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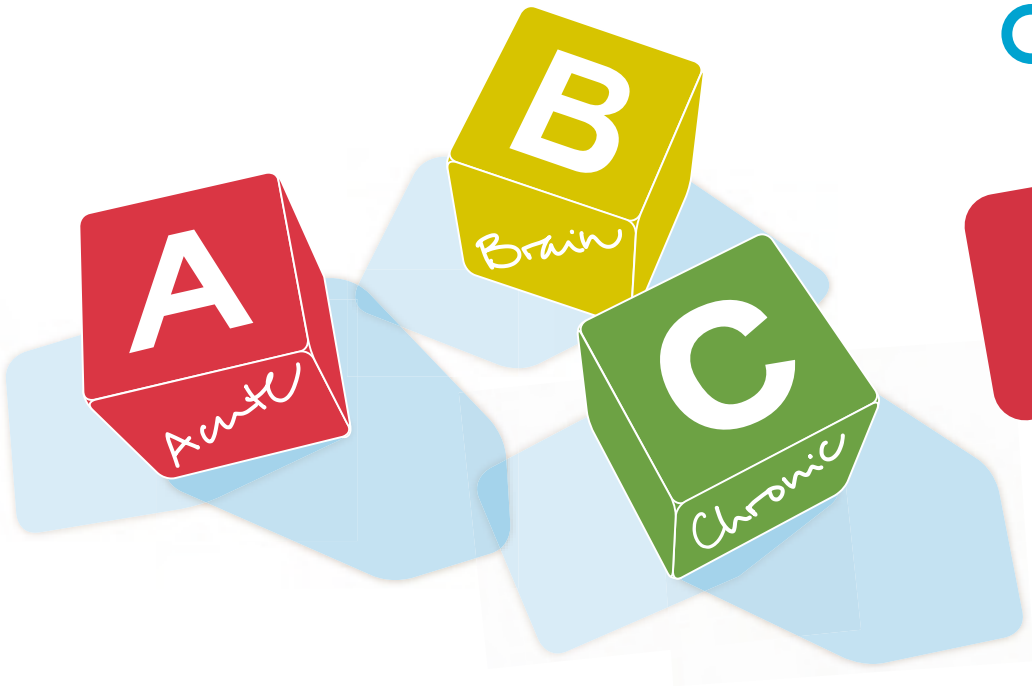

Abstract Book

A · Acute
B · Brain – Science & Health
C · Chronic

Building our alphabet

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ABSTRACTS

Topic: Neurogenetics

EPNS25_16 - Intravitreal Enzyme Replacement Therapy to Prevent Retinal Disease Progression in Children with Neuronal Ceroid Lipofuscinosis Type 2 (CLN2): Interim 3-Year Safety and Efficacy Outcomes

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Objectives

Classic late infantile neuronal ceroid Lipofuscinosis (CLN2) is caused by a mutation of the CLN2 gene. Vision loss begins around age four, resulting in blindness by age 7-10. Intracerebral cerliponase alfa (Brineura, BioMarin) is indicated to slow the loss of ambulation in pediatric patients with CLN2. However, treated children continue to experience visual loss. Intravitreal cerliponase alfa allows access of enzyme to target tissues in the eye, offering a potential treatment.

Methods

This is a phase I/II randomized, masked, clinical trial to determine the safety and evaluate efficacy of intravitreal cerliponase alfa on preventing retinal disease progression in human subjects with CLN2 currently receiving intraventricular cerliponase alfa. One eye of each patient was randomly assigned to monthly treatment for 12-months followed by bilateral treatment for an additional 12-months. Patients that developed disease progression began bilateral treatment earlier than 12-months.

Results

A total of 168 intravitreal injections of cerliponase alfa have been performed in five subjects. There were no serious safety events. Three patients had non-study eye disease progression and began bilateral injections prior to 12-months. Using a linear mixed model, the predicted value of the treatment effect on average central retinal thickness was 8.48 microns.

Conclusions

In our study, intravitreal injection of cerliponase alfa did not result in any serious adverse events. We found treated eyes showed a slower rate of disease progression relative to controls based on OCT imaging. Treated eyes with late stage disease at baseline showed minimal treatment effect, emphasizing the need for early treatment.

ABSTRACTS

Topic: Fetal and Neonatal Neurology

EPNS25_19 - Supplementation with Omega-3 Fatty Acids Rescues Neuroinflammation in an Animal Model of Opiod Exposure

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Objectives Opioid abuse has become a major public health crisis. Oxycodone freely passes through the placenta and can impact the development of a fetus. Currently, mechanisms that lead to impairment in the exposed offspring are not well described. To fill this gap, our study employed a robust preclinical rodent model to test the therapeutic efficacy of omega-3 fatty acids (O3FA) in attenuating neurodevelopmental deficits in offspring exposed to chronic stress (CS) and oxycodone *in utero*.

Methods We employed a 2x2 paradigm: Saline – O3FA + CS (R/S), Saline + O3FA + CS (O3/S), Oxy – O3FA + CS (R/O), and Oxy + O3FA + CS (O3/O). Oxycodone treatment was adapted from an established model in our lab. CS was induced through predator odor simulated with coyote urine. CS treatment stopped once the dam gave birth. O3FA enriched diet was prepared by replacing soybean oil from the AIN-93G base diet with DHASCO oil containing 39.2% DHA. Inflammasome was analyzed using RT-qPCR. Statistical analysis was performed using one-way ANOVA with Tukey's multiple comparison test. Data are represented as mean ± SEM.

Results In the adult (day 60) offsprings' brains, we observed significant upregulation of inflammatory markers CXCL1, IL-10, IL-33, and NLRP1A in the oxy and CS-exposed animals. However, in the O3/O group, we found that the expression of these four markers returned to baseline levels. R/O animals showed significant upregulation of chemokine CXCL1 (fold change difference = 1.213, p = 0.0001), anti-inflammatory cytokine IL-10 (fold change difference = 1.47, p = 0.0061), alarmin cytokine IL-33 (fold change difference = 0.4003, p = 0.0131), and inflammasome NLRP1A (fold change difference = 0.4351, p = 0.016) relative to the R/S animals. In comparison to the R/O animals, the O3/O group returned to baseline expression levels of CXCL1 (fold change difference = -1.123, p = .0012), IL-10 (fold change difference = -1.84, p = .0007), IL-33 (fold change difference = -0.3868, p = .0337), and NLRP1A (fold change difference = -0.4675, p = .0206

Conclusions These findings show that maternal oxy and CS induce neuroinflammation persisting into early adulthood in in utero-exposed offspring but that O3FA treatment could reverse this defect. This study marks a step forward in bridging an important knowledge gap pertinent to maternal-fetal health and enumerates the therapeutic efficacy of O3FA in mitigating neuroinflammation in offspring exposed to in utero oxy and CS**.**

ABSTRACTS

Topic: Headache / Migraine

EPNS25_20 - HIT 6 a New Pediatric Headache Assessment questionnaire

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Objectives

To compare the PED-MIDAS and HIT-6 questionnaires in their ability to assess the degree of impact of headaches on daily functioning.

Methods

A prospective cohort study was conducted. Children aged 6-18 years who visited the Pediatric Headache Clinic at Bnai Zion Medical Center between 11.22- 8.24 due to primary headaches enrolled to the study. All children filled both the PED-MIDAS and HIT-6 questionnaires. Data regarding their headache; diagnosis, frequency and intensity along with demographic data was obtained.

Results

Out of the 96 children participating in the study, 77 completed all the questionnaires. Of these, 57% (44) were female, with an average age of 13.5 years (± 3.3). Migraine was reported by 78% (60) of the participants, 15% of whom experienced aura. Additionally, 22% had tension-type headaches (TTH), and 18% had mixed headache.

PED-MIDAS questionnaires were in positive significant correlation with headache frequency. HIT-6 questionnaire were in positive significant correlation with age and headache strength. PED-MIDAS questionnaire has a positive correlation with HIT-6 and General headache evaluation scale. In linear regression model analysis including patients age gender and headache diagnosis Hit 6 correlated with headache frequency even better (R-squared: 0.255 ,AIC: 408.68 Beta 0.11, CI 0.03, 0.19, p =0.008) than PED-MIDAS (R-squared: 0.245, AIC: 409.83, Beta 0.01, CI 0.00, 0.03, p=0.014).

Conclusions

The HIT-6 questionnaire correlates with the PED-MIDAS questionnaire and can serve as a good alternative for evaluating headache burden among children.

ABSTRACTS

Topic: Miscellaneous

EPNS25_22 - Diagnostic use of transcriptomics in neurodevelopmental disorders: a systematic literature review

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Objectives: RNA sequencing (RNAseq) has emerged as a valuable tool to enhance diagnostic yield in genetic disorders. In this systematic review, we focus on the contribution of transcriptomics to improve the diagnostic yield in neurodevelopmental disorders.

Methods: We performed a systematic literature search in January 2024, including all articles describing diagnostic RNAseq on at least one individual with a primary neurodevelopmental phenotype. We extracted data on cohort size, phenotype, sample tissue, previously used diagnostic methods, added diagnostic yield of RNAseq, the use of control samples, and technical aspects of the RNAseq methodology.

Results: 17 articles were eligible for inclusion in the systematic review. We found an average added diagnostic yield of 17·1% through RNAseq for individuals with neurodevelopmental disorders. There is heterogeneity in the tissue type, reported quality measures, and computational pipelines. Clinically focused papers often lack methodological information, while bioinformatics-oriented papers frequently provide incomplete phenotypic data. Future studies should address this gap by including detailed inclusion criteria and phenotypic information, comprehensive protocol descriptions such as RNA integrity number, sequencing methodologies, read counts per sample, and the data analysis pipelines used for downstream analysis. Transparent reporting of these experimental parameters is crucial for reproducibility and for assessing the reliability of RNAseq studies.

Conclusions: The significantly increased diagnostic yield demonstrates the value of this novel tool in the diagnostic setting of neurodevelopmental disorders. Our results offer an overview of common methodologies for RNAseq and allow us to formulate recommendations for genetic labs and clinicians when implementing RNAseq as a diagnostic tool. Lastly, we provide recommendations for future publications in order to increase transparency and reproducibility.

ABSTRACTS

Topic: Neurodevelopmental Disorders / Developmental Neuroscience

EPNS25_23 - Cognition in children with arachnoid cysts - presurgical and postsurgical evaluations of cognitive functions

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Objectives

Arachnoid cysts of the temporal lobe (AC) are benign, space-occupying, anomalies most commonly identified incidentally during the first decade of life, when a child is undergoing neuroimaging for other reasons. Besides rapid head growth, headaches, seizures, increased intracranial pressure, increased head circumference and focal neurological symptoms, studies with adult patients show results indicating cognitive symptoms and postsurgical improvements. The aim of the studies presented here is to fill the gap in knowledge concerning cognition in children with ACs.

Methods

Study one was a prospective study with presurgical and postsurgical cognitive evaluations. We evaluated 11 children cognitively six months before and six months after microneurosurgery of the AC. Results were analyzed with Students T-test and Wilcoxon Signed Rank Test. Study two was a follow-up of 10 of the initial 11 children. Results were analyzed with ANOVA and the Friedman-test. A neuropsychologist evaluated the children with the same set of psychometric tests on all three occasions; The Wechsler-scales, Boston Naming Test, FAS-test of phonological verbal fluency, Rey Complex Figure Test, Rey Auditory Verbal Learning Test and the Trail Making Test). Significance level was set to p=0.05.

Results

In the initial study the results showed that there were significant improvements after surgery in results on the Wechsler-scales. The children improved in general cognitive ability, with a mean difference of 8.2 IQ-points (95% CI 3.2–13.2, p = 0.005). Significant improvements were seen in verbal comprehension, with a mean difference of 8.0 index points (95% CI 4.2–11.8, p= 0.001) and in processing speed with a mean difference of 11.0 points (95% CI 4.4–17.6, p=0.004). These improvements were stable after five years. There was consistensy between results and the testimonials from children and parents.

Conclusions

To the best of our knowledge this is the first comprehensive long-term postsurgical follow-up of cognitive functions with a set of psychometrically robust instruments in a group of children treated for ACs. In our relatively small sample we found postsurgical improvements in general intellectual ability, verbal comprehension and processing speed. These improvements were stable after five years. This has a potential for an important impact on school performance and future possibilities. Our conclusion is that the risk of cognitive deficits in children with ACs, together with postsurgical improvements and long-term stability, must be considered and cognitive testing should be a part of an investigation before decision on surgery in these patients.

ABSTRACTS

Topic: Infectious and Inflammatory Diseases/ Neuroimmunology

EPNS25_25 - Neurodevelopmental Outcomes in children with Acute Necrotizing Encephalopathy of Childhood from a resource-limited setting

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Objectives

To prospectively assess the neurodevelopmental outcomes in children with acute necrotizing encephalopathy of childhood (ANEC) using standardized scales

Methods

Prospective, single-center study was conducted over 18 months enrolling children upto 18 years of age with a diagnosis of ANEC. All children were assessed in follow-up using modified Rankin score (mRS), Glasgow Outcome Scale- Extended (GOS-E), Developmental Profile-3 (DP3), Vineland Social Maturity Scale (VSMS), Childhood Psychopathology Measurement Schedule (CPMS), children's sleep habit questionnaire- abbreviated (CSHQ-A), Early Childhood Epilepsy Severity Scale (E-CHESS), neuroimaging and electroencephalography. Quality of life of parents was assessed using WHO-QOL-BREF scale.

Results

We enrolled 35 children (median age of presentation 60 months). Mechanical ventilation was needed in 63% children with a median intensive care stay of 12 days. The majority (65%) of children had shock and multiorgan dysfunction at presentation. As per ANE severity score, 55% children were in high-risk category. Classic MRI changes documented in 97%. Mortality rate was 26%. Survivors were followed up for neurodevelopmental assessment (median duration of follow up: 14 months; range: 3-120 months). Overall neurological outcomes by mRS and GOS-E were vegetative state (6%), severe (20%) and moderate disability (14%), and good recovery (34%). Majority (58%) had global developmental delay on DP-3 scale. VSMS showed 4% mild, 4% moderate, 13% severe and 21% profound intellectual disability. Abnormal sleep habit patterns were recorded in 42% using CSHQ-A scale. Focal epilepsy in 8%, generalized epilepsy in 11% and epileptic spasms in 4% were seen. EEG in children with epilepsy revealed multifocal intermittent epileptiform discharges with frequent generalized discharges in 2 children, left frontotemporal discharges and hypsarrhythmia in 1 child each. Movement disorders were observed in 65% children: dystonia 50%, cerebellar ataxia 11% and choreoathetoid movement 4%. Follow-up neuroimaging showed thalamic changes in 87%, cerebral atrophy in 50%, cystic encephalomalacia in 44% and chronic hemorrhage in 31%. Parents reported their quality of life as low in 35%, moderate in 25% and high in 40% by the WHO quality of life scale.

Conclusions

ANEC affects children in the short-term with poor neurodevelopmental outcomes, impaired quality of life and several comorbidities such as poor sleep, epilepsy, behavioral problems, and movement disorders. Hence, children need regular follow-up for early recognition of sequelae and early initiation of rehabilitations, that can improve the overall functioning in the survivors.

ABSTRACTS

Topic: Neuropsychiatric Disorders / Functional Neurological Disorders

EPNS25_26 - Pediatric Acute onset neuropsychiatric syndrome

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A case report on Pediatric Acute Onset Neuropsychiatric syndrome

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Objectives: We report an eight years-old girl with three months history of acute psychosis, behavioral regression, cognitive deterioration, anxiety, repetitive self-soothing, absent verbal responses and tremor of fingers. She diagnosed to have PANS.

Methods: A previously healthy an eight years-old girl, who was hospitalized in our department, presented with acute onset of psychiatric symptoms such as anxiety, severe insomnia, nearly absent communication (both talking and writing), inconsolable crying and screaming, and she was unable to engage in daily life activities including bathing and other personal hygiene activities. All of these symptoms developed over three months and during this period she was diagnosed with bipolar disorder and was treated with medications from nearly every psychotropic medication class with no beneficial effects. Because her condition was refractory to these psychiatric medications, the patient was reffered for a second opinion to the pediatric neurologist in the National Children Medical center. Then who immediately suspected an inflammatory or autoimmune etiology based on the sudden-onset nature of her illness, significant OCD symptoms, poor response to psychotropic, encephalopathic features, persistent tremor, and choreiform movements of her fingers (piano playing finger movements). Based on normal brain and whole spine MRI, negative paraneoplastic panel and specific antibodies for lupus, antiphospholipid, and other autoimmune antibodies in CSF analysis, however, elevated anti-nuclear antibody (ANA) titer (1:252), the patient was diagnosed with PANS (and probably inflammatory brain disease/autoimmune encephalitis). According to diagnose, she was successfully treated with 3 days of high dose methylprednisolone (1000 mg daily for 3 days) two times within month followed by a slow prednisone taper (60 mg p.o daily), IVIG (2 g/kg). The patient returned to 90 % of her baseline functioning. However, when attempts were made to wean the prednisone below 60 mg daily, the patient started to develop a recurrence of symptoms. Then mycophenylate mofetil was added in hopes that this would allow further tapering of prednisone. The patient has now had 10 months of no OCD and other psychiatric symptoms.

Results: These treatments resulted in to complete improvement, even in case in which multiple psychotherapies had failed.

Conclusions: Acute-onset neuropsychiatric symptoms in youth signal a serious risk for cognitive and psychosocial impairment. Alertness to possibility of PANS and cross-discipline coordination can lead to a positive treatment response in youth with the illnesses described as PANS.

ABSTRACTS

Topic: Neurogenetics

EPNS25_28 - Malformation of cortical development disorder in 201 patients: A decade of single center experience

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Objectives

Malformation of cortical development disorders (MCD) are a spectrum of heterogenous disorders that result from a defect in the critical developmental brain process. The process, which is highly genetically regulated, results in mal-positioning and faulty differentiation of cortical grey matter. This study aims to describe the clinical, radiological, and genetic features of MCD.

Methods

We conducted a retrospective descriptive analysis of radiologically and/or genetically confirmed MCD patients who were diagnosed between 2012 and 2022.

Results

MCD was confirmed genetically or radiologically in 201 patients from 181 families. The male were 97 patients and female were 104. Seizure was the most common clinical presentation in 50% followed by developmental delay in 21%. 63% of the patients were presented at neonatal and infancy period. The neurology unit was the first encounter clinic in 56%. Heterotropia and corpus callosum malformation were the most reported radiological features. The germline genetic diagnosis was ascertained in 49% of the (100/201) patients. Different genetic tests were done on 129 patients as follows: Whole exome sequence (n:71, positive: 56), customized gene panel (n: 18, positive 14), chromosomal microarray (n:6, positive: 3), target gene test (n:31, positive 30). Dystrophoglycanopathy was the most common genetic diagnosis in 26/100. We report 5 new clinical phenotypes and 25 novel variants including 11 previously unreported variants.

Conclusions

The rapid expansion of MCD is driven by deep understanding of early brain development; however, our current level of knowledge is insufficient for the development of a comprehensive, or even useful, genetic or pathway-based classification.

ABSTRACTS

Topic: Infectious and Inflammatory Diseases/ Neuroimmunology

EPNS25_31 - Lateral Ventricle Volume is associated with disease severity in Pediatric Multiple Sclerosis.

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Objectives

Up to 10% of all multiple sclerosis patients are diagnosed before the age of 18 years defined as pediatric multiple sclerosis onset (POMS). Although brain volume loss and its involvement in patient deterioration have been established, the effects of changes in the volume of the brain lateral ventricles in pediatric patients have yet to be thoroughly examined.

The purpose of this study was to examine changes in the lateral ventricular volume and its correlation with disease severity in POMS

Methods

Brain MRI performed at baseline and 3 years follow up were analyzed in POMS. The lateral ventricle volumes were measured according to a standard protocol, on 1.5 T MRI scanner. The scans were segmented and quantified for volume using semiautomatic software. The POMS lateral ventricle volumes were matched to age and sex matched healthy subjects.

Results

Sixty six patients, (39 females) with mean ± SE age at onset 13.8 ± 0.4 years, baseline median Expanded Disability Status Scale (EDSS) score of 3.0 (IQR 2.5-4.0), disease duration of 8.1±0.5 years and mean lateral ventricle volume 10602±599 mm3 volume were analyzed. After 3 years follow up the median EDSS were 1.0 (IQR 1.0-2.0) and the lateral ventricle volume 12618±833 mm3. At disease onset, the lower levels of lateral ventricle volume was associated with higher EDSS scores (p=0.05), that could be explained by more exudative inflammation in patients brains leading to reducing of ventricle volumes. In the opposite, after 3 years of the follow up, higher lateral ventricle volumes were now associated with higher EDSS scores (p=0.002), probably as it associated with initiation of neurodegeneration and neuronal loss.

Conclusions

Lateral ventricle volume in POMS associated with higher EDSS at onset and disease severity at 3 years follow up. This able as to follow patients deterioration and disease progression by conventional MRI observations, already in the onset and early disease progression.

ABSTRACTS

Topic: Neurorehabiltation

EPNS25_32 - Reliability und validity of the gait analysis using Gangway in children and adolescents with cerebral palsy

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Objectives

This study's aim was to determine the reliability and validity of the mechanographic gait analysis using Gangway (Leonardo Mechanograph® GW), a force plate system, which automatically analyses typical parameters of gait analysis.

Methods

We conducted a retrospective study, evaluating the data of 846 patients with CP and GMFCS Level I-III, that were examined from May 2007 until January 2020. The age of the patients ranged from 2 to 18 years old. The gross motor function of the patients was evaluated using established clinical tests: GMFM-66, 1MWT and 6MWT. For the validity assessment, these clinical scores were correlated to the equivalent measurements of 3 GW-parameters: “av. length p. step”, “av. velocity horizontal”, “pathlength/distance”. The correlations were performed with the use of Spearman's rank correlation coefficient (rho). For the reliability assessment the intraclass correlation coefficient (ICC) was used as a reliability index in test-retest reliability analysis.

Results

Regarding the validity assessment, all correlation coefficients showed statistical significance ($p<0.05$). All three investigated clinical scores showed a positive correlation to the parameters “av. length p. step” and “av. velocity horizontal” and negative to “pathlength/distance”. The GMFM-66 had a strong correlation to “av. length p. step” (rho 0.665) and to “av. velocity horizontal” (rho 0.752) and moderate to “pathlength/distance” (rho -0.575). In view of the reliability assessment, the ICC for “av. length p. step”, “av. velocity horizontal” and “pathlength/distance” was 0.921, 0.841, 0.559 in average measures.

Conclusions

To summarize, the parameters “av. length p. step” and “av. velocity horizontal” of the Gangway provided reproducible outcomes in young patients with CP and showed the strongest correlations to the GMFM-66. These GW-parameters seem to be a valuable tool for clinical gait analysis in pediatric populations with CP. Further research is needed to explore its utility in other clinical applications and across different age groups.

ABSTRACTS

Topic: Neurogenetics

EPNS25_33 - Identification of Novel SCN1A Gene Variants in Patients with Epilepsy of Uzbek Ethnicity

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Objectives Monogenic forms of epilepsies is detected up to 40 % of severe epilepsies forms. NGS (Next Generation Sequencing) methods can help us to establish monogenic causes of epilepsy in cases of point mutations or Indels (insertion-deletion) in specific genes. The genetic landscape of the Uzbek ethnicity is barely explored and genetic of epilepsies has just been started to be studied. Current study can highlight the most frequent cases of single-gene epilepsies in patients of the Uzbek nationality.

Methods WES (Whole Exome Sequencing) was performed in 70 unrelated Uzbek patients with suspected monogenic epilepsy during 2023-2024. On the base of seizure type, electroencephalographic abnormalities, MRI-findings, anti-seizure treatment response and neurodevelopmental deficits we assume that Dravet syndrome associated with variants in SCN1A in 15 patients. Received WES analysis results were evaluated according to ACMG criterias and next Sanger sequencing in a proband and parents was carried out.

Results In our subgroup of 15 patients with suspected Dravet syndrome it was detected 3 patients (4/15, 26%) with SCN1A-related epilepsy: SCN1A:c.1094T>G (PP3, PM2, PM1, PP2), SCN1A:c.3997A>T(PP3, PM2, PM1, PM5, PP2), SCN1A:c.4362A>C (PM2, PM5, PM1, PP3, PP2), SCN1A:c.603-2A>G(PVS1, PS2, PM2, PP5)**.** Sanger sequencing in a proband and parents confirmed all three SCN1A detected variants are de novo. This de novo occurrence is supported by verification of paternity and maternity and add PS2 criteria. Therefore, all of these variants are conclusively classified as "Pathogenic" according to ACMG guidelines.

Conclusions Newly found genetic variants in the Uzbek ethnicity can improve understanding of pathogenetic mechanisms and establishing of genotype-phenotype correlations among the patients with monogenic forms of epilepsies. SCN1A:c.1094T>G, SCN1A:c.3997A>T, SCN1A:c.4362A>C was not found in literature and databases and demand further functional studies. Also, it is a bright example that monogenic forms of epilepsies in the Uzbek ethnicity demand further large-scale research.

ABSTRACTS

Topic: Neurometabolic Disorders

EPNS25_36 - Iranian Juvenile GM2-gangliosidosis patients:(up to 5 years follow up of treatment with Miglustat)

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Objectives

This study aims to prospectively describe the natural course of clinical changes of juvenile GM2-gangliosidosis and also to present the results of therapeutic interventions performed by prescribing Miglustat in a number of these patients.

Methods

The clinical findings of patients at the time of enrollment in the study, as well as their clinical course and evolutionary changes, along with the care provided, including the prescription of Miglustat and the observation of its impact on the patient's developmental domains

Results

8 patients with GM2-gangliosidosis were enrolled in this study and we followed them between 5 months to 5 years. 5 patients were diagnosed with Tay-Sachs type and 3 patients with Sandhoff type disease. All patients were the result of consanguineous marriages and had undergone a normal course of development before the onset of clinical symptoms of the disease. The most common disorders observed in the course of the disease were seizures, dysphagia, dystonia, and limb contracture.

Miglustat had no clear effect on 4 Tay-Sachs patients, but the drug stopped the progression of the disease in Sandhoff's patients

Conclusions

Miglustat does not have a clear effect on improving developmental domains in patients with juvenile GM2-gangliosidosis of the Tay-Sachs type.

ABSTRACTS

Topic: Epilepsy: Diagnosis and Investigations

EPNS25_38 - Change of heart rate variability in children and adolescents with drug-resistant epilepsy

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Objectives: Heart rate variability (HRV) has been examined and employed as a predictive biomarker for epilepsy. Patients with epilepsy exhibit reduced HRV as a result of heightened sympathetic activity. Reductions in HRV are observed in patients with sudden unexpected death in epilepsy (SUDEP). Our study aims to determine the change in HRV among children and adolescents with drug-resistant epilepsy (DRE) and advocate for its use as a biomarker to assess cardiovascular risk in this population.

Methods: Fifty-four children and adolescents, aged between 6 and 20 years, were enrolled and divided into two groups: the epilepsy group comprised 27 children diagnosed with DRE. Thirty minutes of HRV measurements were performed on both patients and controls.

Results: The median age was 12 years old. Malnutrition was the most common comorbidity in the epilepsy group. Seventy-five percent have been diagnosed with DRE for more than 10 years. Forty-four percent had daily seizures. Generalized tonic-clonic seizures (GTCs) were the most common seizure type, accounting for 55.6% of cases. The most frequent cause of epilepsy was structural brain lesions (55.6%), followed by genetic disorders (18.5%). Patients with DRE had a significant reduction in both HRV's time domain (RMSSD and pNN50) and frequency domain (HF and LF). Patients who had GTC, had epilepsy for more than 10 years, and used more than four anti-seizure medications had a significant reduction in the low-frequency domain of HRV, according to the subgroup analysis.

Conclusions: Children and adolescents with DRE exhibited a marked decrease in HRV measures. These results underscore the heightened sympathetic activity, thereby increasing the likelihood of cardiovascular health issues in these patients. HRV can be used as a biomarker to effectively assess cardiovascular risk in DRE patients.

ABSTRACTS

Topic: Fetal and Neonatal Neurology

EPNS25_39 - The first experience with 16 open microsurgical fetal surgeries for Myelomeningocele in Germany

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Objectives:

Fetal surgery for spina bifida aperta has achieved great advancement in last decade offering three possible methods for surgical repair. Open fetal microsurgical repair still remains the cornerstone considering long-term results available. Since 2016, we established a program offering this modality of treatment in Germany.

Methods:

All patients who underwent interdisciplinary prenatal evaluation following a standardized protocol between June 2016 - June 2024. Sacral lesions were excluded. The surgical technique and protocol used were similar to that described in Management Of Myelomeningocele Study (MOMS).

Results

Sixteen patients underwent surgery for spina bifida aperta without fetal nor maternal deaths. Microsurgical fetal repair was performed between 24th and 25th week of gestation age (GA) (Mean: 24+5 weeks GA). Lesion levels were mainly lumbosacral (n□15) and one thoracolumbar (n□1). Repair was successful in all 16 cases and with reversible hindbrain herniation at time of birth in 13/16 patients (81.3%). Average time of delivery was 33+5 weeks GA, with 8 preterm deliveries occurring before 37 weeks GA; average birth weight was 2193 grams. Maternal complications included 2 patients with uterine scar thinning. Hydrocephalus management was needed in 5/16 patiens (31.25%) via ventriculo-peritoneal shunting.

Conclusions

Open fetal repair of spina bifida aperta in selected fetuses is safe and offers the unborn child a better quality of life but does not cure the disease and is not without risks or complications. Collaboration within the pediatric community is recommended to compile data in a common registry to develop standardized treatment and follow-up protocols.

ABSTRACTS

Topic: Epilepsy: Medical and Surgical treatment

EPNS25_46 - Effectiveness of the use of short-term clobazam in patients with epilepsy

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Objectives:

This retrospective study aimed to evaluate the effectiveness and tolerability of clobazam administered for short courses in inpatients with epilepsy with seizure exacerbations

Methods:

Retrospective study using the electronic patient record search function for:

- Dates 01/06 – 31/07/2024.
- Inpatients seen by paediatric neurology
- Clobazam use <1 month

Data was collated on epilepsy, primary seizure types, changes in seizure frequency, time to response, relapses, and adverse effects. Clinical response was defined as seizure reduction to baseline following treatment with Clobazam.

Results:

Of 115 patients screened, 11 were included aged (mean) 9.4 (3 - 16) years who received Clobazam for (mean) 11 (2 - 30) days with mean dose 0.27 (0.1 – 0.5) mg/kg/day. All eleven had focal impaired awareness seizures (FIAS), with some also having epileptic spasms (ES) (n=2), absence (AS) (n=2), or GTC (GTCS) seizures (n=1). None had seizure freedom following Clobazam. Eight (73%) showed clinical response in primary seizures (FIAS 8/11, ES in 1/2, AS in 2/2 and GTCs in 0/1).

Only one patient discontinued treatment due to respiratory difficulty. The patients (n=3) who didn't respond well to Clobazam were on lower doses(<0.2mg/kg/day) compared to the others who responded well(>0.2mg/kg/day). Response times varied with (mean) 8.7(1 – 21) days. At end of follow-up, 3 of the eleven patients successfully weaned off Clobazam after 4 weeks, whilst five relapsed (repeat course of Clobazam given in five, adjustments to anti-seizure medications in 5.

Conclusion:

Seventy three percent of patients (8/11) showed clinical response although most had a relapse during follow up, which required changes to other drugs and a second course of clobazam. The patients who didn't respond had a smaller dose of Clobazam in this study.

ABSTRACTS

Topic: Infectious and Inflammatory Diseases/ Neuroimmunology

EPNS25_49 - Prevalence and Risk Factors of Pediatric Seizures inCOVID-19 Infection: A Study from Thailand

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Objectives: COVID-19 is an emerging disease primarily presenting with respiratory tract infections in children. Recent reports have highlighted neurological manifestations, including seizures. However, there is a lack of studies regarding the prevalence and risk factors for pediatric seizures associated with COVID-19 in Thailand, which prompted our research.
Methods: This retrospective study involved pediatric patients aged 1 month to 15 years who exhibited clinical seizures as a primary symptom alongside COVID-19 infection. Patients diagnosed with Multisystem Inflammatory Syndrome in Children (MIS-C) were excluded. The study was conducted at Maharat Nakhon Ratchasima Hospital from December 1, 2019, to December 30, 2022. Demographic data and risk factors were assessed, and the prevalence of seizures was calculated.
Results: A total of 963 pediatric patients were included in the study, with ages ranging from 1 month to 15 years. The mean age of the cohort was 6.8 years (± 4.6 SD), with a male predominance (53.2% male, 46.8% female). Among these, 40 cases presented with clinical seizures, resulting in a seizure prevalence of 0.76%. In the seizure group, ages ranged from 8 months to 14 years, with a mean age of 3.67 years (± 3.45 SD). This group also showed male predominance. Notably, 70% of the patients were under the age of 5 years, and the majority (95%) experienced febrile seizures associated with the Omicron variant. The identified risk factors for seizures included younger age (less than 5 years) and the severity of COVID-19 infection. A long-term follow-up at 2 years indicated favorable neurodevelopment outcomes.
Conclusions: The prevalence of seizures in pediatric patients with COVID-19 varied according to the viral variant, with the Omicron variant being associated with a surge in febrile seizures. Younger age and the severity of COVID-19 were found to increase the risk of seizure occurrence.

ABSTRACTS

Topic: Epilepsy: Diagnosis and Investigations

EPNS25_55 - Antiseizure Medication Regimen Adjustment After Fenfluramine Initiation: Lessons Learned From European Early Access Program in Pediatric and Adult Patients With Dravet Syndrome

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Objectives: Dravet syndrome (DS) is a rare developmental and epileptic encephalopathy characterized by seizure onset within the first year of life and developmental delay thereafter. Fenfluramine (FFA) is approved in the US, EU, UK, Israel, and Japan for the treatment of seizures associated with DS in patients ≥2 years old. Because DS persists into adulthood, long-term FFA usage data in this population are needed. We report FFA dosage and concomitant ASM dose adjustments from a clinical practice setting in adult and pediatric patients who participated in the European early access program (EAP; supported by Zogenix/UCB).

Methods: The EAP was open from 2018 until European Medicines Agency approval in 2020, when patients transitioned at country reimbursement. Patients were eligible through their physician if they had a confirmed DS diagnosis, no alternative treatment, and were ineligible for clinical trial enrollment. Key contraindications included hypersensitivity to FFA, valvular heart disease, pulmonary artery hypertension, or monoamine oxidase inhibitor use within 14 days prior.

Results: Of 269 total patients (Germany-43.9%; Italy-39.0%; Spain-10.8%; UK-4.5%; Ireland-1.9%), 192 (71.4%) were pediatric (3-17 years old) and 77 (28.6%) were adults (≥18 years old) at last request. Overall, 41 (15.2%) patients withdrew for various reasons, including FFA commercial availability in respective countries. 48.3% of patients were female. Concomitant STP use at initial request was reported in 54.7% and 44.2% of pediatric and adult patients, respectively. Mean (SD) weight: initial request, 26.0kg (12.6kg) and 68.5kg (22.2kg), respectively; noninitial (follow-up) requests, 27.8kg (13.5kg) and 66.8kg (17.2kg), respectively. Mean (SD) FFA dosage: initial request, 9.63mg/d (6.07mg/d) and 17.52mg/d (5.99mg/d), respectively; noninitial requests, 12.33mg/d (5.19mg/d) and 18.89mg/d (5.15mg/d), respectively. 93% of patients had concomitant ASM adjustments after FFA initiation. ASM dose reductions were observed in 56.8% and 61.7% of pediatric and adult patients, respectively; STP was the most common dose-reduced ASM (33.8% and 27.6%, respectively). ASM withdrawals were observed in 20.8% and 38.3% of pediatric and adult patients, respectively; STP was the most common ASM withdrawal (96.2% and 33.3%, respectively). ASM dose increases were observed in 28.8% and 14.9% of pediatric and adult patients, respectively; valproate was the most common dose-increased ASM (27.0% and 71.4%, respectively).

Conclusions: Patients with DS received FFA doses within the recommended maximum dose ranges for pediatric and adult patients. In the largest adult population treated with FFA to date, we observed meaningful ASM dose reductions and withdrawals that reflect the effectiveness of FFA.

ABSTRACTS

Topic: Neurometabolic Disorders

EPNS25_56 - Preclinical study of AAV.GT5 gene therapy for OTC deficiency

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Objectives

The liver is a key target for gene therapy in treating various genetic and neurometabolic disorders. Among these disorders, ornithine transcarbamylase (OTC) deficiency is a strong candidate for liver-directed gene therapy. OTC, an essential enzyme in the urea cycle, is primarily expressed in hepatocytes, and its significant reduction leads to toxic hyperammonemia. Although specific medications and lifelong low-protein diets can help manage symptoms, they cannot prevent irreversible central nervous system damage. Currently, liver transplantation remains the only curative treatment. Despite ongoing clinical trials, the urgent need for curative therapies persists, especially in infancy.

Methods

We previously developed a triple mutant AAV3 (AAV.GT5) vector with reduced reactivity to anti-AAV capsid-neutralizing antibodies by introducing three surface substitutions (S472A, S587A, and N706A) into the AAV3B capsid protein. In this study, we evaluated the therapeutic potential of an AAV.GT5-based vector expressing human OTC under a liver-specific promoter in a mouse model of OTC deficiency. Humanized chimeric mice (PXB-OTCD) were generated by transplanting primary human hepatocytes derived from OTC-deficient patients into the spleens of 2- to 4-week-old female homozygous cDNA-uPA/SCID mice.

Results

The transduction efficiency of AAV.GT5 in human hepatocellular carcinoma cell lines was comparable to that of the parental AAV3B vector. Remarkably, in hepatocytes derived from humanized PXB mice, AAV.GT5 demonstrated a 50-fold higher transduction efficiency than the commonly used AAV8 vector. While untreated PXB-OTCD mice succumbed within four weeks, mice treated with AAV.GT5-OTC (1×10^{12} vg/mouse) survived and exhibited reduced serum ammonia levels. Histological analysis confirmed OTC expression in human-derived hepatocytes without abnormal findings such as fibrosis. Post-treatment, OTC activity in transduced hepatocytes reached approximately 50% of the levels observed in healthy hepatocytes, comparable to asymptomatic carrier family members. No significant toxicity or adverse effects related to AAV injection were observed in infantile rat. Furthermore, we evaluated safety and viral shedding in cynomolgus monkeys, which supported the tolerability of this gene therapy.

Conclusions

AAV.GT5-OTC demonstrated favorable efficacy and safety in a humanized mouse model of OTC deficiency. Although reduction in the proportion of transduced hepatocytes by proliferation remains a challenge, AAV.GT5-OTC with its superior gene transfer efficiency has great potential as a disease-modifying therapy for OTC deficiency.

ABSTRACTS

Topic: Neurodevelopmental Disorders / Developmental Neuroscience

EPNS25_57 - Impact of tDCS on Social Interaction in ASD: A Systematic Review and Meta-Analysis

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Objectives This study investigated the effectiveness of transcranial Direct Current Stimulation (tDCS) in improving social interaction among children and adolescents with autism spectrum disorder (ASD).

Methods This prospective systematic review and meta-analysis followed PRISMA 2020 guidelines. A comprehensive search of four databases (Medline, Web of Science, Scopus, and Embase) was conducted up to November 6, 2024, identifying studies published in English. Included studies were randomized controlled trials (RCTs) and non-RCTs examining the impact of tDCS on social interaction in individuals under 18 years old diagnosed with ASD, using standardized criteria such as the DSM-5. Studies involving comorbidities or focusing on gene interactions were excluded. Data extraction was performed using a standardized form, with independent review by two authors. The Cochrane Risk of Bias 2 (RoB2) and ROBINS-I tools were used to assess bias in RCTs and non-randomized studies, respectively. Meta-analysis was conducted using Revman software, calculating Hedges' g (g) to determine effect size. Heterogeneity was evaluated using the I^2 statistic, and publication bias was assessed via funnel plot and Egger's test.

Results Twelve studies met the inclusion criteria, encompassing various tDCS protocols, target areas, and age groups. Six studies directly assessed the effects of tDCS on social interaction. Positive effects on social functioning were observed in several studies, with improvements noted in social responsiveness, communication skills, and emotion recognition. Notably, cathodal tDCS combined with cognitive training showed significant enhancement in social functioning, potentially by modulating the theta-band excitation/inhibition balance in relevant brain regions. Anodal tDCS also demonstrated positive effects, possibly through the enhancement of functional connectivity in the social brain network. Meta-analyses were performed on studies using the Social Responsiveness Scale-2nd Edition (SRS-2).

Conclusions The findings suggest that tDCS may be a promising intervention for enhancing social interaction in individuals with ASD. However, further research is needed to optimize tDCS protocols, understand individual differences, and evaluate long-term effects. Combining tDCS with other interventions warrants further investigation to develop comprehensive treatment strategies for ASD.

ABSTRACTS

Topic: Epilepsy: Diagnosis and Investigations

EPNS25_59 - Social outcome of young adults with previous self-limited epilepsy with centrotemporal spikes

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Objectives: Children with self-limited epilepsy with centrotemporal spikes (SeLECTS), may have psychosocial issues. Although the adult outcome is expected to be good, reports suggest persistent problems.

Methods: Patients with SeLECTS treated in a single center from 2006 to 2013, currently over 18 years old, were assessed with a semi-structured telephone interview. It covered academic performance, employment, behavioral issues, relations with family, friends, and romantic partners, and overall satisfaction with different aspects of life. Their epilepsy history is obtained from chart review.

Results: Of the 200 adults with previous SeLECTS, cases without long-term follow-up (n=83) and those unavailable for the survey (n=37) were omitted. We collected data from 80 adults aged 22.8±3.4 years with a follow-up of 15.3±3.3 years. Seven continued therapy - five were never seizure-free, and two relapsed after 5-6 years of drug cessation. The others finished treatment at an average age of 13.5 years. EEG was normalized at 12.9±2.4 years. Twelve patients had a history of continuous spike-wave in slow sleep syndrome. None developed Landau-Kleffner syndrome or status epilepticus.

Thirty-four patients had behavior problems during school years, 18 were treated with stimulants for ADHD. Seven were briefly suspended from school, 13 repeated a grade. Seven adults experienced minor legal issues, there was no drug/alcohol abuse. Seventy-seven graduated from high school, 54 of those went on to university and 3 of them to PhD. Currently, 32 are still in education and 35 are employed with a regular income.

Forty-nine reported close, while 9 reported cold familial relations. Sixty-three preferred socializing with friends to spending time alone. Only 24 went out with friends more than once a month. Thirty-four were currently single, and 15 never had a previous romantic relationship.

When asked about life satisfaction, there was no health-related dissatisfaction. Half were very satisfied with their health and friendships. Work-life and social life showed more scattered results. Dissatisfaction in romantic life was 50%.

Conclusions: There is a complex interplay between epilepsy and psychosocial abilities. We observed that although they felt good about their health and friendships and were academically successful, they felt less satisfied with their work-life and especially romantic relations. This shows the need for more support in psychosocial issues alongside seizure control.

ABSTRACTS

Topic: Neuromuscular Disorders

EPNS25_63 - Long-term functional outcomes, safety, and micro-dystrophin expression following delandistrogene moxeparvovec treatment in DMD: EMBARK 2-year results

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Objectives: Delandistrogene moxeparvovec (rAAVrh74 vector-based gene therapy approved in the US and other select countries) delivers a transgene encoding delandistrogene moxeparvovec micro-dystrophin, an engineered, functional form of dystrophin that stabilizes or slows Duchenne muscular dystrophy (DMD) progression. EMBARK (NCT05096221), a Phase 3, randomized, double-blind, placebo-controlled, two-part study, assesses delandistrogene moxeparvovec in DMD.
Methods: EMBARK enrolled ambulatory males with DMD aged ≥4—<8 years (Mendell. *Nat Med*. 2024). In Part 1 (52 weeks), patients received delandistrogene moxeparvovec (single intravenous dose 1.33×10^{14} vg/kg) or placebo; in Part 2, patients crossed over. Muscle biopsies were performed at Weeks 12 and 64. Due to the crossover, 2-year functional outcomes from Part 1 delandistrogene moxeparvovec-treated patients were compared with external controls (EC), matched using prespecified propensity-score-weighted analyses based on baseline prognostic factors that impact DMD progression.
Results: At 2 years, Part 1 delandistrogene moxeparvovec-treated patients (N=63) demonstrated statistically significant and clinically meaningful functional benefit versus EC (N=113–115, per functional assessment). Mean change from baseline: North Star Ambulatory Assessment total score, 2.63 versus –0.25 points (between-group difference: 2.88 points); Time to Rise, 0.65 versus 2.71 seconds (–2.06 seconds); 10-meter Walk/Run, –0.04 versus 1.32 seconds (–1.36 seconds); all $P<0.01$. Mean micro-dystrophin expression was sustained from Weeks 12 (n=17) to 64 (n=16) (34.29% vs. 45.68%; western blot). Between Weeks 52 and 104, 15 (23.8%) patients experienced 34 treatment-related treatment-emergent adverse events (AEs): troponin-I increase (6.3%); proteinuria, headache, gamma-glutamyl transferase increase, and nausea (3.2% each) the most frequent. One patient experienced two treatment-related serious AEs of rhabdomyolysis; both resolved. There were no deaths, discontinuations, or clinically significant complement-mediated AEs.
Conclusions: 2-year results indicate favorable treatment effect of delandistrogene moxeparvovec on disease progression versus a well-matched EC. Stabilized functional outcomes, prognostic for delaying loss of ambulation, and sustained micro-dystrophin expression demonstrate durability of treatment. Safety was consistent with prior experience.

ABSTRACTS

Topic: Neuropsychiatric Disorders / Functional Neurological Disorders

EPNS25_64 - Exploring the Role of AI-Enhanced Radiography and Ultrasound in Early Diagnosis of Pediatric Neurological Disorders

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Introduction

Paediatric neurological disorders often present with subtle symptoms, making early and accurate diagnosis crucial. While advanced imaging modalities like MRI and CT are commonly used, X-rays and ultrasound are more accessible, cost-effective, and frequently used as initial screening tools. AI and machine learning offer the potential to enhance the diagnostic capabilities of these imaging modalities, enabling earlier detection of neurological conditions in children.

This study aims to evaluate the effectiveness of AI-enhanced X-rays and ultrasound in diagnosing paediatric neurological disorders, particularly those that may be missed by traditional imaging methods. By applying AI to routine imaging, we aim to improve diagnostic accuracy, aid early intervention, and offer personalized treatment strategies.

Objectives: 1. Evaluate the diagnostic accuracy of AI-enhanced X-rays and ultrasound in detecting paediatric neurological disorders, such as epilepsy, cerebral palsy, and intracranial lesions. 2. Compare AI-driven imaging results with clinical diagnoses and advanced imaging (e.g., MRI). 3. Assess how AI can improve clinical decision-making, particularly in early diagnosis and treatment planning. 4. Examine the cost-effectiveness and feasibility of AI-driven X-rays and ultrasound as early screening tools.

Methods: 1. Design: A multi-center cohort study involving paediatric patients (0-18 years) presenting with neurological symptoms. Participants will undergo standard X-ray and ultrasound imaging as part of their diagnostic work-up.2. AI Image Analysis: AI algorithms, such as deep learning, will analyze the X-ray and ultrasound images to detect abnormalities related to neurological conditions (e.g., brain malformations, lesions, or atrophy). 3. Clinical Comparison: The AI findings will be compared to clinical diagnoses and advanced imaging techniques (MRI or CT). 4. Outcome Measures: The primary outcomes will be sensitivity, specificity, and diagnostic accuracy of AI-enhanced X-rays and ultrasound.

Results: AI will likely improve diagnostic accuracy, detecting abnormalities that may be missed with conventional imaging interpretation. The study is expected to demonstrate that AI can enable earlier diagnosis, leading to timely interventions and better outcomes for paediatric patients. The feasibility and cost-effectiveness of AI-driven X-rays and ultrasound will be assessed, highlighting their potential as accessible tools for early screening.

Conclusions: This study will explore the potential of AI-enhanced X-rays and ultrasound to improve early diagnosis and intervention for pediatric neurological disorders. By leveraging affordable imaging modalities with AI, the study could lead to more accessible, cost-effective, and accurate diagnostics, ultimately improving patient outcomes.

ABSTRACTS

Topic: Traumatic Brain Injury

EPNS25_65 - Striking Differences: Analyzing Concussion Incidence and Impacts in Boxing Versus Taekwondo

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Objectives

The World Health Organization has described traumatic brain injury (TBI) as one of the leading causes of acquired neurological illness, making TBI a major public health issue. Despite the high incidence of TBI and the milder concussion, the regulations and risk factors that lead to these injuries remain largely unexplored in boxing and Taekwondo. This paper comprehensively examines the influence of age, sex, and weight on concussion rates and the short and long-term consequences of head injuries.

Methods

A search using Google Scholar and PubMed databases provided peer-reviewed articles, published within the last 15 years. Articles were literature reviews, controlled studies, epidemiology reports, and surveys. The search terms used were “Taekwondo,” “Boxing,” “Combat Sports,” “injuries,” “concussion,” “return-to-play,” “history,” “age,” “sex,” “weight” and “rule changes.” All articles were analyzed thoroughly, and information was organized into a consolidated report.

Results

Both boxing and Taekwondo exhibit high rates of head injuries, with Taekwondo having an incidence four times higher than other contact sports. Despite fewer head blows per minute compared to boxing, Taekwondo athletes experience significant concussion-related injuries, with 28% of youth injuries being concussion-related. Other factors such as weight, gender and age all impacted injury rates.

Conclusions

Fighters are at an increased risk of developing cognitive impairment and headache, persistent post-concussion syndrome, and CTE. Psychological sequelae of concussions include memory disturbances and mood disorders. Given the concern for TBI in combat sports, this paper proposes protocol changes such as enhanced return-to-play algorithms, ringside medical care, and protective equipment to improve concussion safety and prevention.

ABSTRACTS

Topic: Epilepsy: Diagnosis and Investigations

EPNS25_67 - A Retrospective Assessment of Febrile Seizures Over the Age of Five

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A Retrospective Assessment of Febrile Seizures Over The Age of Five

Objectives: Febrile seizure (FS) is a convulsive event associated with fever (body temperature ≥38°C) and the absence of central nervous system infection, commonly occurring in children aged 6 to 60 months. Certain children encounter febrile seizures during late childhood. In contrast to standard febrile seizures, febrile seizures occurring in late childhood necessitate additional evaluation. This study evaluated the clinical findings associated with febrile convulsions in late childhood.

Methods: This study retrospectively evaluated FS patients older than 60 months who presented to the pediatric neurology clinic from October 2022 to January 2023. Clinical findings, prior febrile seizure (FS) history of patients, family history of epilepsy or FS, body temperature during FS, seizure semiology and duration, infection focus, and neuroimaging tests were analyzed.

Results: From October 2022 to January 2023, 46 patients aged over 60 months with FS were identified at the pediatric neurology clinic. Of the patients, 11 were female and 35 were male. The average age was 79.07 months, with a minimum of 61 months and a maximum of 182 months. In 16 patients, there was no history of FS, while 30 patients exhibited a history of FS. Eighteen out of 30 patients with a history of febrile seizures (FS) reported experiencing two or more episodes of FS. Body temperature was most frequently recorded between 38 and 39 during the seizure. The predominant seizure semiology observed was generalized tonic-clonic, with the majority lasting under 5 minutes. The predominant site of infection was the upper respiratory tract. Abnormal findings were observed in the electroencephalography of nine patients, while heterotopia was identified in the neuroimaging of one patient.

Conclusions: This study found that 65% of patients with febrile seizures (FS) lasting over 60 months had a prior history of FS, with 60% of this subgroup reporting a history of two or more FS episodes. Two or more febrile seizure experiences, along with a family history of febrile seizures within the typical age range of 6 to 60 months, may be identified as risk factors for febrile seizures in late childhood.

ABSTRACTS

Topic: Neurorehabiltation

EPNS25_69 - Quality of Life, Knowledge, and Awareness among caregivers of Children and adolescents with autism spectrum disorder in Kuwait: A Cross-Sectional Study

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Objectives:

The main aim of this research was to examine the Quality of Life, the level of knowledge and awareness among caregivers of children and adolescents with ASD in Kuwait. also to fill the gap in the literature by assessing the QoL, knowledge, and awareness of caregivers of children and adolescents withASD in Kuwait, providing insights into the support needed to improve their well-being.

Methods

A descriptive cross-sectional study was conducted targeting caregivers with autism spectrum disorder. A totalof 130 caregivers completed the study questionnaire. Data were collected from participants using a self- reported questionnaire. A demographic form was completed by all participants to gather background information, which was used to describe the sample. Two instruments were used. The Autistic Spectrum Disorder Parent/Caregiver Quality of Life (ASDPC-QoL) and the knowledge and awareness scale. This (ASDPC-QoL) instrument comprises 28 questions divided into four domains with good psychometric properties. The knowledge and awareness scale was reviewed by a panel of three experts in developmental disorders from the medical college of King Khalid University to check clarity and content validity. Tool reliability was assessed using a pilot study of 25 participants. The tool covered the following data: parents' socio-demographic data.Parents' knowledge regarding autism was assessed using 31 questions covering general knowledge, clinical features, social effects, consequences, and curability. The last section covered parents' perceptionsregarding autism frequency in Saudi Arabia, stigma, and awareness level in the study region

Results

The survey included 130 caregivers, primarily females (69.2%), Kuwaitis (91.5%), aged 30-49 (66.9%), with a diploma or bachelor's degree (86.2%), and mothers of children with ASD (68.5%). Mostfamilies consisted of 4 to 9 members. The results showed that the average caregiver answered only 50.72% of the questions correctly, indicating a generally low level of ASD knowledge. The findings revealed average QoL scores ranging from 61 to 69.8 across different dimensions, with physical health scoring the lowest and mental health the highest. This suggests a moderate QoL among the caregivers in Kuwait.

Conclusions

The study revealed misconceptions among caregivers concerning ASD, emphasizing the importance of education. Higher levels of education were associated with improved comprehension. Gender variations in mental health were obvious, with women scoring lower. The importance of support for these families was highlighted by highlighting the obstacles that parents of children with ASD face in their marriages.

ABSTRACTS

Topic: Neurodevelopmental Disorders / Developmental Neuroscience

EPNS25_70 - Neurodevelopmental Outcomes in Infants with Congenital Heart Disease: The Role of Neuromarkers, Brain MRI, and Perioperative Data

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Objectives

Congenital heart diseases (CHD) affect approximately 8 in 1,000 live births, with many requiring surgical intervention. Children with CHD are at risk for neurodevelopmental issues, that may be influenced by a range of perioperative factors and brain injuries.

This study aims to investigate the association between perioperative events, MRI imaging; serum neuromarker and short-term neurodevelopmental outcomes for various types of complexCHD.

Methods

We conducted a prospective cohort study involving 27 neonates with complex CHD, monitored at the Clinique d'Investigation Neuro-Cardiaque (CINC). Participants underwent cardiac surgery requiring cardiopulmonary bypass within the first two months of life. Serum levels of neuron-specific enolase (NSE) and S100B were measured at several time points. Brain MRI imaging was performed postoperatively 2 weeks after surgery. Neurodevelopmental assessments were performed using the Alberta Infant Motor Scales (AIMS) at four months of age.

Results

In the cohort, the median AIMS score was 11 (IQR: 10-12), with 15 infants (65.21%) scoring at or below the 10th percentile. A significant correlation was observed between elevated NSE and S100B levels and lower AIMS scores (preoperative NSE: $r = -0.59$, $p < 0.005$, S100B on Day 3: $r = -0.63$, $p < 0.005$), but also between microbleed on Brain MRI and prone position ($r = -0.64$, $p < 0.005$). Clustering analysis revealed two distinct profiles of patients based on their perioperative events and neurodevelopmental outcomes. Patients in cluster 1 had better neurodevelopmental scores, fewer brain lesions and lower NSE levels compared to those in cluster 2. A multivariate regression model was developed for each cluster, obtaining the regression coefficient for each variable. Application of this model enabled us to predict a new patient's AIMS score with good accuracy.

Conclusions

The study highlights the critical role of perioperative management and the monitoring of neurological biomarkers in predicting neurodevelopmental outcomes in infants with complex CHD. In the CINC study, children are followed by a multidisciplinary team until 24 months of age. The expected results will contribute to a better understanding of neurodevelopmental outcomes in infants with complex CHD.

ABSTRACTS

Topic: Epilepsy: Diagnosis and Investigations

EPNS25_71 - EpiTrack Junior test for the assessment of cognitive abilities in children with idiopathic and symptomatic epilepsy syndromes

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Objectives. To assess cognitive abilities in children with idiopathic and symptomatic epilepsy syndromes using the EpiTrack Junior test.

Methods. 79 children with idiopathic and 13 children with symptomatic epilepsy syndromes. This 15-minute EpiTrack Junior test assesses the cognitive functions of attention, executive functions, and working memory in children aged 6 to 18 along with antiepileptic therapy. Assessment of current test performance: up to 28 points -"significantly impaired" (SI), 29 to 30 points -"mildly impaired" (MI), 31-35 points -"average" (A) and from 36 points -"good" (G).

Results. Children with idiopathic epilepsy syndromes (N=79, M±m): Rolandic epilepsy (24 children)-29,5±0,52 (MI); Childhood absence epilepsy (16 children)-31,9±0,5 (A); Epilepsy with generalized tonic-clonic seizures alone (30 children)- 29,37±0,5 (MI); Jeavons syndrome (1 child)-29 points (MI); Panayiotopoulos syndrome (1 child)-33 points (A); Watanabe syndrome (1 child)-33 points (A); Juvenile myoclonic epilepsy (3 children)-32,29,29 points (A,MI,MI); Reflex epilepsies (3 children)-31,30,25 points (A,MI,SI). Children with symptomatic epilepsy syndromes (N=13, M±m): congenital cortical malformations of the central nervous system (6 children)-28,33±2,2 (SI); history of traumatic brain injury (1 child)-26 points (SI); history of thrombosis of the sinus rectus and vein of Galen (1 child)-23 points (SB); history of encephalitis (1 child)-23 points (SI); history of meningitis with Sepsis (1 child)-26 points (SI); Multilocal vacuolating neuronal tumor (MVNT) (1 child)-29 points (MI); history of hypoxic-ischemic encephalopathy (1 child)-31 points (A); large temporal arachnoid cyst (1 child)-29 points (MI). There were no results in the “good” (G) category in any of the groups. It was noted that oxcarbazepine and higher doses of valproate (Orfiril Long) were used more often in children with symptomatic epilepsy syndromes compared to patients with idiopathic epilepsy syndromes.

Conclusions. The results showed a significant dominance of the “average” (A) category in patients with idiopathic epilepsy syndromes compared to patients with symptomatic epilepsy syndromes. This depends on the etiological factors of the epilepsy syndromes, the cognitive abilities of the children and the antiepileptic therapy. The EpiTrack Unior test is an effective screening test for the detection and tracking of cognitive abilities, attention and executive functions in children with epilepsy.

ABSTRACTS

Topic: Neurogenetics

EPNS25_76 - Clinical manifestations and long-term neurological outcomes of biallelic SHQ1 variant-related pediatric neurodevelopmental disorder with dystonia and seizures

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Objectives

Biallelic *SHQ1* variant-related neurodevelopmental disorder with dystonia and seizures (NEDDS) (MIM #619922) in pediatric patients is extremely rare. The aim of this study is to report the clinical manifestations and long-term neurological outcomes of this disease entity.

Methods

Night individuals, from eight unrelated families, who exhibited developmental delay, hypotonia, and dystonia, received whole-genome sequencing, and had inherited biallelic *SHQ1* variants, were recruited. Clinical features and neurological outcomes were analyzed.

Results

The median age at disease onset was 3.5 months old. All 9 individuals exhibited normal eye contact, profound hypotonia, and paroxysmal dystonia at the first visit, as well as varying degrees of autonomic dysfunction. Two individuals had cerebellar atrophy at the initial neuroimaging study; however, five individuals showed cerebellar atrophy at follow-up. Eight individuals who underwent cerebral spinal fluid analysis all had a low level of homovanillic acid in neurotransmitter metabolites. Five individuals who received ^{99m}Tc-TRODAT-1 scan had moderate to severe decreased tracer uptake in the striatum. Four novel *SHQ1* variants in 18 alleles were identified: 10 alleles (56%) were c.997C>G (p.L333V); 5 (28%) were c.195T>A (p.Y65X); 2 (11%) were c.812T>A (p.V271E); and 1 (6%) was c.146T>C (p.L49S). The median follow-up duration was 3 years and 9 months, ranging from 18 years and 8 months to 3 years and 2 months. During the follow-up period, 6 individuals still exhibited hypotonia and paroxysmal dystonia; 2 showed dystonia; and 1 had hypotonia only. All patients exhibited profound psychomotor impairment despite selegiline, carbidopa/levodopa (25/100), or trihexyphenidyl administration. Eight individuals were non-ambulatory, and one could walk with ataxic gait. One patient died of respiratory failure at the age of 9 years and 8 months old.

Conclusions

Clinical features of pediatric patients with biallelic *SHQ1* variant-related NEDDS vary and the neurological outcomes are devastating. The underlying pathomechanism among movement disorders, dopaminergic pathways, and the neuroanatomic circuit needs further study to clarify the roles of the *SHQ1* gene and protein in neurodevelopment, furthermore, to provide personalized healthcare.

ABSTRACTS

Topic: Movement Disorders/ Cerebral Palsy

EPNS25_77 - Patients with Allan-Herndon-Dudley Syndrome (MCT8 Deficiency) Display Symptoms of Parkinsonism in Childhood and Respond to Levodopa/Carbidopa Treatment

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Objectives Patients with mutations in the monocarboxylate transporter 8 (MCT8) suffer from Allan-Herndon-Dudley syndrome (AHDS), characterized by developmental delay and a highly disabling movement disorder. Despite the potential of thyroid hormone derivatives to overcome the transporter defect, current trials did not achieve patient-oriented therapeutic goals. Since most neurological symptoms are related to the dopaminergic system, we investigated the role of dopamine and its metabolites in MCT8 deficiency with regard to pathophysiology and potential therapeutic strategies in an observational cohort study.

Methods We present longitudinal data from the DEEPTYPE registry of twelve patients with video-documentation, standardized phenotyping, cerebrospinal fluid analysis, treatment response to levodopa/carbidopa supplementation, and neuroimaging data. To establish a cell-based model for pathophysiological studies, we differentiated healthy human induced pluripotent stem cells (hiPSCs) into dopaminergic neurons.

Results Children presented with signs of parkinsonism in childhood, including hypokinesia, hypomimia, inability to sit or stand, rigidity, dystonia, and autonomic dysfunction along the

ABSTRACTS

classification of Leuzzi and colleagues. Cerebrospinal fluid homovanillic acid concentrations were decreased (n=12), suggesting isolated dopamine pathway impairment. Six out of seven patients responded favorably to levodopa/carbidopa supplementation and we did not see any adverse drug reactions. Our cell-based studies showed that hiPSC-derived dopaminergic neurons expressed MCT8 and produced quantifiable levels of biogenic amines.

Conclusions Parkinsonism is part of AHDS's clinical presentation and may be amenable to treatment. The precise impact of MCT8 deficiency on the dopamine metabolism needs to be further elucidated, e.g. by using patient iPSC-derived dopaminergic neurons in future studies.

ABSTRACTS

Topic: Epilepsy: Diagnosis and Investigations

EPNS25_86 - Interictal changes of tension in new onset childhood epilepsy: A Cause or consequence?

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Objectives: Seizures are known to cause blood pressure (BP) changes by modulating the blood-brain barrier as a result of cerebral inflammation caused by sympathetic hyperactivation Autonomic response may be variable as a result of stimulation/inhibition by epileptic activity in different neuronal networks. In our study, we aimed to determine interictal BP changes in new-onset epilepsy (NOE).

Methods: Fifty-six patients aged 6-16 years diagnosed with idiopathic generalized epilepsy (childhood absence epilepsy) and self-limited focal epilepsy with centrotemporal spikes (SELECTS) were included in the study. Ambulatory BP monitoring was performed for 24 hours and interictal BP changes were compared between groups. BP values above the 95th percentile according to gender and height were determined as hypertension. BP load refers to the percentage of total readings over the hypertension threshold. Decrement of mean systolic or diastolic BP over 10% between daytime and nighttime BP measurements was defined as dipping pattern.

Results: The mean age of NOE participants (56 patients) was 108 months (28.3 SD; 98 months median, range 73-178 months). There was no difference according to BMI percentile and weight for height (p=0.871; p=0.849). Mean of daytime systolic BP load was found to be higher in patients with childhood absence epilepsy than SELECTS (p=0.001). Non- dipping pattern were more frequent in SELECTS (p=0.02). There was no difference according to epileptic activity (unilateral or bilateral) (p=0.759; 0.822, respectively). Prevalence of hypertension (one patient with absence and one patient with SELECTS) were similar in both groups. Low-dose amlodipine treatment was initiated to one patient with SELECTS due to the detection of end organ damage on neuro-ophthalmological examination

Conclusions: This study is a pioneer for further studies to elucidate interictal BP changes in NOE. Epileptic patients may show impaired interictal autonomic function depends on seizure type and duration. Non-dipping patern was common among patients with SELECTS and this could be attributed to the increased nocturnal interictal activity.

ABSTRACTS

Topic: Fetal and Neonatal Neurology

EPNS25_88 - A quantitative and qualitative study of the brain development of fetuses with Spina Bifida: insights from gestational ages 15-23 weeks

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Objectives

Spina bifida aperta is often related to secondary brain anomalies such as Chiari malformation type II (CMII), hydrocephalus, agenesis of the corpus collosum, tectal beaking and abnormal morphology of the cerebral cortex. The aim of this study was to find qualitative and quantitative changes in specific brain structures, including the brainstem, cerebellum, corpus callosum, ventricles and cerebral cortex, as an effect of spina bifida. This is the first time to conduct volumetric or morphometric studies in micro-CT in this specific area of research on human fetuses.

Methods

We analyzed six microfocus Computed Tomography (micro-CT) scans. The study included three human fetuses with SB aged 15-23 weeks of gestation and three age-matched healthy fetuses for comparison. Fetuses were scanned using micro-CT providing high quality imaging. To measure brain structure volumes, a process of segmentation was performed.

Results

The fetus with gestational age of 15 and 19 weeks both exhibit an opening in the spine at the level of L3, while the fetus with GA 23 has the defect at the level of S2. While analyzing the morphology of critical brain structures, several visual features were identified. However, not all of these findings can be directly attributed to SB; some may be influenced or associated with other factors such as the premature labor or the staining and fixing techniques, like rupture of the corpus callosum in all fetuses. The severity of the CMII defect appears to increase in the older fetuses as the cerebellum is more descended and flattened than in the younger SB fetuses. Furthermore, especially the older SB specimens exhibited visually a smaller fossa posterior, and in addition a smaller cerebellum in comparison to the healthy control group. The volume of cortex was smaller in fetuses with spina bifida and the differences increase over time.

Conclusions

This study highlights the progressive nature of cerebral en cerebellar anomalies over time during the fetal period. By using micro-CT scanning, we introduce a novel approach to researching this condition. This study provides highly detailed imaging of early human development stages, at level of detail rarely achieved before.

ABSTRACTS

Topic: Neurometabolic Disorders

EPNS25_89 - Leriglitazone Achieved a Primary Endpoint Based on Disease Arrest in Patients with Childhood Cerebral Adrenoleukodystrophy in the NEXUS Open-Label Phase 2/3 Study

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Objectives: Cerebral adrenoleukodystrophy (cALD) is a rapidly fatal, X-linked neurodegenerative disorder characterized by inflammatory brain demyelination. Haematopoietic stem cell transplantation (HSCT) may halt disease progression, but there is an unmet need for less invasive therapies that can be administered immediately upon lesion identification. Leriglitazone is a peroxisome proliferator-activated receptor γ agonist with potential to treat cALD. We assessed the efficacy and safety of leriglitazone in boys with cALD.

Methods: NEXUS (NCT04528706) was a phase 2/3, 96-week, open-label, multicentre study of once-daily oral leriglitazone, which recruited boys aged 2–12 years with cALD, with or without gadolinium-enhancing lesions. The primary endpoint was the proportion of patients with clinically and radiologically arrested disease at week 96 or last visit before HSCT. The primary endpoint success criterion was a greater proportion of patients with arrested disease compared with natural history (one-sided 95% confidence interval > 10%). Arrested disease was defined as change in neurological function score (NFS) ≤ 5 from baseline, no major functional disabilities (MFD) and no lesion progression on MRI. Secondary endpoints included change from baseline in NFS and Loes score. Exploratory endpoints included volumetric assessment (trajectory of lesion fold change over time), MFD-free survival and change in plasma biomarker concentrations.

Results: Of 23 patients recruited, 20 were evaluable at week 96 or visit before HSCT. Seven patients (35%) met arrested disease criteria, fulfilling the primary endpoint success criterion, a significantly higher proportion than would be expected from natural history data (10%, $p < 0.05$). All patients remained clinically stable (MFD free and stable NFS) during treatment. There were no treatment-related serious adverse events or discontinuations due to adverse events. Further data on secondary and exploratory endpoints, including volumetric lesion growth data, will be presented.

Conclusions: Leriglitazone treatment resulted in cerebral disease arrest with clinical and radiological stabilization in a significant number of patients and was well tolerated. These data demonstrate the efficacy and safety profile of leriglitazone in treating childhood cALD, with potential to address the significant unmet treatment need for this patient population.

ABSTRACTS

Topic: Neuromuscular Disorders

EPNS25_91 - Evaluation of Vaccination Status in Children Diagnosed with Duchenne Muscular Dystrophy

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Objectives: Duchenne muscular dystrophy (DMD) is the most common neuromuscular disease in childhood with high mortality and morbidity. According to the rare diseases report published by the Turkish Public Health Agency in 2019, it is estimated that there are approximately 15,000 DMD patients (aged 1-60) in our country and 140-150 new cases are added annually. DMD patients are particularly at risk for respiratory tract infections. Vaccines are the most effective practice against infectious diseases today, as they were in the past. We aimed to determine the vaccination status of DMD patients followed in our clinic.

Methods: The status of influenza and national vaccination calendar vaccinations of DMD patients who came for routine follow-up between June 15 and December 15, 2024, at the Neuromuscular Clinic of the Muscle Diseases Center of İzmir Tepecik Education and Research Hospital was examined. Patients were divided into three groups according to their influenza vaccination status: every year, irregularly and never. Vaccines in the national vaccination calendar were evaluated through the patients' vaccination card and medical record system.

Results: Total of 100 patients were included in the study. The mean age of the patients was 8.95 years (1-17 years), and the mean age at diagnosis was 2.76 years (6 months-9 years). The rate of hospitalization in the last year was 7% (n=7). Influenza was the causative agent in 3 of them (42%), and the cause of lower respiratory tract infection was not determined in the others. 65% (n=39) of the patients were receiving steroid treatment, and 8.3% (n=5) were receiving translarna treatment. It was determined that 7% (n=7) had influenza vaccination every year, 7% (n=7) had it irregularly, and 86% (n=86) had never had it. In 21% (n=21) of the cases, deficiencies in the vaccinations in the Turkish national vaccination calendar were detected. The most frequently missed vaccines in the vaccination schedule were; chickenpox 17% (n=17), measles-mumps-rubella (MMR) 15% (n=15), hepatitis-A 15% (n=15), oral polio vaccine (OPA) 10% (n=10), pneumococcal vaccine (PV) 8% (n=8), respectively.

Conclusions: In our study, we found that DMD patients were undervaccinated for many vaccines, especially influenza. Live vaccines are contraindicated in patients receiving high-dose steroid therapy (>2 mg/kg/d or >20 mg/d) for more than 14 days. Therefore, it is important to identify and complete the deficiencies in our patients' vaccination program before steroid therapy. We should recommend influenza vaccination and follow up on the vaccinations in our national vaccination calendar.

ABSTRACTS

Topic: Neurodevelopmental Disorders / Developmental Neuroscience

EPNS25_92 - Genetic background and phenotypic manifestation of 10 cases with atypical rett syndrome

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Objectives

"Atypical Rett syndrome" is a term traditionally used to integrate a group of rare neurodevelopmental disorders, which present many similarities but do not meet the clinical criteria of Rett syndrome. The purpose of our study is to underline the varied genetic etiology and clinical manifestations behind this diagnosis.

Methods

We present 10 cases of Atypical Rett syndrome treated in our clinic. Patients are assessed every 6 months after initial diagnosis. Every visit includes: neurological, developmental, cardiologic, respiratory and general pediatric examination. EEG-study and serum laboratory tests are performed as well.

Results

8 of our patients are girls and the genetic background includes mutations in CDKL5 (5 girls), FOXG1 (1 girl and 1 boy), GABBR2 (1 girl) and STXBP1 (1 girl and 1 boy) genes.

Epilepsy was the initial symptom in all CDKL5 and STXBP1 cases within the first 6 months their lives and epileptic encephalopathy was present soon after. In both STXBP1 cases it manifested in the form of West syndrome. All of the other patients developed epilepsy later on, with the exception of the GABBR2 case. Valproic acid is used in 9 of our patients in combination with other antiepileptic medication. Two of the patients that developed epilepsy have remained seizure free - the girls with FOXG1 and STXBP1 mutations. Epilepsy seems refractory in the rest.

Neurodevelopmental retardation and microcephaly were the initial signs in the FOXG1 and GABBR2 cases. All of the rest manifested them after the onset of seizures. None of our patients developed speech. All have autistic signs and stereotypical hand movements. None of the patients in the CDKL5 and FOXG1 groups managed to stand or walk. The girl with the GABBR2 mutation and both patients with STXBP1 mutations, managed to walk after the age of four.

All patients have feeding difficulties, with most of them avoiding solid foods and one girl with CDKL5 gene mutation is fed through gastrostomy. Altered breathing patterns are present in all patients as well.

Conclusions

Atypical and typical Rett syndrome share many symptoms such as neurodevelopmental delay, microcephaly, epilepsy, feeding and breathing abnormalities. On the other hand patients with Atypical Rett syndrome seem to have an overall worse clinical condition, with epilepsy appearing earlier and being more difficult to control. Lately CDKL5 and FOXG1 encephalopathies tend to be considered as distinct entities and maybe that should be the case for the rest genotypes under the Atypical Rett syndrome umbrella.

ABSTRACTS

Topic: Neurodevelopmental Disorders / Developmental Neuroscience

EPNS25_93 - Gait development in 40 patients with rett syndrome

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Objectives

Rett syndrome is a rare neurodevelopmental disorder, which affects girls and is caused by mutations in the MECP2 gene. Typically affected individuals show regression after a period of normal development, with gradual loss of purposeful hand skills, loss of acquired spoken language and development of gait abnormalities. Autistic behavior and epileptic seizures are also common. The goal of our study is to explore changes in the ability of our patients to move, walk and stand in different stages of the disease.

Methods

We present 40 cases of Rett syndrome treated in our clinic. Patients are assessed every 6 months after initial diagnosis. Every visit includes: neurological, developmental, cardiologic, respiratory, orthopedic and general pediatric examination. EEG-study and serum laboratory tests are performed as well. All of our patients have confirmed MECP2 mutations. All patients undergo physiotherapy sessions.

Results

26 of our patients started walking at the appropriate age (12-18 months), while 3 at the age of 20-24 months and 3 more after the age of 24 months. On the other hand 6 patients never achieved walking and 2 although did manage to stand, they never walked. The earliest age that one of the walkers started to show signs of regression was 18 months-old, in a girl that started walking at 12 months-old. By the age of 5, all of the still ambulant girls had developed ataxia. The earliest a girl became non ambulatory was at the age of 7 years-old. On the other hand 1 patient still walks independently at the age of 31 years-old and 1 more walks with ataxia at 17 years-old and. The oldest one of our patients was when she lost the ability to walk was 23 years-old.

Conclusions

In our experience gait development in girls with Rett syndrome shows great variability. Initially normal motor development followed by regression and loss of walking ability is the norm in patients with Rett syndrome, but variations exist. Improvement in palliative care and better standards of care seem to play a significant role in delaying and altering the disease progression.

ABSTRACTS

Topic: Epilepsy: Medical and Surgical treatment

EPNS25_96 - Subjective Parental Considerations for Monitoring Requirements of Responsive Vagal Nerve Stimulation in Paediatric Drug Refractory Epilepsy

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Background: Since the late 1990s VNS (Vagal Nerve Stimulation) has been approved as a surgical adjunct for drug refractory epilepsy. Over time it has evolved into a closed-loop responsive therapy known as AutoStim which automatically delivers VNS in the absence of a magnet, with the aim of shortening and reducing the incidence of seizure activity in response to ictal tachycardia.

Objectives: To assess subjective parental perceptions on improvements in their child's quality of life, percentage reduction in seizure frequency and any reported adverse effects or troubleshooting with the VNS (Vagal Nerve Stimulation). The patients' initial and current VNS settings in comparison to manufacturer initial programming instructions have been reviewed. The findings inform our recommendations for monitoring protocols and follow up requirements in VNS clinics.

Methods: Our audit retrospectively analyses clinical records of paediatric patients across the Northeast of Scotland with intractable epilepsy requiring VNS. Subjective comments from carers were obtained through telephone surveys. Potential associations between patient age, VNS settings, seizure type and age of implantation were explored.

Results: Eight patient records were reviewed with a focus on subjective parental outcomes. Only one patient had differing initial programming settings from the standard manufacturer instructions. Seizure reduction >50% was observed in 37.5% (3) of cases, though 50% (4) of patients could not determine the percentage of reduction due to recent implantation, coinciding pubertal changes or medication adjustments. 50% (4) of carers reported improvements in quality of life, the other 50% (4) noticed negative or no improvement. It was observed that the patients with no improvements in quality of life of seizure reduction, had <2mA AutoStim, unknown or no AutoStim output current. The only adverse effects reported were mild coughs and slight changes in voice. Two patients experienced issues with the physical device.

Conclusions: The audit identified the need for consistent monitoring of adverse effects and troubleshooting processes in VNS clinics to ensure timely management of significant complications, thereby maintaining optimal VNS therapy. Furthermore, the results indicate that carers find it challenging to confirm improvements in seizure outcome as the impact of confounding variable such as coinciding medication adjustments or preexisting comorbidities were unknown. Enhanced focus on monitoring parental perceptions and confounding variables in VNS clinics, could offer a more precise evaluation of device effectiveness and enable earlier intervention through programming adjustments.

ABSTRACTS

Topic: Neurogenetics

EPNS25_97 - Radial microbrain (micrencephaly) is caused by a recurrent variant in the RTTN gene

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Objectives

Genetic Primary Microcephaly (PM) is a defect in early brain development leading to congenital microcephaly, mostly recessively inherited, and mild to moderate intellectual disability. PM has been largely elucidated thanks to exome and genome sequencing. However, radial microbrain, the most severe form of genetic PM or micrencephaly described in the 1980s, which leads to early lethality or very severe intellectual handicap, remains without a molecular diagnosis. We sought to identify the cause of radial microbrain by analyzing the genotype of children/adults and fetuses with an extremely small brain.

Methods

We searched for individuals with the smallest head circumference among patients with a confirmed diagnosis of PM included in two French and European observational studies coordinated at the Robert Debré Children's Hospital in Paris. Their neurodevelopment and brain imaging were analyzed, as well as next generation sequencing for a panel of microcephaly genes or exome sequencing. Neuropathological and immunohistological analysis of extremely severe microcephalic fetal brains and stage-matched controls were carried out. A paired t test with Welch's correction was used to compare the cortical thickness between groups.

Results

We identified 5 individuals (4 females, 7 years 10 months – 19 years) with a particularly small brain among a series of 50, all suffering from a severe neurodevelopmental disorder with no ability to communicate verbally and, in 3 of them, no ability to walk. Genetic analysis revealed the presence in all individuals of the same homozygous variant c.2953A>G (p.R985G) in the *RTTN* gene (ROTATIN). The same variant was found in 2 fetuses whose neuropathological evaluation showed a major reduction in the thickness of the ventricular zone and neuronal heterotopias. The cortical plate was reduced by 70% compared to controls, irrespective of the region considered. Immunostaining with VIMENTIN showed a 50% loss of radial glial columns, characteristic of radial microbrain.

Conclusions

Our data shows that the homozygous c.2953A>G substitution in *RTTN* is a recurrent variant responsible for radial microbrain, the most severe form of primary microcephaly. Our combined neurological, imaging and histopathological approaches provide a better understanding of the severity of this condition and its prognosis.

ABSTRACTS

Topic: Epilepsy: Medical and Surgical treatment

EPNS25_98 - Stepwise Multimodal Treatment Approaches and Seizure-Free Outcomes in Patients with Lennox-Gastaut Syndrome: A Retrospective Analysis

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Objectives

Multimodal treatment approaches are often considered for patients with Lennox-Gastaut syndrome (LGS) due to the resistance of seizures to drug treatment in this condition. Developing a treatment algorithm to guide providers remains challenging. This study aimed to assess seizure-free outcomes of stepwise multimodal treatments in LGS patients.

Methods

We retrospectively analyzed 377 patients with LGS who underwent multimodal treatments, including antiepileptic drugs (AEDs), diet therapy (DT), resective epilepsy surgery (r-ES), and palliative epilepsy surgery (p-ES). Treatment steps were categorized as follows: first-line therapy consisted of AEDs alone; second-line therapy included AEDs combined with DT, r-ES, or p-ES; and third-line therapy involved AEDs combined with both DT and surgical treatments (r-ES or p-ES). Seizure-free outcomes of at least one year were assessed, and clinical factors, including age and etiology, were compared among the treatment groups.

Results

Over a mean follow-up period of 12.5 years (range, 1.5–35.2), 174 patients (46%) achieved seizure freedom for ≥1 year, including 56 (15%) who remained seizure free for ≥5 years. Among the 377 patients, 78 (20.7%) were treated with AEDs alone as first-line therapy. For second-line therapy, 105 patients (27.9%) received AEDs+DT, 60 patients (15.9%) received AEDs+r-ES, and 38 patients (10.1%) received AEDs+p-ES. For third-line therapy, 96 patients (25.5%) underwent combined AEDs+DT+ES. Seizure-free outcomes of ≥1 year were achieved by 49 patients (13.0%) in the AEDs+DT group, 25 patients (6.6%) in the AEDs+r-ES group, and 16 patients (4.2%) in the AEDs+p-ES group, with no statistically significant differences among the groups. Clinical factors, including age and etiology, significantly differed across the treatment groups ($P<0.001$, Bonferroni post-hoc correction).

Conclusions

No single treatment strategy proved to be superior for patients with LGS. However, stepwise multimodal treatment approaches, including combinations of AEDs, diet therapy, and surgery, achieved relatively high rates of seizure freedom. These findings emphasize the importance of individualized treatment strategies for LGS patients and highlight the potential efficacy of a stepwise multimodal approach in achieving long-term seizure control in this challenging population.

ABSTRACTS

Topic: Neuromuscular Disorders

EPNS25_99 - Clinical management and unmet Needs of Duchenne Muscular Dystrophy in Spain: Results from the DMD-NEEDS Study

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Objectives: Duchenne muscular dystrophy (DMD) is an X-linked neuromuscular disorder marked by clinical and management variability. While therapeutic advancements have been made, limited data on healthcare practices and patient care trajectories contribute to disparate clinical outcomes. This study aimed to assess the management strategies for DMD patients in Spain, identify unmet medical needs, and evaluate the clinical and therapeutic approaches employed by neuropaediatricians.

Methods: The DMD-NEEDS study was a non-interventional, cross-sectional investigation conducted in collaboration with the Spanish Society of Paediatric Neurology and Duchenne Parent Project. Data were obtained through an electronic survey designed to capture information on diagnostic methods, clinical practices, patient demographics, and therapeutic strategies in DMD care.

Results: A total of 41 neuropaediatricians (56.1% female) participated, managing 1–10 patients each and reporting a mean of 13.3 years (SD 7.1) of experience in DMD care. Most diagnoses were established between ages 2 and 3 years (53.7%), with diagnostic confirmation achieved in under 6 months for 46.3% of cases. Corticosteroids, predominantly deflazacort, were prescribed as first-line therapy in 95.1% of cases, with initiation typically occurring at ages 4–5 years (66.7%). Multidisciplinary care was available in 68.3% of centers, commonly involving cardiologists (96.4%) and physiotherapists (85.7%). However, key gaps included delays in treatment initiation and underutilization of quality-of-life (QoL) assessment tools, with 58.5% of clinicians not routinely employing these measures.

Conclusions: Despite early diagnosis and widespread corticosteroid use, deficiencies remain in timely treatment initiation, access to multidisciplinary care, and integration of QoL assessments into routine practice. These findings emphasize the critical need for standardized care pathways and improved education for healthcare providers to optimize outcomes for DMD patients.

ABSTRACTS

Topic: Infectious and Inflammatory Diseases/ Neuroimmunology

EPNS25_100 - A case of prodromal RIS (pre-RIS) in a 17-Year-Old Patient with Focal Seizures

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Objectives: Radiologically isolated syndrome (RIS) is considered a pre-symptomatic stage of Multiple Sclerosis (MS), characterized by incidentally identified lesions on MRI with features suggestive of MS, without accompanying clinical symptoms. While RIS is well-documented in adults, data in the pediatric population is limited and specific criteria for pediatric RIS (ped-RIS) are not yet established. Prodromal RIS (pre-RIS) is a newly proposed term, describing imaging findings typical of MS that do not fully meet the revised 2023 diagnostic criteria for RIS, reflecting the spectrum of subclinical disease activity prior to symptom onset. We describe the case of a 17-year-old female with focal seizures and MRI findings suggestive of demyelination and we discuss the potential recognition of a pre-RIS stage, as well as its therapeutic implications.

Methods: This case report includes a detailed review of the patient's clinical history, imaging, and laboratory findings, along with a comprehensive review of relevant literature.

Results: The patient, previously treated for generalized epilepsy until age 7, developed focal seizures at 15 years of age. MRI revealed chronic, typical demyelinating lesions, located in subcortical and infratentorial white matter, while CSF analysis demonstrated the presence of type 3 oligoclonal bands. No prior definitive demyelinating event was identified by medical history and neurological examination.

Conclusions: The indicated therapeutic approach for RIS in adults remains elusive, with even greater uncertainty surrounding management in ped-RIS cases. Furthermore, the pre-RIS stage lacks a clear definition in global literature, presenting additional challenges. The association of epilepsy with MS is particularly complex, as seizures are not a common initial manifestation in adults, but they can occasionally present as the first symptom in typical pediatric relapsing MS. Gray matter involvement and cortical lesions may contribute to epileptogenesis in these patients. Notably, patients identified as pre-RIS appear to carry an elevated risk of progression to a first demyelinating event, especially in the presence of high-risk prognostic factors, such as cerebellar or spinal cord lesions and positive oligoclonal bands. Comprehensive evaluation of imaging and laboratory findings, alongside recognition of atypical MS manifestations—such as seizures or psychiatric symptoms—are vital for the reliable identification of pre-RIS. Recently established serum biomarkers, especially neurofilament light chain, could be particularly useful to clinicians, as they confirm the diagnosis and facilitate patients' stratification. Early diagnosis and intervention are crucial to ensure favorable long-term outcomes, and more research is considered mandatory.

ABSTRACTS

Topic: Epilepsy: Medical and Surgical treatment

EPNS25_103 - Results of DIAVEY, the European post-marketing safety study on stiripentol use

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Objectives

In 2007, stiripentol received conditional marketing authorization in the European Union (EU), and the European Medicines Agency required a post-marketing surveillance study. The aim was to collect real-world safety information on stiripentol use in patients with Dravet syndrome (DS) and other epilepsies, focusing on neutropenia, hepatotoxic potential, failure to thrive, behavior issues, and psychomotor development.

Methods

DIAVEY was a non-interventional EU-wide post-marketing study. Patients with refractory generalized tonic-clonic or clonic seizures newly prescribed stiripentol were eligible. The study period was from January 2007 to May 2012, with yearly evaluations. Patients were included for at least one year.

Results

227 patients from 57 centers in 11 European countries were enrolled: 152 had DS and 75 had other epilepsies. Mean age at inclusion was 7.2 years (6.4 years in DS and 8.6 years in non-Dravet). 16 DS patients were less than 1 year-old, and 46 were between 1 and 3 years of age.

At stiripentol start, 79% of DS patients were receiving valproate, 71% clobazam, and 24% topiramate, while 56% of non-Dravet patients were receiving clobazam, 36% valproate, and 25% carbamazepine. Mean ± standard deviation (SD) stiripentol dosage at inclusion was 38.9 ± 16.8 mg/kg/day in DS and 33.5 ± 17.6 mg/kg/day in non-Dravet.
Mean ± SD treatment duration was 22.4 ± 13.8 months in DS and 15.9 ± 13.7 months in non-Dravet. A total of 83 patients (36.6%) discontinued stiripentol: 41 (27%) with DS and 42 (56%) with other epilepsies due mainly to lack of efficacy or adverse drug reactions (ADRs).

Overall, 130 patients (57%) experienced 387 ADRs, serious in 28 patients and leading to stiripentol discontinuation in 34 patients. Increased γ-glutamyl transferase levels (17%), increased aspartate aminotransferase levels (14%), decreased appetite (13%), somnolence (9%), fatigue (8%), neutropenia (7%). Also, 9 cases of thrombopenia were reported in 7 patients; thrombocytopenia was added as a rare undesirable effect in the Summary of Product Characteristics (SmPC).

No negative impact of stiripentol on patients' growth in height or weight was observed.

Despite efficacy evaluation was not the aim of the study, a decrease in seizure frequency was noted in most patients.

Conclusions

DIAVEY did not identify new ADRs; only thrombocytopenia was added to the SmPC. Discontinuations were mainly due to lack of efficacy and/or ADRs and were more frequent in non-Dravet patients.

ABSTRACTS

Topic: Neuromuscular Disorders

EPNS25_105 - Safety and Efficacy from the Ongoing Phase 1/2 DELIVER Trial of DYNE-251 in Males with DMD Mutations Amenable to Exon 51 Skipping

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Objectives

DMD is a rare, progressive neuromuscular disorder caused by mutations in the *DMD* gene, which result in the absence of functional dystrophin protein. DYNE-251, an investigational therapeutic for DMD, leverages the transferrin receptor 1 to deliver an exon 51-skipping PMO to affected tissues with the goal of restoring dystrophin expression. The safety and efficacy of DYNE-251 are being investigated in the Phase 1/2 DELIVER trial (NCT05524883) in 4-16-year-old males with *DMD* mutations amenable to exon 51-skipping.

Methods

In the MAD portion of DELIVER, participants are randomized to receive DYNE-251 or placebo Q4W or Q8W for 6 months; participants subsequently enter the OLE/LTE. All 54 enrolled participants are at the 20 mg/kg dose level.

Results

DYNE-251 drove dose-dependent increases in mean PMO muscle concentration and exon skipping, resulting in 3.22% and 3.72% of normal mean dystrophin in the 10 mg/kg and 20 mg/kg cohorts, respectively, at 6 months. The mean corresponding muscle content-adjusted dystrophin levels were 7.64% and 8.72% of normal. DYNE-251 led to improvements across multiple functional endpoints, including the North Star Ambulatory Assessment, Time to Rise from Floor, 10-Meter Walk/Run Test, and Stride Velocity 95th Centile. Improvements were noted as of 6 months in the 10 mg/kg and 20 mg/kg cohorts, with a continued effect through 12 months in the 10 mg/kg cohort. DYNE-251 had a favorable safety profile as of the analysis date with most TEAEs reported as mild or moderate. Three serious TEAEs potentially related to study drug occurred in two participants in a 40 mg/kg Q4W cohort. These events had multiple confounding factors suggestive of infection or background risk that may have contributed to their presentation. Subsequently, all participants in the 40 mg/kg cohorts were lowered to the 20 mg/kg dose level.

Conclusions

DYNE-251 had a favorable safety profile and resulted in early improvements across multiple functional endpoints. Longer-term follow-up data for patients included in this abstract will be presented.

ABSTRACTS

Topic: Neuromuscular Disorders

EPNS25_107 - Evaluation of the Experiences of Caregivers of Children Diagnosed with SMA Type-1

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Objectives: Muscular Atrophy (SMA) is a rapidly progressive disease characterized by denervation of the neuromuscular junction caused by SMN gene mutation. Patients diagnosed with SMA face disruptions in basic life activities that bring along the need for care by their families and in addition to the health problems experienced by the patient, caregivers face some psychosocial/economic problems. The aim of our study is addressing these problems faced by caregivers of children with SMA type 1 in depth.

Methods: The study is a qualitative research in which online in-depth interviews were conducted. Purposive sampling was used and terminated when the data reached saturation. Our study included the caregivers of 12 patients who were diagnosed with SMA type-1 and followed up by Department of Pediatric Neurology. Mini questionnaire including questions about sociodemographic characteristics was applied. Data were collected through in-depth interviews using a semi-structured question guide and analyzed by content analysis method. Thematic analysis was conducted considering themes and sub-themes.

Results: All of the participant caregivers were family members. Ten were female, 2 were male, 2 were employed and 10 were not employed. The themes of the study are: “Diagnosis - disease and treatment process, Effects of the process on caregivers, Aid and Campaigns, Stigmas, Suggestions - Expectations”. The majority mentioned they met diagnosis process with great sadness, becoming very tired and worn out during process which caused them to not being able to give enough care for other family members and children. Their social life was greatly reduced/ended after their children were diagnosed with SMA, and the caregiving process was also very negative in terms of mental impact. Ten of the participants stated that their relationships with their spouses were not affected and even became more united, while others mentioned that their relationships were negatively affected. All of the participants complained that they had financial difficulties and had some demands in this regard. Many of the caregivers mentioned the problems in accessing treatment and medication and shared their negative experiences.

Conclusions: Caregivers of patients diagnosed with SMA type-1 encountered various difficulties in the caregiving process. The challanges were exhausting process, lack of help, decrease in work life, decreased or ended social life, not being able to have a spare time for the other kids, bad affected mental health and financial problems due to the drug supplying process. They needed financial and moral support for various reasons. This study voice families' expectations.

ABSTRACTS

Topic: Epilepsy: Diagnosis and Investigations

EPNS25_110 - Early developmental outcome in Dravet syndrome: a scoping review of cognitive, language, behavioural and motor development in the first six years of life

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Objectives

Dravet syndrome (DS) is a severe developmental and epileptic encephalopathy with intractable epilepsy, developmental delay and behavioural difficulties. In the majority of the patients DS is associated with a SCN1A gene mutation. However, a substantial number of children with an SCN1A mutation do not develop DS, but a less severe phenotype. As the phenotypic diagnosis of DS relies on the presence of developmental delay there may be a long diagnostic gap, making it crucial to identify early prognostic developmental biomarkers for DS.

Our objective was therefore to review existing evidence on developmental delay in various developmental domains in the first six years of life in children with DS.

Methods

The scoping review was performed according to the PRISMA-ScR checklist (Preferred Reporting Items for Systematic reviews and Meta-Analysis extension for Scoping Reviews). A literature search in PubMed was performed to identify studies published up unto June 2024. MeSH terms and free text terms were applied to create a search string. Inclusion criteria for studies were: peer-reviewed articles with full text published in English, German, or French and studies should concern humans. Studies should include at least five children with Dravet syndrome aged six years or younger. Exclusion criteria were single case reports, review articles without new patient data and medication studies. Information is presented on developmental domains important for functioning: cognitive development, language and speech development, behaviour and motor development.

Results

The systematic literature search yielded ten articles which met the in- and exclusion criteria. Nine studies investigated cognition, four assessed language and speech development, five assessed behaviour and five evaluated motor development. Some studies were based on retrospective data from medical records, some used parental surveys and others actually applied developmental assessments.

Altogether, the findings suggest that developmental delay in DS already starts before the age of two years in the majority of children and is present in several developmental domains. It is first visible in the domain of motor development where it already appears after the first half year of life in part of the children, and is becoming apparent in the cognitive, language and behavioural domain after the age of one year in most children.

Conclusions

Developmental delay in DS starts well before the age of two years and is first visible in the domain of motor development. Data available are limited. There is a need for prospective developmental studies in DS in infancy and pre-school age.

ABSTRACTS

Topic: Epilepsy: Medical and Surgical treatment

EPNS25_111 - Indications and outcomes of hemispherotomy: a tertiary pediatric epilepsy center experience

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Objective

Epilepsy is one of the most common neurological diseases. Despite the appropriate use of two antiepileptic drugs, 30-40% of patients continue to experience refractory seizures that impair their quality of life and cognitive functions. This study aimed to evaluate the indications, outcomes, and effectiveness of hemispherotomy in children with drug-resistant epilepsy.

Methods

Twenty-seven children, aged between 9 months and 17 years, who were evaluated at Gazi University Faculty of Medicine Pediatric Neurology-Epilepsy Center and decided to undergo hemispherotomy, were retrospectively analyzed. Detailed histories, Video EEG monitoring results, MRI findings, and postoperative seizure-free statuses were thoroughly reviewed.

Results

Of the 27 patients, 16 (59.25%) were female and 11 (40.75%) were male. Hemispherotomy was performed on 18 (66.6%) of the patients. The etiologies included cortical development malformations in 13 patients (48.1%), encephalitis sequelae in 10 (37%) (of which 7, or 25.9%, were Rasmussen encephalitis), and MCA infarcts in 2 (7.4%).

The epileptogenic zone was unilateral in 19 patients (70.3%) and bilateral with a dominant hemisphere in 8 patients (29.6%). MRI findings revealed pathology in a single hemisphere in 25 patients (92.5%). Among the hemispherotomies performed, 10 (55.5%) were on the left side and 8 (44.4%) on the right. Surgeries involved the nondominant hemisphere in 11 patients (61.1%) and the dominant hemisphere in 2 (11.1%).

Ictal EEG findings were consistent with the pathological hemisphere in 10 patients (55.5%). Preoperative hemiparesis was present in 6 patients (33.3%). Postoperatively, 27.7% of the patients achieved complete seizure freedom.

Conclusions

Hemispherotomy is a highly effective surgical method, particularly in cases of drug-resistant epilepsy originating from a single hemisphere. The timing of epilepsy surgery is crucial for achieving seizure freedom and improving quality of life. Developing well-equipped, multidisciplinary centers for epilepsy surgery is essential in this regard.

ABSTRACTS

Topic: Headache / Migraine

EPNS25_113 - Physiopathology of migraine and neuromodulation by central sensitization, the new challenge in children

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Objectives

Mainly, our objective is to demonstrate the arguments of central sensitization as a means of neuromodulation of migraine pain in children, then secondarily it is to highlight the interest of innovative therapies as an effective therapeutic alternative.

Methods

Our study is longitudinal, prospective, with 24 months of recruitment, during which 26 children with migraine were included. We worked with an investigation sheet, which includes the patient's demographic data, the explorations, the evaluation tests, the treatment and its evolution. Children of all ages, both sexes, with confirmed migraine were included and those not included were complicated cases or with pathologies interfering with migraine headaches.

Results

The average age of our population is 12.53 years, the sex ratio is 4.33 M/F, 84.61% of children presented anxiety and 07.69% depression. No correlation between the intensity of the headaches and the medication used as well as the duration of progression. Self-medication was present in 12.46%, constituting a major risk of perpetuation of the disease. 88.46% had school retention. Analytically, the VAS classes and the CRP average before and after treatment are statistically significant ($p<0.05$). Clear correlation between the improvement of children and the preventive means used ($p=0.03$). The non-significance of our results in terms of headache intensity and duration of progression could be linked to the type of study (longitudinal), the small size of the sample and the traditional therapeutic protocols used versus immunotherapy (Tessa De Vries et al, 2020). Self-medication was largely present due to lack of therapeutic education of our patients (Licia Grazzi et al, 2023). The same goes for the socio-professional impact of the disease. The results of CRP monitoring are in clear agreement with the study by (FH Vanmolkot, 2007). Preventive means are effective and consistent with the literature (Roberta Messin et al, 2023).

Conclusions

In children, treat migraine headaches early and anticipate them and do not wait for signs of central sensitization to appear. The neuro-modulation of pain in itself is a synonym for the risk of becoming chronic. Preventive measures are effective in the same respect as therapeutics. Immunological monitoring of migraine headaches can be a very reliable means of monitoring.

ABSTRACTS

Topic: Epilepsy: Diagnosis and Investigations

EPNS25_114 - Extrahippocampal Radiomics Analysis: Identifying Laterality in MRI-negative Temporal Lobe Epilepsy

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Objectives

Temporal lobe epilepsy (TLE) is a condition where identifying the epileptogenic focus is essential for successful surgical outcomes. This study hypothesizes that radiomics features in extrahippocampal regions can provide valuable insights into lateralization, even in MRI-negative TLE cases. We investigated whether these features differ between affected and unaffected sides in TLE patients and compared them to healthy controls to evaluate their diagnostic utility.

Methods

A retrospective study was conducted including three participant groups: (1) patients with focal TLE and hippocampal sclerosis (n = 36), (2) age- and sex-matched healthy controls (n = 50), and (3) patients with MRI-negative TLE, forming the validation set. Radiomics models were developed using supervised learning techniques. Feature selection employed t-tests with false discovery rate correction, followed by logistic regression with elastic net regularization. Model performance was assessed via receiver operating characteristic (ROC) curves and area under the curve (AUC) metrics. Statistical analyses were performed using R software, with significance set at $P < 0.05$.

Results

Among 684 hippocampal features, 48 were identified as predictive of epilepsy laterality, with the hippocampal model achieving an AUC of 0.99 in training but only 0.69 in external validation. Conversely, 815 extrahippocampal features revealed 99 predictive features, yielding an extrahippocampal model with an AUC of 0.92 in external validation. This model demonstrated superior sensitivity (92%) and specificity (96%) in MRI-negative TLE cases.

Conclusions

This study highlights the diagnostic potential of extrahippocampal radiomics in identifying laterality in TLE, particularly in MRI-negative cases. These findings underscore the value of non-invasive radiomics analysis in enhancing presurgical evaluation and facilitating better clinical outcomes for patients with TLE.

ABSTRACTS

Topic: Epilepsy: Medical and Surgical treatment

EPNS25_116 - Effects of Ketogenic Diet Therapy in Outpatient Anti Epileptic Drug Cost Reduction and Parental Satisfaction among Children with Intractable Epilepsy

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Objectives

This study aims to compare the cost of AED treatment in children with drug-resistant epilepsy before the initiation and after 6 months completion of KDT

Methods

This study is a retrospective with descriptive-analytical approach using outpatient medical records of 16 patients aged 5–18 years with drug-resistant epilepsy who underwent a ketogenic diet for up to 6 months. The evaluation of patient's costs was done based on the prescribed AED, using prices set by the government, both before the initiation of KDT and after its completion in 6 months.

Results

There was a 21% reduction in the cost of prescribed AED among the 16 patients in this study, comparing before the initiation of KDT and after its completion at 6 months. This reduction was statistically significant, with amount Rp 3,757,812 or 235 USD ($p < 0.001$). However, no significant difference in costs was found between 3 months and 6 months after KDT ($p = 0.484$). Most parents in the study (87,5%) gave positive remarks about the affordability and ease of ketogenic diet therapy in managing epilepsy (100%).

Conclusions

This study showed a reduction in the cost of prescribed AEDs between the period prior to the initiation of KDT and after six months of its completion.

ABSTRACTS

Topic: Basic Science

EPNS25_118 - Diagnostic Utility of Visual Evoked Potential (VEP) Testing in Pediatric Age

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Objectives: Visual Evoked Potential (VEP) is a non-invasive neurophysiological method that objectively evaluates the functionality of the visual system. By recording cortical responses to visual stimuli, VEP identifies dysfunctions in the visual pathways, including the retina, optic nerve, and occipital cortex. This study aimed to evaluate the diagnostic power of VEP in pediatric patients with diseases affecting the visual pathways

Methods: This retrospective study reviewed 552 VEP records, analyzing data from 292 patients aged 10–18 years. Clinical data, including age, gender, preliminary and final diagnoses, pattern VEP findings, brain and orbital MRI results, and serum 25OH vitamin D levels, were obtained from medical records. A total of 584 eyes were evaluated based on VEP test results. VEP abnormalities, such as P100 latency changes, were assessed, and the diagnostic performance of a 120 ms P100 latency cut-off for multiple sclerosis (MS) was analyzed using ROC curves.

Results: VEP abnormalities were identified in 106 patients, including 86 with bilateral abnormalities. All patients with abnormal VEP findings had pathologies affecting the visual pathways. VEP testing contributed to the diagnosis in 47% of eyes and 36% of patients. The most common presenting complaint was visual impairment (52%). ROC analysis confirmed the diagnostic performance of the 120 ms P100 latency cut-off for MS patients.

Conclusions: This study highlights the value of VEP in diagnosing optic neuritis, MS, and post-traumatic syndrome (PTS). VEP testing provided significant diagnostic support, particularly when combined with other diagnostic methods such as MRI. These findings emphasize the utility of VEP in evaluating pediatric patients with visual pathway diseases

ABSTRACTS

Topic: Epilepsy: Diagnosis and Investigations

EPNS25_119 - Epidemiology of Epilepsy and Associated Comorbidities in Saudi Pediatric Population: A Cross-Sectional Analysis

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Objectives

This research focuses on Saudi children, examining the prevalence of epilepsy, cognitive impairments, and psychiatric comorbidities. By addressing these issues, the study aims to contribute to effectively managing epilepsy in this population—furthermore, the research aims to develop interventions to enhance the cognitive and mental health of these children.

Methods

A cross-sectional survey was conducted among 1085 Saudi children aged 2 to 18 years, drawn from hospitals and clinics across various regions in Saudi Arabia. The survey employed a comprehensive questionnaire to collect demographic information and data related to epilepsy prevalence, cognitive impairments, and psychiatric comorbidities. This study specifically focused on identifying the factors contributing to cognitive impairments and psychiatric disorders in Saudi children with epilepsy.

Results

The estimated prevalence of epilepsy among the surveyed Saudi children was 22.6% (245 out of 1085). Cognitive impairments were identified in 12.9% of the children, with attention deficits (8.8%) and memory issues (4.6%) being the most affected cognitive domains. A notable finding is that 68.2% of children with epilepsy experienced cognitive impairments, in contrast to 31.8% without epilepsy. Psychiatric comorbidities were more prevalent, with attention deficit hyperactivity disorder (ADHD) affecting 6.5% and anxiety disorder affecting 4.1% of the children. Interestingly, 77.2% of children with epilepsy were diagnosed with psychiatric comorbidities, compared to 22.8% without epilepsy. These results underscore the higher likelihood of cognitive impairments and psychiatric comorbidities in children with epilepsy.

Conclusions

This study provides critical insights into the epidemiology of epilepsy and its associated cognitive impairments and psychiatric comorbidities in Saudi children. The findings highlight the substantial impact of epilepsy on cognitive function and psychiatric well-being in this population. The observed associations between epilepsy and both cognitive impairments and psychiatric comorbidities emphasize the need for a comprehensive approach to care. Addressing these complex interactions is essential for enhancing the quality of life for children with epilepsy. Ultimately, this research underscores the multifaceted challenges faced by Saudi children with epilepsy and suggests avenues for improved clinical management and supportive strategies.

ABSTRACTS

Topic: Neurogenetics

EPNS25_120 - Safety and Efficacy of Trofintide in Treating Patients with Rett Syndrome: A Systematic Review and Meta-Analysis of the RCTs

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Objectives

To assess the safety and effectiveness of trofinetide in randomized controlled trials (RCTs) involving patients with Rett syndrome.

Methods

A total of 224 articles were identified from multiple databases. After duplicates were removed, 92 articles remained for further evaluation, Randomized controlled trials (RCTs) assessing the efficacy and safety of trofinetide in Rett syndrome patients were included, with five studies meeting the eligibility criteria. Titles, abstracts, and full texts of the identified studies were reviewed independently by two reviewers, and relevant data were extracted. The quality of the included studies was assessed using the Cochrane Risk of Bias (RoB) 2.0 tool. A meta-analysis was performed using a fixed-effects model in cases of insignificant heterogeneity or a random-effects model when heterogeneity was present. Depending on the outcome, the mean difference or odds ratio was analyzed.

Results

Among the analyzed outcomes for 181 patients in the trofinetide group and 134 patients in the placebo group, a significant improvement in Rett Syndrome Behavior Questionnaire (RSBQ) scores was observed at a 200 mg dosage (overall mean difference: -3.53, $p = 0.001$). Clinical Global Impression-Improvement (CGI-I) scores also showed considerable improvement at the 200 mg dosage (overall mean difference: -0.34, $p < 0.0001$). No significant changes were observed in Motor Behavioral Assessment (MBA) scores or Top 3 Caregiver Concerns. Treatment-Emergent Adverse Events (TEAEs) were evaluated across various dosages, with significant associations identified for diarrhea (200 mg), vomiting (200 mg), and irritability (200 mg). No significant association was found between any dosage and the incidence of decreased appetite.

Conclusions

Trofinetide showed potential in improving RSBQ and CGI-I scores at a 200 mg dosage, though no significant changes were observed in MBA scores or the top three caregiver concerns. Adverse events were associated with specific dosages. More RCTs should be conducted.

ABSTRACTS

Topic: Fetal and Neonatal Neurology

EPNS25_122 - Neurological and motor development trajectories of children with neonatal hypoxic-ischaemic encephalopathy who did not develop cerebral palsy

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Objectives

Neonatal hypoxic-ischaemic encephalopathy (HIE) carries a risk of long-term neurodevelopmental impairment, even with hypothermia treatment (TH). This study aimed to investigate neurology and motor development trajectories from infancy to school age in those who survived without severe neuromotor impairment, i.e. Cerebral Palsy.

Methods

Sixty-eight children with neonatal HIE treated with TH who did not develop CP were assessed with a standardised neurological examination for movements, posture, muscle tone at ages 3, 12, 24 months, and at mean age 6,2 years (SD: 0.94) with the simplified Touwen neurological examination to identify minor neurological dysfunction (MND). Motor development was assessed with the Alberta Infant Motor Scale (AIMS) at 3, Ages and Stages Questionnaire-3 (ASQ) at 12, and Bayley-3 Scales at 24 months. At school age the Movement Assessment Battery for Children-2 (MABC-2) was used for assessment of motor skills. Correlations between early assessments and school age outcomes were examined with Spearman's correlation coefficient.

Results

At school age 73.5% had normal neurology, 20.6% had MND1, 5.9% had MND2. 14/68 children (20.6%) had a total M-ABC-2 score ≤15th percentile, indicating difficulties with motor skills at school age. Neurological findings at 12 and 24 months were strongly correlated ($r=0.807$, $p<0.001$). None of the early motor and neurological assessments showed significant correlation with school-age neurology. There was no significant correlation between early motor assessments and total MABC scores; however, early motor assessments including, AIMS at 3 months ($r=0.501$, $p=0.007$), ASQ gross motor at 12 months ($r=0.398$, $p=0.026$), and Bayley gross motor scores at 24 months ($r = 0.308$, $p = 0.031$), showed a moderate positive correlation with MABC-2 balance subtest scores. Hypoxic-ischaemic (HI) brain injury on neonatal MRI moderately correlated with neurology at school age ($r=0.30$, $p=0.019$), but not with early and school-age motor development/skills assessments.

Conclusions

In children with neonatal HIE who do not develop CP, early motor assessments provide moderate predictive value for motor (balance domain) outcomes at school age. However, early motor and neurological assessments have limited predictive value for MND at school age. The moderate correlation between signs of HI injury on neonatal MRI and school-age neurological outcomes, supports the necessity of combining imaging and neurological assessments to improve prediction of long-term outcome in this population.

ABSTRACTS

Topic: Neurometabolic Disorders

EPNS25_123 - A Rare Cause of Neurodegenerative Disorder with the Value of MRI Findings: Infantile Neuroaxonal Dystrophy

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Objectives: Infantile neuroaxonal dystrophy (INAD, NBIA2A; MIM: 256600) is a rare neurodegenerative disorder affecting 1 in 1,000,000 children. Symptoms typically manifest between 6 and 18 months, leading to motor and cognitive decline involving the central, peripheral, and autonomic systems.

Methods: This is a retrospective study of patients diagnosed with INAD in two tertiary university hospital centers in Türkiye from 2019 to 2024. Seven patients with a PLA2G6 gene mutation were included in the study. All demographic, clinical, and neurological examinations were documented. Biochemical analyses of plasma amino acids, acylcarnitine profiles, urinary organic acids, lactate, and lysosomal enzymes were conducted. Magnetic resonance imaging (MRI) of the brain was performed on all patients except one who was 6 months old at the time of their initial complaint upon admission to the hospital.

Results: Among these patients, the second and third patients and the fourth and fifth patients were siblings. 28% were girls and 71% were boys. The median age of the patients was 4 years (min: 6 months, max: 11 years), with the initial presentation occurring at a median of 18 months (min: 6 months, max: 4 years). A notable 85% of the cases involved consanguineous marriages. All patients were born at term without complications and exhibited neurodegeneration around 1 year old. Each patient experienced developmental delays in sitting and walking milestones. Initial symptoms included an unsteady gait and inability to sit unaided. None of the patients can speak. Normal deep tendon reflexes (DTR) were present in 28% of patients; 14% had brisk reflexes, while 57% showed absent DTR. Spasticity was seen in 42%, whereas 58% displayed hypotonicity. Furthermore, 71% were bedridden, and 14% were deceased. Routine biochemical and metabolic screenings were normal for all children. Regarding visual evoked potential (VEP) tests, 42% were normal, and 57% exhibited sensorimotor polyneuropathy in electromyography (EMG). The brain MRI showed only cerebellar atrophy, except for the 6-month-old patient. At least one pathogenic variant in the PLA2G6 gene was detected in all patients by whole exome sequencing methods (WES). The patients were followed up with the physical therapy and rehabilitation clinic.

Conclusions: We want to emphasize that in children experiencing neuromotor degeneration or decline, particularly in the motor area at one year of age, normal metabolic and other laboratory test results, along with cerebellar atrophy without significant cortical involvement, indicate INAD, which is an extremely rare neurometabolic disorder.

Table 1: Demographic findings of the patients

patients	current years of age	gender	consanguinity	gestational age	age of initial presentation	neurodegeneration
1. case	11years	girl	no	38gh	4years	yes
2. case	7,5years	boy	yes	38gh	18 m	yes
3. case	4years	boy	yes	38gh	12 m	yes
4. case	2years	boy	yes	39gh	6m	yes
5. case	6month	boy	yes	40gh	6m	yes
6. case	22month	boy	yes	38gh	18m	yes
7. case	7years	girl	yes	36gh	36m	yes

ABSTRACTS

Table 2: Clinical features of the patients

Patients	The months of neck-holding/sitting/walking	Initial finding	DTR	Tonus	Ataxia	Prognosis
1. case	3m/7m/18m	unsteady gait	brisk	spasticity	yes	bedridden
2. case	6m/12m/no	cannot sit without support	normal	spasticity		bedridden
3. case	6m/12m/no	cannot sit without support	normal	spasticity	no	bedridden
4. case	4m/6m/no	deterioration of unsupported sitting	no	hypotonicity	no	exitus
5. case	4m/no/no	cannot sit without support	normal	hypotonicity	no	alive
6. case	6m/12m/no	cannot walk without support	normal	hypotonicity	no	bedridden
7. case	3m/7m/18m	cannot walk without support	no	hypotonicity	no	bedridden

Table 3: Laboratory and neuroimaging findings

Patients	Lab results (routine biochemistry, metabolic screening, hemogram)	vep	emg	Brain MRI	Genetic study (Pla2g6)
1. case	normal	-	-	cerebellar atrophy	c.1630A>G(p.544V) c.1748T>C(p.M583T) compound heterozygote, pathogen
2. case	normal	-	sensorimotor polyneuropathy	cerebellar atrophy	c.1772G>A(p.R591Q) homozygote mutation
3. case	normal	-	sensorimotor polyneuropathy	cerebellar atrophy	c.1772G>A(p.R591Q) homozygot mutation
4. case	normal	normal	sensorimotor polyneuropathy	cerebellar atrophy	c.1957>A (p.Gly653Ser)
5. case	normal			no	c.1957>A (p.Gly653Ser)
6. case	normal	normal	sensorimotor polyneuropathy	cerebellar atrophy	exome 3-4 homozygote deletion
7. case	normal	normal	normal	cerebellar atrophy	c.1610G>A(p.R537Q) homozygot mutation

ABSTRACTS

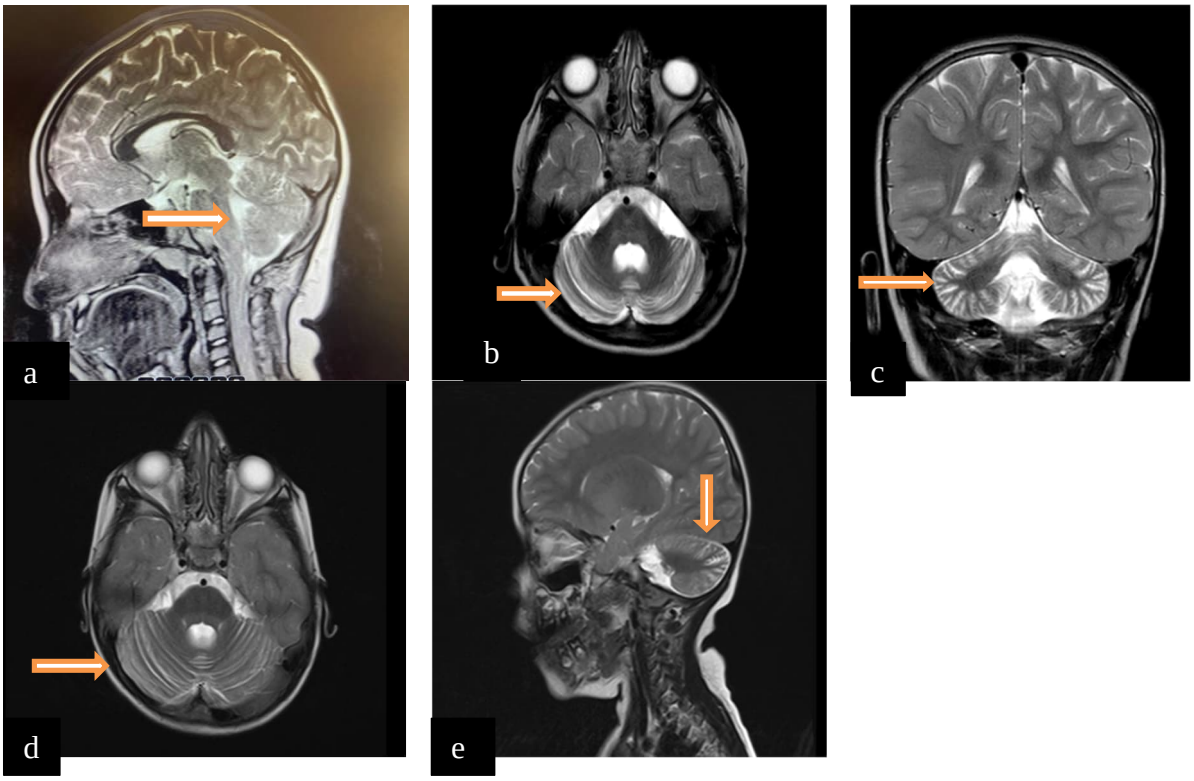
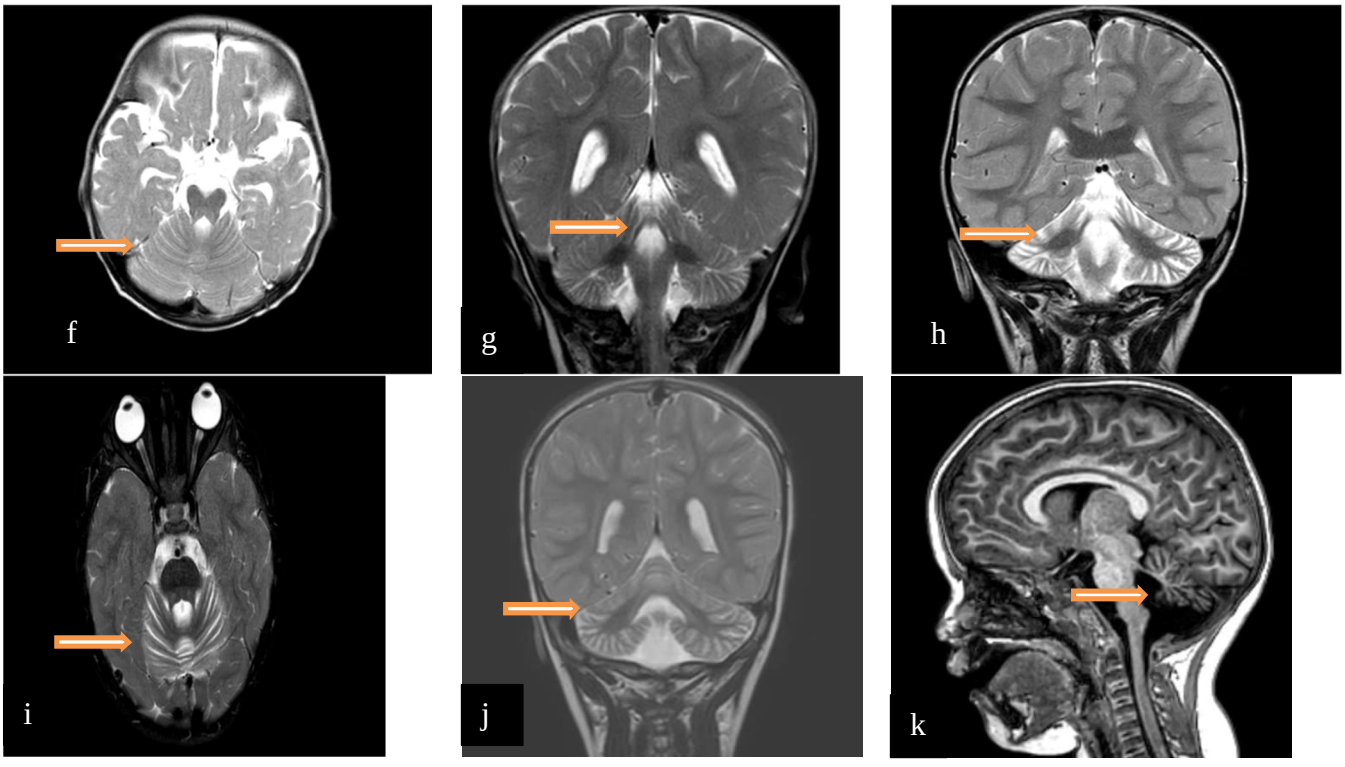


Figure 1: Brain MRI of the patients. (a) is the T2 sagittal section of patient 1, which shows cerebellar atrophy. (b) and (c) show the coronal and axial sections of patient 2, respectively, demonstrating severe cerebellar atrophy. (d) and (e) show the sagittal and coronal sections of patient 3, which show mild cerebellar atrophy.



ABSTRACTS

Figure 2: (f) and (g) are the coronal and axial sections of patient 4, showing mild cerebral and cerebellar atrophy. (h) and (i) show severe cerebellar atrophy in patient 6. (j) and (k) are sagittal and coronal sections of patient 7, demonstrating cerebellar atrophy.

ABSTRACTS

Topic: Miscellaneous

EPNS25_124 - Exploring the Correlation Between Electroencephalography and Electrocardiography in Children with Dizziness

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Objectives

Dizziness in children manifests as light-headedness or a sensation of faintness and can be associated with various underlying conditions, such as vertigo, headache, or cardiovascular dysfunction. This study aimed to investigate the correlation between electroencephalography (EEG) and electrocardiography (EKG) findings in pediatric patients presenting with dizziness.

Methods

We retrospectively reviewed medical records of patients under 18 years old who visited the pediatric neurology outpatient clinic at Taipei City Hospital, Zhongxiao Branch, for dizziness between January 2016 and December 2024. EEG and EKG examination reports were analyzed to identify correlations between their findings.

Results

A total of 171 medical charts were initially reviewed, and 93 patients (44 males, 44.1%; 52 females, 55.9%) with complete EEG and EKG studies were included in the analysis. Based on EEG results, patients were categorized into a normal EEG group (n=68) and an abnormal EEG group (n=25), the latter characterized by focal (n=23, 92%) or generalized (n=3, 12%) epileptiform discharges. No significant differences were found between the two groups in terms of age, gender, or the incidence of syncope and headache. However, vertigo was significantly more frequent in the abnormal EEG group. Children with abnormal EEG findings were also significantly more likely to have abnormal EKG results compared to those with normal EEG findings (88.0% vs. 19.1%; $p<0.0001$), with a relative risk (RR) of 2.553 (95% CI: 1.754–4.106) and an odds ratio (OR) of 31.03 (95% CI: 8.683–104.5). The most common EKG abnormalities in the abnormal EEG group were arrhythmias, including tachycardia, bradycardia, and ectopic atrial rhythm. Other EKG parameters, such as PR interval and QTc interval, showed no significant differences.

Conclusions

This retrospective study highlights a significant correlation between EEG and EKG findings in children presenting with dizziness, with abnormal EEG findings strongly associated with a higher likelihood of EKG abnormalities. These results may support the brain-heart axis hypothesis and emphasize the importance of conducting both EEG and EKG evaluations in pediatric patients with dizziness.

ABSTRACTS

Topic: Neurorehabiltation

EPNS25_125 - Abobotulinumtoxin A injections for the chronic sialorrhea in children: a retrospective multicenter study

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Objectives to analyze the multicenter experience of the off-label use of AbobotulinumtoxinA (AboA) injections for the correction of chronic sialorrhea in children.
Methods 608 injections (from 1 to 5 repeated injections) of the AboA into the salivary glands for 226 patients aged 2.0 to 17.8 years (Me — 5.1 years) with different neurological diseases and neurodevelopmental disorders in 12 medical and rehabilitation centers were retrospectively analyzed. A history of aspiration pneumonia, including repeated cases, was noted in 79 (35%) children; 12 (5.3%) patients had a tracheostomy, 10 (4.4%) - gastrostomy, 10 (4.4%) - both a tracheostomy and a gastrostomy. The patients' representatives have provided informed consent for off-label AboA injections. The study was approved by the local ethical committee.
Results AboA was the first botulinum toxin A (BTA) used to correct drooling in 180 patients (79.6%); 46 (20.4%) patients had previous experience with other BTA for sialorrhea. 177 (78.3%) children received combined injections into the salivary glands and body muscles to correct spasticity. The total doses of AboA (in units (U) and units per kg (U/kg)) administered into the salivary glands during the first injection were (Med; min-max; 25-75%): 150 U (7.7 U/kg); 30-400 U (1.9-27.3); 100-200 U (4.8-15.3). Doses to both parotid glands — 80 U (4.1 U/kg); 18-250 U (0.8-15.4 U/kg); 60-120 U (2.7-8.5 U/kg); in both submandibular — 70 U (3.3 U/kg); 12-160 U (0.5-13.6 U/kg); 40-80 U (2.1-6.1 U/kg). After the first injection of AboA, a significant decrease in salivation was observed in 212 cases (93.8%). The effect lasted for an average of 4.9 months (0.5 to 24 months). Changes in the Drooling Impact Scale and subjective duration of effect were not significantly different after repeated injections. Adverse events were noted in 30 (13.3%) cases and persisted up to 2-3 weeks after injection.
Conclusions off-label AboA injections for the chronic sialorrhea in children have shown effectiveness and safety in real multicenter practice, also in combination with concomitant spasticity treatment. The identified dosages can be used as a possible reference for AboA salivary gland injections until the formal clinical studies.

ABSTRACTS

Topic: Neurodevelopmental Disorders / Developmental Neuroscience

EPNS25_127 - Early Onset and Increasing Disparities in Neurodevelopmental Delays From Birth to Age 6 in Children from Low Socioeconomic Backgrounds

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Objectives

To analyze the complex relationship between socioeconomic status (SES) and neurodevelopmental achievements by investigating the temporal dynamics of these associations from birth to age 6

Methods

This retrospective cohort study was conducted over 6 years using population-based data from the National Health Insurance Service and integrated data from the National Health Screening Program for Infants and Children. Participants were children born between 2009 and 2011 in Korea without neurodevelopmental delays with potential developmental implications. We analyzed results from the Korean Developmental Screening Test, administered at age 6, which covered overall assessment and six domains of gross and fine motor function, cognition, language, sociality, and self-care. The secondary outcome was to determine when neurodevelopmental outcomes began after birth and how these differences changed over time.

Results

Of 276,167 individuals (49.2% males), 66,325, 138,980, and 60,862 had low, intermediate, and high SES, respectively. Neurodevelopmental delays observed across all developmental domains were more prevalent in the low-SES group than in the high-SES group. Disparities in neurodevelopment according to these statuses were apparent as early as age 2 and tended to increase over time (interaction, $P<0.001$). The cognition and language domains exhibited the most substantial disparities between SES levels. These disparities persisted in subgroup analyses of sex, birthweight, head circumference, birth data, and breastfeeding variables.

Conclusions

Low SES was significantly associated with an increased risk of adverse neurodevelopmental outcomes in preschool children, particularly those affecting cognitive and language domains. These differences manifested in early childhood and widened over time.

ABSTRACTS

Topic: Traumatic Brain Injury

EPNS25_129 - EEG Monitoring in TBI Rehabilitation: Decoding the Journey

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Objectives:
Traumatic brain injury (TBI) often leads to post-traumatic epilepsy (PTE). Prolonged EEG monitoring during the acute stage has revealed subclinical seizures, spikes, and paroxysmal events that do not manifest as overt seizures. This study aims to systematically characterize key EEG features (e.g., slowing, spikes, increased sigma activity) in pediatric TBI patients at different stages of rehabilitation.

Methods:
At ALYN Pediatric Rehabilitation Hospital, retrospective EEG data were collected over five years from 35 children (ages 1–20 years) with acquired brain injuries (ABI) hospitalized for rehabilitation, followed by outpatient follow-up. The cohort includes ABI cases due to falls, road accidents, trauma, intracerebral haemorrhage from vascular malformations, or neurosurgical tumour resection complications. The first EEG was conducted within the first month post-injury, with repeated monitoring every 3–4 months over 1–2 years. EEG recordings were analysed by a pediatric neurologist and an external pediatric epileptologist.

Results:
Preliminary data from 11 patients (9 males, 2 females; mean age 9.9 ± 3.9 years) are presented. Most (n=8) underwent 3–4 EEG exams, while 3 had more than 5. Six patients experienced late seizures (>7 days post-admission): two had focal seizures, and four had generalized seizures. Pathological EEG features observed during rehabilitation included intermittent slowing (6/11), continuous slowing (5/11), epileptiform discharges (9/11), absence of sleep spindles (7/11), and increased sigma activity (3/11). Clinical outcomes revealed: 10/11 patients required anti-seizure medications; 8 received Amantadine therapy; 7 were treated with psychiatric medications (e.g., SSRIs, Risperdal); 5 received stimulants.

Conclusions:
Comprehensive data on epileptic phenomena in pediatric TBI patients, particularly subclinical events, are limited. Preliminary findings show that while most patients regain basic functional abilities, EEG follow-ups frequently detect epileptic features, often accompanied by late clinical seizures, cognitive challenges, and psychiatric comorbidities. Further analysis will focus on the time course of these features throughout rehabilitation.

ABSTRACTS

Topic: Neurometabolic Disorders

EPNS25_132 - Cerebral creatin deficiency syndromes ,case series from Iran

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Objectives

Creatine and phosphocreatine--its phosphorylated form--play an essential role in maintaining and transmission of energy in most tissues, especially in high-energy demanding tissues such as brain and skeletal muscles (1). This energy is produced by exchanging high-energy phosphate bond with adenosine triphosphate (ATP) that is catalyzed by creatine kinases (CK) (2). Creatine can be absorbed from food mostly from meat and dairy products by intestinal absorption or it can be synthesized in body, mostly by liver, pancreas and kidneys. Two enzymes are involved in creatine synthesis.

We must note that some causes of autism as CCDS may be treatable and early diagnosis and early treatment can improved their outcome.

Methods

We reported 5 cases of cerebral creatine deficiency syndromes (GAMT type) with their clinical symptoms ,EEG pattern, Brain MRI and MRS and biochemical profile.

Results

In all of our cases, patients had similar findings in electroencephalography (EEG). Therefore, EEG can be considered as a good suggesting tests for this disease in autistic patients.

Conclusions

The clinician must think about treatable causes of Autism spectrum disorders and if there is positive familial history, Consanguinity between parents, refractory seizures and abnormal movements combination with ASDs and specific EEG pattern, performing urinary and serum creatine panel is needed.

ABSTRACTS

Topic: Movement Disorders/ Cerebral Palsy

EPNS25_133 - Extrapyramidal Disorders in Childhood-Onset Hereditary Spastic Paraplegia: A Cross-Sectional Study of over 400 Cases

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Objectives

Extrapyramidal movement disorders have been reported in certain forms of hereditary spastic paraplegia (HSP); however, their prevalence, characteristics and natural history remain insufficiently defined. We aim to: 1) Define the spectrum of movement disorders in a well-characterized cohort of children and young adults with genetically-confirmed HSP, and 2) Identify gene variants associated with these symptoms.

Methods

In this cross-sectional study, we evaluated 428 patients with molecularly confirmed childhood-onset HSP. We systematically reviewed clinical, imaging, and molecular data, and analyzed longitudinal video recordings. Statistical analyses focused on the prevalence and types of extrapyramidal movements, as well as genotype-phenotype correlations.

Results

Among 41 unique HSP-associated genes identified, the most frequently observed variants were in AP4B1 (SPG47), AP4M1 (SPG50), SPAST (SPG4), AP4S1 (SPG52) and ZFYVE26 (SPG15). Overall, 95 patients (22.6%) exhibited at least one extrapyramidal movement disorder, with 48 (11.1%) having two or more types. Dystonia (16.4%) and ataxia (10%) were most prevalent, while brady/hypokinesia (7.9%) and postural instability (7%) were less common. Ataxia was predominantly observed in ZFYVE26-related HSP (SPG15), whereas dystonia was more common in children with HSP-SPAST (SPG4) due to de novo variants.

Conclusions

Our findings highlight that childhood-onset HSP often includes extrapyramidal movement disorders in addition to spasticity, expanding the known clinical spectrum. Recognizing these coexisting movement disorders and their underlying genetic causes is crucial for precise diagnosis, informed counseling, and targeted treatment strategies. These observations also underscore the need for robust natural history studies in rare disease cohorts – studies that help capture the full breadth of the phenotypic spectrum and guide the development of more effective clinical trial designs for emerging therapies. Finally, our comprehensive video archive serves as a key resource for advancing research, promoting education, and fostering innovative therapeutic approaches in the future.

ABSTRACTS

Topic: Epilepsy: Diagnosis and Investigations

EPNS25_134 - Childhood Occipital Epilepsy: Long-Term Experience of a Tertiary Center

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Objectives: Childhood occipital epilepsy (COE) can primarily be classified into idiopathic occipital lobe epilepsy (IOLE) and symptomatic occipital lobe epilepsy (SOLE). This study aims to retrospectively evaluate the demographic and clinical characteristics of a large pediatric patient group diagnosed with COE, presenting experiences regarding follow-up characteristics, patient management, and prognosis.

Methods: Medical records of 203 children diagnosed with COE were evaluated. Data were analyzed in terms of demographic features, family history, seizure types and semiology, ictal symptoms, electroencephalography and magnetic resonance imaging findings, treatment responses, and prognostic features.

Results: Among the 203 patients (60% male, mean age 109.6 months) followed for an average of 2 years with COE diagnosis, 7.3% had a history of hypoglycemia, with a median age of seizure onset at 5 years and a median age of last seizure at 7 years. Of the patients, 11.8% had SOLE, while 19.3% were diagnosed with self-limited epilepsy with autonomic seizures (SeLEAS). Focal seizures with retained awareness were observed in 26.6%, generalized tonic-clonic seizures in 21.2%, visual symptoms in 21.6%, ictal-postictal headaches in 11.3%, and ictal vomiting in 27% of the patients. Status epilepticus was reported in 2.9% of cases. Antiseizure medication (ASM) was discontinued in 17.2% of patients after an average use of 46.3 months, with a seizure recurrence rate of 9.1% in this group. Medication adherence was high at 97.6%. No statistically significant relationship was found between the number of seizures and the presence of visual symptoms, ictal vomiting, ictal headaches, or status epilepticus. However, patients with a higher number of seizures before initiating ASM were found to have a greater risk of seizures during follow-up.

Conclusions: This study highlights that early seizure frequency impacts prognosis in COE, medication adherence is high, and patients should be carefully monitored for seizure recurrence after ASM discontinuation.

ABSTRACTS

Topic: Basic Science

EPNS25_138 - The role of kynurenic acid and kynurenine pathway in the efficacy of ketogenic diet in epilepsy and neurodegeneration

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Objectives

To show the evidence of the involvement of kynurenne pathway and the role of kynurenic acid, a putative endogenous neuroprotectant and antiepileptic agent in the antiseizure and neuroprotective effect of ketogenic diet. This is to present a state of the art and an outline of the concept based on authors' own publications.

Methods

Following varied methods were employed: high performance liquid chromatography, NMDA-induced neuronal degeneration, analysis of in vitro production of kynurenines in bovine slices, pathomorphological evaluation, scrutiny and clinical evaluation.

Results

Experimental chronic exposure to ketogenic diet increased kynurenic acid concentration in the discrete rat brain structures. In vitro, decreased production of kynurenic acid in bovine retinal slices was attenuated by chief ketone bodies, acetoacetate and beta-hydroxybutyrate. Ketogenic diet and independently ketone bodies each had a neuroprotective effect on retinal ganglion cells in a rat model of NMDA-induced neuronal damage. We report a pattern of changes in the blood level of kynurenines in patients with refractory epilepsy who started the KD. Higher concentrations of kynurenic acid and lower concentrations of kynurenine were found in patients who attained a higher reduction in seizure frequencies on the KD.

Conclusions

Data presented here though very promising awaits further experimental and clinical verification and it needs to be elucidated how alterations of kynurenine pathway translate into a clinically significant improvement of epilepsy and other neurodegenerative diseases.

ABSTRACTS

Topic: Epilepsy: Diagnosis and Investigations

EPNS25_139 - A personalized approach to the diagnosis of epilepsy in children with obesity

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Objectives

To identify key metabolic changes in childhood epilepsy associated with obesity in order to develop a personalized approach to diagnosing this pathological condition.

Methods

The study included 22 patients aged 1 to 16 years (mean age 11.7 years): 16 patients with various epileptic syndromes associated with obesity and 6 patients in the comparison group. The profile of 60 organic acids in urine was studied using High-Performance Liquid Chromatography-Mass Spectrometry. To compare the mean value and differences in a number of indicators of the level of organic acids in urine in the group of patients with epilepsy against the background of obesity and in the comparison group, the Student's t-test for unrelated populations with a significance limit of P=0.05 and the Mann-Whitney criterion with the same significance limit were calculated. Statistical calculations were performed in the Statistica 10.0 program.

Results

In the group of patients with epilepsy against the background of obesity, an excess of the upper reference limit of a number of markers of the Krebs cycle (fumaric and 2-ketoglutaric acids), bacterial dysbiosis and lactic acid levels were detected. Also in the sample of patients, in contrast to the comparison group, an increase in the levels of a number of markers of mitochondrial dysfunction (adipic, ethylmalonic and methylsuccinic acids) was found.

Conclusions

Thus, we identified a number of metabolic markers associated with obesity-associated epilepsy in children. The results of the study confirm the importance of a personalized approach to the diagnosis and treatment of this pathological condition.

ABSTRACTS

Topic: Neuromuscular Disorders

EPNS25_141 - Integrated approch: pharmacological, standards of care and kinetotherapeutic interventions, including advanced assistance in patients with spinal muscular atrophy type i

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Objectives: Spinal muscular atrophy (SMA) is a nervous system degenerative disorder with autosomal recessive genetic transmission, affecting motor neurons in the anterior medullary horn, often those in the brainstem and leading to their death with loss of muscle mass and motor deficiency. SMA type I is the most severe form of the disease. There are currently three therapies approved by the Food and Drug Administration and the European Medicine Agency: Onasemnogene Abeparvovec, Nusinersen and Risdiplam. Besides these treatments, it is critical to follow correct and comprehensive standards of care and kinetotherapeutic interventions, including advanced assistance. Wishing treatment efficiency for SMA patients type I, aware of the need to apply the standards of care in this disease, we have designed this paper in order to share the expertise of NCHCN and to guide all our colleagues who care for this pathology.

Methods: The paper aims to reproduce images with patients, methods of diagnosis and innovative treatments used in our hospital. Current options are effective in improving mobility, good ventilation and improvements in ventilation free survival in the patient who have started early treatment.

Results: We have observed disease trajectories that differ significantly from the known natural history of the disease. These new phenotypes now also cross the traditional subtypes of SMA.It is now more appropriate to rely on a combination of age of onset, number of SMN2 copies, and age at start of drug treatment rather than the traditional subtypes to define a clinical phenotype of SMA.

Conclusions: An early treatment leads to a better result and we need to improve our diagnostic ability and reduce all the procedures in order to ensure a fast treatment. We need to guarantee the best standards of care to get the best results and to describe new phenotypes in SMA patients. We need consensus on SMA-type classification and endpoints that determine intervention efficacy of any treatment. Standard newborn screening seems to be an appropriate tool to achieve maximum treatment effects, a timely diagnosis and treatment initiation.

ABSTRACTS

Topic: Neuropsychiatric Disorders / Functional Neurological Disorders

EPNS25_143 - The Role of Genetic Variants of Folate Cycle Genes in the Etiopathogenesis of Autism Spectrum Disorder (ASD) in Children

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Objectives

Changes in the folate cycle may be a factor in hereditary predisposition to ASD. Some key genetic factors associated with the folate cycle include the C677T and A1298C variants in the methylenetetrahydrofolate reductase (MTHFR) gene and the A66G variant in the methionine synthase reductase (MTRR) gene. We studied the association of three genetic variants with ASD.

Methods

Changes in the folate cycle may be a factor in hereditary predisposition to ASD. Some key genetic factors associated with the folate cycle include the C677T and A1298C variants in the methylenetetrahydrofolate reductase (MTHFR) gene and the A66G variant in the methionine synthase reductase (MTRR) gene. We studied the association of three genetic variants with ASD.

Results

When analyzing the frequency of the rare TT genotype of the MTHFR C677T variant between the ASD group with hyperhomocysteinemia (average value 20.1±3 μmol/L) and the control group, the OR value was 3.2 (CI: 2.0–4.2) ($P < 0.0001$).

When analyzing the frequency of the risk CC genotype of the MTHFR A1298C variant between the ASD group and the control group, the OR value was 2.7 (CI: 1.9–3.6) ($P < 0.0001$).

When analyzing the combined risk genetic profile of the TT MTHFR C677T and CC MTHFR A1298C variants, a higher OR value of 6.6 (CI: 5.4–11.0) ($P < 0.0001$) was obtained.

When analyzing the combined risk genetic profile of the TT MTHFR C677T and GG MTRR A66G variants, an even higher OR value of 7.6 (CI: 4.4–13.1) ($P < 0.0001$) was obtained.

Conclusions

Our study revealed an association between ASD and the genetic variants of MTHFR and MTRR.

ABSTRACTS

Topic: Epilepsy: Medical and Surgical treatment

EPNS25_145 - The Ketogenic Diet in the Treatment of Pharmacoresistant Epilepsy in Children in Russia

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Objectives

To analyze the effectiveness of the ketogenic diet (KD) in children with pharmacoresistant epilepsy (PRE) and to evaluate changes in psychomotor functions during diet therapy.

Methods

To analyze the effectiveness of the ketogenic diet (KD) in children with pharmacoresistant epilepsy (PRE) and to evaluate changes in psychomotor functions during diet therapy.

Results

The overall effectiveness of KD was observed in 269 patients (54%): 100% seizure control: 105 patients (21%), 75% seizure reduction: 95 patients (19%), 50% seizure reduction: 69 patients (14%), <50% seizure reduction: 70 patients (14%), The highest effectiveness of KD was noted in the 0–6 years age group, accounting for 76% of all positive outcomes. Improvement in motor and cognitive functions was reported in 92% of patients, regardless of seizure reduction effectiveness. Lack of KD effectiveness was observed in 146 children (29%). Diet therapy was discontinued in 15 children (3%) due to side effects.
Among the 30 patients with GLUT1 syndrome: 100% seizure control on KD: 23 patients (78%), KD + antiepileptic drugs (AEDs) with 100% control: 1 patient (3%), 75% seizure reduction: 3 patients (10%), <50% seizure reduction: 1 patient (3%), Not on KD: 1 patient (3%), No effect: 1 patient (3%)

Conclusions

The ketogenic diet has shown high efficacy in all forms of PRE, with the greatest effectiveness observed in genetic forms of epilepsy. For GLUT1 syndrome, a 100% seizure-free effect was achieved in 78% of patients. The highest success rate was seen in children aged 0–6 years (76% of all positive outcomes).

Motor and cognitive function improvements were observed in 92% of patients, which, along with seizure reduction, significantly enhanced their quality of life. KD is an effective and cost-efficient treatment method that improves the quality of life for patients with PRE.

ABSTRACTS

Topic: Neuromuscular Disorders

EPNS25_146 - SMA Care UK: A national initiative to ensure that those living with SMA in the UK receive the best possible care

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Objectives: The 2018 international recommendations for care in spinal muscular atrophy (SMA) were published prior to the introduction of disease modifying treatments. These drugs have revolutionised SMA disease progression and prognosis. The original recommendations were based on the minimal care and support that anyone with SMA should receive, irrespective of country of residence. They were focused largely on the paediatric population and made no reference to management of the novel and evolving disease phenotypes that have emerged as a result of treatment.

SMA CARE UK is a collaborative initiative between patients, health care professionals and other stakeholders that aims to update, harmonise and support the implementation of evidence-based standards of care for all those living with SMA across the UK, focusing on those aspects of care delivery that are of particular concern for those living with SMA.

Methods: The current recommendations are being reviewed and areas that require revision identified, on the basis of new evidence, changing practice and unmet need. The aim is to produce relevant and, where possible, evidence-based recommendations for specific areas of care; Where there are 'gaps' in knowledge, these will be highlighted and potential strategies to gather relevant evidence will be explored.

The project is hosted by SMA UK and rolled out over 3 years with the support of the University of Newcastle and the SMA Reach clinical networks. A steering group has been convened and has identified the priority areas of care to be addressed. Expert 'working groups' of patient representatives, neuromuscular and other clinical experts have been formed to address specific care topics. Final recommendations will be published after consultation with wider clinical and patient networks in the form of both professional and 'patient- friendly' guidance. Endorsement for the guidance will be sought from relevant professional bodies and recommendations will be presented at academic and patient conferences.

Results: N/A

Conclusions: It is hoped that the development of a 'minimum' UK standard of care will support professionals and families in addressing any inequalities in care across different services/regions of the UK. Highlighting aspects of care where knowledge base is limited should foster more open dialogue with carers seeking the 'best' management for their loved ones. Collaboration with global networks will support further data gathering and effective research in this rare disease and ensure that guidance produced is consistent with international standards.

ABSTRACTS

Topic: Neurometabolic Disorders

EPNS25_147 - Rapid-Onset Obesity with Hypothalamic Dysfunction, Hypoventilation, and Autonomic Dysregulation (ROHHAD Syndrome): Diagnostic Criteria and Effective Treatment Scenarios

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Objectives

To improve treatment outcomes for respiratory failure in patients with ROHHAD syndrome.

Methods

The study included data on 8 pediatric patients with ROHHAD syndrome treated between 2019 and 2024. Four patients had neurogenic tumors. Two patients presented with paraneoplastic syndrome and were treated with immunoglobulins and rituximab; one of them showed no response to treatment. Five patients underwent surgery with diaphragmatic stimulators (DS) implantation.

Results

Following implantation, one patient requires DS activation only during sleep, two patients are on continuous DS support, and one patient uses DS during wakefulness and requires continuous invasive or non-invasive mechanical ventilation during sleep. One patient could not transition to DS due to severe obesity. In one case, implantation was deemed infeasible due to extensive pulmonary fibrosis. One patient does not require respiratory support.

Conclusions

ROHHAD syndrome is an extremely rare, life-threatening condition characterized by respiratory failure, predominantly resembling central hypoventilation syndrome. Early recognition of the disease by pediatricians, neurologists, endocrinologists, dietitians, and oncologists is crucial for timely diagnosis and appropriate treatment. In the absence of effective etiopathogenetic therapy, early respiratory function prosthetics and syndrome-targeted therapy stabilize patient conditions. Diaphragmatic nerve stimulator implantation reduces the need for mechanical ventilation and improves quality of life.

ABSTRACTS

Topic: Epilepsy: Diagnosis and Investigations

EPNS25_150 - Current Classifications of Epileptic Seizures, Epilepsy and Epilepsy Syndromes and Their Application in Practice

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Objectives: International League Against Epilepsy (ILAE) published a new classification of epilepsy and epileptic seizures in 2017 and a new classification of epilepsy syndromes in 2022. These classifications enable the use of unified terminology, which is essential for establishing an accurate diagnosis, management, treatment and prognosis. Overall, this leads to an improved quality of life for patients and their caregivers.

Methods: The aim of this study was to determine the occurrence of epileptic seizures, types of epilepsy, and epilepsy syndromes according to the new ILAE classifications from 2017 a 2022. We retrospectively reviewed medical records from hospital database of patients aged 0-19 years hospitalized at the Department of Paediatric Neurology, Faculty of Medicine of Comenius University and National Institute of Children´s Diseases between January 1, 2020 and June 30, 2022.

Results: We identified 443 patients, including 200 females and 243 males. The etiology of seizures or epilepsy was established in 26.64% of patients, with structural etiology being the most frequent (51.69%). The patients were divided into three groups according to the type of seizure, type of epilepsy, or type of epilepsy syndrome. The type of seizure was established in 17.83% of cases, the type of epilepsy in 47.40%, and type of epilepsy syndrome in 36.76% of patients. Focal seizures and epilepsy were the most common (50.63% and 53.33%). The most frequent epilepsy syndromes were syndrome of infantile epileptic spasms (20.13%), self-limited epilepsy with centrotemporal spikes (13%), and developmental and epileptic encephalopathy with spike-wave activation in sleep (11%).

Conclusion: The new ILAE classifications are applicable in clinical practice. The results of our study align in many aspects with those of other similar studies investigating the prevalence of epilepsy.

ABSTRACTS

Topic: Neurometabolic Disorders

EPNS25_151 - Pyridoxine-dependent epilepsy, Pyridox(am)ine 5'-phosphate oxidase deficiency, and Biotinidase deficiency: Experience from a Middle Eastern tertiary center

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Objectives

This study aims to investigate the demographics, clinical presentation and diagnostic patterns, of pyridoxine-dependent epilepsy (PDE), pyridox(am)ine 5'-phosphate oxidase deficiency (PNPOD) and biotinidase deficiency (BD) among patients at a tertiary children's hospital in the Middle East.

Methods

A retrospective study examined electronic health records (EHRs) of patients aged 0-18 years with PDE, PNPOD, or BD at a tertiary center. Data was collected from September 2016 to September 2023 after ethical approval. SPSS v26 was used for data analysis, including chi-square tests for associations.

Results

A total of 29 EHRs were examined. 21 patients were diagnosed with BD, 7 with PDE, and 1 patient had PNPOD. The majority of the patients (86.2%) were from Arab ethnicity. Rate of consanguinity was 20.1%. Neuroimaging was abnormal in 17.2%, with 1 in BD group, and 4 in PDE group. The most useful test that yielded positive results was genetic testing (86.2%). 34.5 % of patients were diagnosed with BD via the national newborn screening program and biotin treatment was initiated promptly.

Seizures were experienced by all in the PDE and PNPOD groups but by only one patient in the BD group. Skin rash and alopecia were seen in 14.2% in the BD group. At their initial presentation, 44.8% of all patients exhibited neurodevelopmental delays. 34.5% of patients continued to experience neurodevelopmental sequelae despite intervention. Among patients with seizures, 31.6% also presented with other symptoms.

The mean age at seizure onset was 27.33 days (SD = 47.25), with 5 patients presenting in the neonatal period, 3 in the infantile period, and 1 in early childhood. Patients were diagnosed at a mean age of 74.5 months (SD = 64.3 months), ranging from 8 months to 14 years.

Conclusions

Early and prompt initiation of specific vitamin treatments is crucial in improving outcomes. Given their heterogeneity and varied presentations, the diagnosis of these conditions requires maintaining a high suspicion index. Genetic testing appears to be the most useful tool.

ABSTRACTS

Topic: Miscellaneous

EPNS25_152 - Neuroimaging findings in patients with central precocious puberty at initial diagnosis

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Objectives

The overall incidence of central precocious puberty (CPP) has increased in recent decades, and cranial magnetic resonance imaging (MRI) is recommended to identify intracranial lesions in patients with CPP. This study aimed to investigate the prevalence of MRI abnormalities and to evaluate the need for routine brain MRI in patients with newly diagnosed CPP.

Methods

This retrospective study obtained data of patients newly diagnosed with CPP who underwent routine brain MRI from January 2022 to February 2023. A total of 85 girls and 11 boys was enrolled in this study. Positive MRI findings were categorized as abnormal pituitary, nonpituitary incidental, and pathological. In addition, we investigated the incidence of MRI abnormalities and evaluated their associations with clinical and biochemical parameters.

Results

Positive brain MRI findings were observed in 21 patients (21.4%). Pituitary abnormalities were found in 13 patients (13.5%), with Rathke cleft cysts being the most common (11.5%). Incidental nonpituitary findings such as pineal gland cyst and arachnoid cyst were observed in 6 patients (6.3%). Pathological brain findings were observed in 2 patients (2.1%), one male patient of germinoma, and one female patient of hypothalamic hamartoma.

Conclusions

True pathological findings were rare, even though the prevalence of abnormalities on pituitary MRI in patients with CPP was relatively high. Considering its cost-effectiveness, MRI screenings should be carefully considered in patients with CPP.

ABSTRACTS

Topic: Neurodevelopmental Disorders / Developmental Neuroscience

EPNS25_153 - Qualitative Research to Define the Symptoms and Impact of GRIN-related Neurodevelopmental Disorder

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Objectives

GRIN-related neurodevelopmental disorder is associated with developmental delays, behavioral symptoms, and drug-resistant seizures, among other symptoms. The natural history and burden of this rare disease are poorly understood. This qualitative study characterized manifestations of GRIN-related neurodevelopmental disorder from caregivers' perspectives.

Methods

Caregivers of patients (age ≤18 years) with a clinical diagnosis of GRIN-related neurodevelopmental disorder and a *GRIN1*, *GRIN2A*, *GRIN2B*, or *GRIN2D* variant were recruited through patient advocacy groups to complete an online survey. Survey results were used to develop a guide for a 90-minute qualitative interview completed by a subset of caregivers. Data were analyzed separately in cohorts with or without seizures. A conceptual model was developed based on survey results and refined after interview analysis.

Results

Fifty-seven caregivers of 58 children with GRIN-related neurodevelopmental disorder (mean age: 7.4 y [SD: 4.4]; male: 55.2%; *GRIN2B*: 55.2%) participated in the online survey; 20 survey respondents participated in the qualitative interviews. Caregivers reported a range of neurologic, physical, behavioral, and gastrointestinal symptoms. Frequently reported signs and symptoms included developmental delays, fine and gross motor delays, behavioral symptoms, hypotonia, and constipation. Patients frequently needed assistance with activities of daily living and had difficulties with expressive and receptive communication. Half of survey respondents and 55% of interview participants reported patients were currently or previously experiencing seizures. These symptoms were identified by caregivers as being important to treat.

Conclusions

This is the first qualitative research characterizing the complex nature of the signs and symptoms and their impact on those living with GRIN-related neurodevelopmental disorder. Motor delays, communication difficulties, behavioral symptoms, and seizures are prevalent and prioritized by caregivers for treatment. The conceptual model will inform selecting clinically meaningful endpoints for a Phase 3 study of radiprodil in this patient population.

ABSTRACTS

Topic: Epilepsy: Diagnosis and Investigations

EPNS25_154 - Prognostic Evaluation of Pediatric Epilepsy Patients with Occipital Discharges

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Objectives

This study aims to evaluate the demographic, clinical, laboratory, and imaging characteristics of pediatric epilepsy patients with occipital discharges. Additionally, the study investigates prognostic factors by comparing patients who responded to treatment within the first 36 months (Group 1) and those who did not respond within the same timeframe (Group 2).

Methods

This retrospective study included 84 pediatric patients diagnosed with epilepsy with occipital discharges between 2018 and 2023. Patients' demographic, clinical, and laboratory data, as well as electroencephalography (EEG) and magnetic resonance imaging (MRI) findings, were analyzed. Statistical analyses utilized Odds Ratios and multivariate logistic regression.

Results

Among the patients, 32% (n=27) were classified as Group 1, while 68% (n=57) were in Group 2. Structural brain abnormalities were more common in Group 2, along with higher rates of psychiatric comorbidities and social adaptation issues. The age of diagnosis was significantly lower in Group 2 ($p=0.003$), and the prevalence of mental retardation was higher ($p=0.05$). The follow-up period for epilepsy was significantly longer in Group 2 ($p<0.001$). Systemic comorbidities were present in 23.8% of patients, none of whom achieved remission ($p=0.018$).

Conclusions

The findings highlight the prolonged treatment duration for pediatric epilepsy patients with occipital discharges, emphasizing the need for individualized and multidisciplinary approaches for cases unresponsive to treatment within 36 months.

ABSTRACTS

Topic: Cerebrovascular Disorders

EPNS25_155 - Neurological sequellae of pediatric cerebral ischemic stroke: case series in a tertiary care hospital

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Objectives
To evaluate the neurological features, neuroimaging findings, and neurological outcomes of seven pediatric patients with MRI-confirmed cerebral ischemic stroke, all presenting with hemiparesis and seizures, and to investigate factors contributing to the variability in their neurological sequelae.

Methods
Included are even children with cerebral ischemic stroke confirmed via magnetic resonance imaging (MRI). Clinical data, including neurological sign and symptoms, and neuroimaging results, were collected. Due to seizures electroencephalography was performed. Genetic analyses for thrombophilic gene mutations were also performed as well as cardiological examination including echocardiography and electrocardiography.

Results
All seven patients had ischemic lesions identified on MRI, with lesion locations varying among individuals. Six of the seven patients presented with hemiparesis; in one case, the hemiparesis was transient and resolved completely during follow-up. Five patients had abnormalities detected on thrombophilic gene panel testing, revealing homozygous mutations associated with hypercoagulability. All patients were initiated on antiepileptic therapy due to seizures. Long-term outcomes varied, with differences in motor, cognitive, and sensory deficits observed.

Conclusions
Pediatric ischemic stroke poses significant diagnostic and therapeutic challenges due to its diverse presentations and multifactorial etiologies. Early recognition and comprehensive evaluation, including neuroimaging and genetic testing, are crucial for optimizing outcomes. Additionally, a structured rehabilitation approach, incorporating physiotherapy and neurorehabilitation, plays a vital role in enhancing motor recovery and mitigating long-term neurological deficits. Multidisciplinary care remains essential for improving functional outcomes and quality of life in this population.

ABSTRACTS

Topic: Fetal and Neonatal Neurology

EPNS25_156 - The neurobiological requisites of fetal sentience

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Objectives

The emergent properties of the conscious state, its cerebral location, neural substrate, and scale are aspects of developmental neuroscience research. Knowledge of human brain development advances through neurophysiology, behavioral observations (e.g., the recording of unconscious involuntary fetal movements by 4D ultrasonography), neuroimaging (e.g., fetal brain connectivity networks by fetal functional MRI), and the microscopic description of fetal brain tissue. We review these measures of emerging prenatal neuronal connectivity.

Methods

Fetal brain tissue was assessed from normal fetal brains between 2004 and 2024 (n=80; age range 6-41 weeks' gestation) obtained from autopsies after spontaneous stillbirth or pregnancy termination for severe fetal anomalies in other organ systems. Neuronal maturation and function were measured by immunocytochemical markers (e.g. neuronal nuclear antigen and synaptophysin immunoreactivity).

Results

In cerebral cortical ontogeny, neuroanatomical processes of brain maturation are precisely time-linked to gestational age and are constant between fetuses of the same age. Trajectories of brain development follow reproducible patterns of maturation in sequential stages. Thalamo-cortical axonal projections mainly occur between 15- and 27-weeks' gestation. Around 23 weeks' gestation, the first projections from the thalamus into the cortical subplate become apparent. The subplate gradually disappears through apoptosis as the overlying cortical plate matures. Neuronal lamination occurs as neuroblast migration ceases, followed by the process of neurite outgrowth, axonal development, and synaptogenesis (peak 30–39 weeks' gestation) required for the mature cerebral cortex and its capacity for sentience. Certain immunocytochemical markers are expressed only late in neuronal maturation, when neurons are beginning to function.

Conclusions

Emerging human consciousness requires functional thalamocortical connections with integrative capacity. The earliest anatomic appearance of these connections begins around 15 weeks' gestation, but the connections do not become physiologically functional until at least 24 to 30 weeks' gestational age. Both the neuroanatomical formation and physiological function of synaptic circuitry are requisite to the emergence of sentience in fetal life. Epistemologically, cortical synaptic integration appears to be insufficient to facilitate human consciousness before the age of fetal viability.

ABSTRACTS

Topic: Palliativ Care

EPNS25_157 - Addressing the perpetual controversies surrounding pediatric brain death declaration

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Objectives

To consider practical strategies for addressing the many controversies associated with brain death or death by neurologic criteria (BD/DNC) in discussions with family members expressing doubt about its diagnostic validity or objections to its clinical determination.

Methods

A review of the most important controversies related to BC/DNC with sensible responses to each of them.

Results

Persistent controversies surrounding BD/DNC include 1) its definition—including debates regarding “all function of the entire brain”; 2) variability in diagnostic criteria between jurisdictions; 3) conceptual equivalency to “biological death”—including claims of “legal fiction”; 4) religious objections—including assertions of individual variation in beliefs; 5) public misperception leading to distrust in the diagnostic process; 6) informed consent requirements in performing a BD/DNC examination; 7) legal and ethical implications about the timing and process of discussing organ donation; 8) moral status, legal personhood, and the dignity of the dead; 9) requests for accommodations or the continuation of ventilator support; and 10) justice—including healthcare resource utilization after BD/DNC declaration. Pediatric neurologists must be both knowledgeable of the updated guidelines for BD/DNC determination and aware of the various controversies. Pediatric neurologists and neurointensivists must follow the standardized and meticulous evaluation processes outlined in the guidelines to reduce diagnostic error and ensure no false positive determinations. Sociocultural sensitivity and transparent, respectful communication with families regarding the diagnosis of BD/DNC is crucial, addressing any concerns or questions they may have. When faced with objections based on religious or cultural beliefs, neurologists should attempt to understand the specific concerns and explore potential accommodations within ethical boundaries.

Conclusions

Accurate determination of death is a necessary responsibility of the medical profession. Pediatric neurologists must be prepared to address the many historical and perpetual controversies surrounding the definition of BD/DNC, its clinical determination and legal declaration.

ABSTRACTS

Topic: Neuromuscular Disorders

EPNS25_158 - Long-Term Follow-Up of Spinal Muscular Atrophy Cases Diagnosed by Newborn Screening

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Objectives: Spinal muscular atrophy (SMA) is one of the most common neuromuscular disorders of childhood. The aim of our study is to share the long-term follow-up of SMA patients diagnosed through a newborn screening program.

Methods: CHOP-INTEND and Bayley-III scores, and nusinersen treatments of patients diagnosed with SMA from the newborn screening program between May 2022 and May 2024 in the Southeastern and Eastern regions of Turkey were examined.

Results: Fifteen patients diagnosed with SMA through the newborn screening program were followed up. The SMN2 gene copy number was found to be 2 copies in 14 patients and 4 copies in 1 patient. Five patients were symptomatic at the initial examination (absence of deep tendon reflexes, hypotonicity, respiratory and feeding problems). During our follow-up, a total of four patients died, one from congenital heart disease and three from respiratory failure. CHOP-INTEND scores of 7 patients who completed 24 months of follow-up were 40.1 on average before nusinersen treatment and 51.2 on average after loading doses. The mean Bayley-III scores of these patients were 84.1 for the cognitive domain, 90.6 for the language domain, and 71.6 for the movement domain. Two patients were breathing with mechanical ventilation, and three patients were being fed with a nasogastric tube. Five of the six patients who were older than 12 months were able to walk independently. The 2-year survival rate was 73%.

Conclusions: It is seen that the outcomes of SMA are better with early diagnosis and treatment through newborn screening programs. We think that the incidence, clinical picture and prognosis of SMA may change significantly in the coming years with the combination of carrier tests, newborn screening and early treatment. For this reason, we would like to emphasize the importance of long-term follow-up results.

ABSTRACTS

Topic: Neurogenetics

EPNS25_159 - The role of allelic polymorphism of the CDKN2A and CDKN2B genes with AVMs

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Objectives. The existence of linked arteries between arterial and venous segments is a congenital vascular abnormality known as arteriovenous malformations (AVMs). The tissue surrounding the afflicted arteries alters as a result of this condition's abnormal capillary network. This region has a high blood flow rate, which raises the possibility of rupture, which can cause serious problems and death. The pathological process in the future malformation area can be started by a number of sources. These include genetic variables, angiogenic growth factors, inflammatory cytokines, and environmental factors that promote angiogenesis, or the development of new blood vessels. It is an uncommon, progressive brain vascular disease that has a significant hereditary component.

Numerous genome-wide association studies (GWAS) have linked intracranial aneurysms and stroke to single nucleotide polymorphisms (SNPs) on chromosome 9p21. The purpose of this study is to investigate the role of allelic polymorphism of the CDKN2A (rs7865618), CDKN2B (rs1333040) genes in the genetic predisposition to cerebral AVM and rupture in Uzbek individuals.

Methods. The study included 85 individuals diagnosed with AVM. The determination of polymorphic gene variants was performed using real-time PCR with competitive TaqMan probes.

Results. In our research, patients with the GG genotype and G allele were significantly associated with AVMs compared to those with the GA and AA genotypes for the polymorphic variable rs7865618 of the CDKN2A gene (OR=1.915, CI=[1.158-3.167], p=0.01).

Conclusions. In Uzbek population, the GG genotype significantly associated with sporadic AVMs. For the remaining examined polymorphic loci, there were no statistically significant differences between the control and patient groups in terms of allele and genotype occurrence frequency. The significance of the 9p21 chromosome region as a shared risk factor for cerebrovascular disorders is strengthened and expanded by these findings.

ABSTRACTS

Topic: Epilepsy: Diagnosis and Investigations

EPNS25_161 - Senescence Markers in Peripheral Blood Mononuclear Cells in Pediatric Drug-Resistant Epilepsy

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Objectives: Senescence, a steady loss of proliferative capacity triggered by complex pathways, has received attention in neurodegenerative diseases but remains obscure in epilepsy. This study aims to investigate whether the stress of frequent seizures in children triggers cellular senescence.

Methods: Peripheral blood mononuclear cells (PBMC) from children under 12 years of age were analyzed for activity, telomere length, expression of cell cycle arrest genes [p53, p16, p21, retinoblastoma (RB)] along with telomerase reverse transcriptase (TERT), insulin-like growth factors (IGF), and interleukin-6 (IL-6)/tumor necrosis factor-alpha (TNF-alpha) levels. We compared these markers in drug-resistant epilepsy patients with malformations of cortical development to those in drug-responsive epilepsy patients and healthy controls. (n = 10 each).

Results: Our study showed similar PBMC SA-βGal levels across all groups. CD8+ T cell subgroup analysis from the drug-resistant epilepsy group exhibited higher SA-βGal activity. Drug-resistant epilepsy group was associated with the longest telomeres and high TERT expression. p53 and RB expressions were similar to healthy controls in drug-resistant epilepsy group, whereas p21 and p16 expressions were higher. Children with drug-resistant epilepsy with MDC showed significantly higher levels of IL-6 and TNF-alpha than healthy controls or children with drug-responsive epilepsy.

Conclusions: We observed no evidence of established stress-induced premature or replicative senescence in drug-resistant epilepsy patients. However, elevated proinflammatory cytokines and high p21/p16 expression in the drug-resistant group may suggest ongoing seizures cause cellular stress which could increase susceptibility to senescence in drug-resistant pediatric epilepsy patients over time.

ABSTRACTS

Topic: Neurogenetics

EPNS25_162 - Establishing an International network registry for Megalencephalic Leukoencephalopathy with Subcortical Cysts

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Objectives Megalencephalic Leukoencephalopathy with Subcortical Cysts (MLC) is a rare genetic disorder with infantile onset, characterized by chronic brain white matter edema, leading to macrocephaly and motor and cognitive impairment. Pathogenic variants in the genes MLC1, GLIALCAM, GPRC5B, and AQP4 result in MLC. Depending on the mutated gene, five MLC subtypes have been identified: MLC1, MLC2A, MLC2B, MLC3, and MLC4. The two main clinical phenotypes are classic (MLC, MLC2A, MLC3) with slow neurological decline, and remitting (MLC2B and MLC4) without decline. Studies on phenotype are scarce. No curative treatment is available; only management of symptoms. The absence of a registry hampers research progress. This initiative aims to define standardized clinical outcome measures (COMs), facilitating phenotypic characterization of MLC patients, thereby enabling natural history studies and preparation for clinical trials.

Methods The registry intends to combine a retrospective and prospective observational approach and longitudinally collect clinical data, including genetic information, in MLC patients from different areas of the world. First, we formed an International Consortium of clinical MLC experts. Second, we identified standardized COMs for the MLC registry using a modified Delphi procedure. This modified approach aimed to attain consensus among consortium members while minimizing the required rounds. To guide the selection process current literature was collected through a review, and input from consortium members and patient advocates (Alliance MLC) was used. Third, the consortium developed customized questionnaires to inventory the clinical disease course, incorporating input from Alliance MLC.

Results The MLC consortium decided on eight performance outcomes, eight clinical-reported outcomes, and six observer-reported outcomes. Customized questionnaires specific to MLC were developed for initial and follow-up inventories. Currently, a Castor-based secure registry with a platform for pseudonymized data sharing is being built.

Conclusions In communication with patient advocates, we defined a package of assessments and questionnaires, aiming at balancing data completeness and meeting regulatory requirements versus the burden and time demands on patients and families. Establishing an international MLC network registry is crucial for advancing disease insight, standardizing patient care and therapy development.

ABSTRACTS

Topic: Neurodevelopmental Disorders / Developmental Neuroscience

EPNS25_165 - Characteristics and timing of neurodevelopmental disorders in preterm infants: a prospective study

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Objectives

Neurodevelopmental disorders are long-term neuropsychiatric complications that occur in preterm infants. Although Japan has the lowest neonatal mortality rate worldwide, the incidence of neurodevelopmental disorders is not lower than that in other countries. These disorders often lead to psychosocial problems during school-age, and “early diagnosis and rehabilitation” are essential. This study prospectively examined trends in psychological test results to investigate the timing of onset and compare outcomes between extremely preterm (EPI, gestation < 28 weeks) and very preterm infants (VPI, gestation 28–< 32 weeks).

Methods

The preterm follow-up outpatient clinic included 25 infants with EPI (n=12) or VPI (n=13). Neurodevelopment was evaluated with Vineland Adaptive Behavior Scale-II (VABS-II) at modified 9–11 months, the Kyoto Scale of Psychological Development (KSPD) and Japanese-modified Check List for Autism in Toddlers (M-CHAT) at corrected 1.5 years, VABS-II and Parent-interview ASD Rating Scale-text Revision (PARS-TR) at modified 2 years. This study was approved by the Ethical Review Committee, and informed consent was obtained from the parents.

Results

In VABS-2, the standard scores were lower in the EPI group than in the VPI group; however, the difference decreased with age (p=0.032 at corrected 9–11 months, p=0.811 at modified 2 years). Comparing the changes in VABS-2 at corrected age 9–12 months and 2 years, communication skills decreased in both groups, and the rate of decline was higher in the EPI group than in the VPT group (p=0.01). There were no significant differences in the KSPD, M-CHAT, or PARS-TR between both groups. Eight patients (EPI, n=4; VPI, n=4) were suspected to have ASD (>9 points) on the PARS-TR, of whom four (EPI, n=1; VPI, n=3) were in the normal range on all three other tests up to 2 years of age.

Conclusion

Early preterm infants showed delayed communication skills at 2 years of age, and there was a more obvious trend towards delays in VPI than in EPI. Although several test batteries were within the normal range, a higher proportion of the VPIs had developmental characteristics. It has been suggested that there is a need to support all preterm infants, including those with VPIs that are seemingly in the normal range, to promote the development of communication during infancy before developmental differences occur.

ABSTRACTS

Topic: Infectious and Inflammatory Diseases/ Neuroimmunology

EPNS25_166 - Receiver operating characteristics analysis of peripheral blood cell count ratios for pediatric autoimmune encephalitides: a single center retrospective study

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Objectives: to evaluate the accuracy of peripheral blood cell count (PBCC) ratios at disease onset in differentiating autoimmune encephalitides (AE) from other non-inflammatory neurological disorders (OND) in children. AE is a challenging diagnosis, and patients often require appropriate treatment before a formal diagnosis of the condition is definitively secured.

Methods: a retrospective chart review between 2016 and 2024 identified patients with definite or probable AE (AE group - AEG) who had a first PBCC before any immunomodulatory medication was administered. An age-matched control group of patients with OND and nominally normal PBCC were included in the control group (ONDCG). Ratios of neutrophils (NLR), monocytes (MLR) and platelets (PLR) to lymphocytes were computed, as well as more complex indices: systemic immune-inflammation index (SII), systemic inflammation response index (SIRI) and the aggregate index of systemic inflammation (AISI). Receiver operating characteristics (ROC) curves and area under the curve (AUC) were used to assess test performance in distinguishing AEG from ONDCG. Youden's J index was computed to further assess sensitivity (Se) and Specificity (Sp).

Results: 41 patients with definite or probable AE were identified and 38 fulfilled the inclusion criteria. 38 children with OND were included as controls. Patients with AE exhibit higher overall neutrophil count and lower lymphocytes. No significant differences between groups are present regarding red blood cell counts or platelets. The best discrimination performance between AEG and ONDCG are shown by NLR (AUC 0.76, $p<0.001$, CI 0.65-0.85; Youden's $J > 1.4$, Se 60.5%, Sp 87.8%) and SII (AUC 0.74, $p<0.01$, CI 0.62-0.83; Youden's $J > 534.6$, Se 47.4%, Sp 94.7%), with lower AUC for the rest of the evaluated ratios and indices.

Conclusions: NLR and SII exhibit fair performance in distinguishing between AEG and age-matched ONDCG, with overall good specificity. These could be useful ancillary tests to help guide a clinician's judgement when faced with the initial presentation of cases that often require prompt empirical treatment before a definite diagnosis can be firmly established. These results should encourage replication in larger cohorts of both patients and controls as well as computation of effect size differences to help refine test thresholds.

ABSTRACTS

Topic: Neurogenetics

EPNS25_168 - A new leukodystrophy with chronic brain edema

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Objectives

We identified 3 unrelated paediatric patients with an identical MRI pattern, characterized by signal abnormalities in the subcortical cerebral white matter and pyramids in the brain stem. Whole exome sequencing (WES) was unrevealing.

Methods

We collected clinical and MRI information on the patients. We performed WES in two patients and compared the results to identify the mutated gene. We analyzed the likely causative gene variant in the third patient and his mother by Sanger sequencing. The consequences of the variant on protein function were characterized in cell-based studies.

Results

We identified the same *de novo* heterozygous variant in a novel gene, encoding a transporter, in the two paediatric patients. We confirmed the same heterozygous variant in the third patient and his mother. The paediatric patients presented in infancy with progressive macrocephaly. They displayed cognitive impairment, autism, epilepsy and motor impairment with ataxia and spasticity. All three had occasional episodes of increased intracranial pressure with papiloedema, which were sometimes life-threatening and required aggressive treatment with steroids and acetazolamide. The first two patients are currently 4 and 7 years old. The third patient died of unknown cause at 20 years of age. The clinical disease of the mother was less well documented, but clearly much less severe. She is still alive and ambulant at age 51 years. Sequential MRIs showed increasing cerebral white matter signal abnormalities and swelling in the three paediatric patients with in later childhood secondary remission and development of atrophy in the third patient. MRI of the mother revealed no white matter abnormalities and significant atrophy. Volumetric Brain MRI demonstrated that not only white matter, but also the grey matter, especially the cerebral cortex, contributed to the megalencephaly. The type of transporter defect was characterized in cell-based studies. Based on the findings, metabolic treatment was installed in two children, which led to clinical and MRI improvement.

Conclusions

In cases with a leukodystrophy of unknown origin and negative next generation sequencing findings, MRI pattern recognition facilitates gene identification by allowing comparison of patients. Short-0term treatment effects are promising, but long-term effects have to be awaited.

ABSTRACTS

Topic: Neurometabolic Disorders

EPNS25_169 - Exploring the Role of Variants of Uncertain Significance in Newborn Screening for X-Linked Adrenoleukodystrophy

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Objective: In 2016, California implemented newborn screening (NBS) for X-linked adrenoleukodystrophy (ALD) using a tiered combination of biochemical and genetic testing. This study aimed to determine whether individuals with an ABCD1 gene variant of uncertain significance (VUS) detected through NBS for ALD exhibit a distinct natural history of symptom development compared to those with likely pathogenic (LP) and pathogenic variants (P). Additionally, we investigated the relationship between phenotype, genotype, and C26:0-LPC levels.

Methods: This retrospective cohort study was conducted at Stanford University. Patients were identified through the Stanford Research Repository tool using ICD-10 codes for ALD. Inclusion criteria were males with one X chromosome and a genetically and biochemically confirmed ALD diagnosis, identified due to NBS. Data included demographics, mortality, clinical presentation, genotype, biochemical testing results, and disease progression. Individuals were grouped according to genotype classification provided by the state of California at the time of screening. Statistical analyses included Kaplan-Meier curves to estimate survival probabilities for symptom onset and multiple linear regression to assess the relationship between genotype classification, C26:0-LPC levels, and symptom onset.

Results: We included 59 patients from Stanford. The median age at last follow-up was 4.1 years (range: 0.1-12.2 years). Among these patients, 28 had a VUS, 11 had LP variants and 20 had P variants. At the time of data collection, 15 patients had developed adrenal insufficiency (AI), 14 of whom had LP/P variants. The median age of onset of AI insufficiency was 1.6 years (range: 0.58-9.9 years). Our survival analysis shows that at 120 months, the survival probability of remaining free from AI among patients with an LP/P variant is 14% (95% confidence interval (CI): 0%-36%), compared to 96% (95% CI: 88%-100%) in the VUS group. Two patients with P variants had developed cALD. Multiple linear regression shows that C26:0-LPC levels in second-tier testing were significantly higher for patients in the LP/P group compared to the VUS group ($p<0.001$). Furthermore, patients who had already developed AI had significantly higher C26:0-LPC levels ($p<0.001$) compared to those who had not developed AI.

Conclusions: We found that natural history varied by ABCD1 genotype classification. Individuals with VUS exhibited lower rates of adrenal insufficiency and cerebral development and had lower C26:0-LPC levels compared to those with LP/P variants. These results highlight a potential correlation between biochemical markers, symptom development, and genotype. Further study and validation are required, but our findings could inform thresholds for ALD NBS.

ABSTRACTS

Topic: Epilepsy: Medical and Surgical treatment

EPNS25_173 - Long-term outcomes and management of infantile epileptic spasm syndrome: a multicenter retrospective cohort study

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Objectives

Infantile epileptic spasms syndrome (IESS) is a severe infantile epilepsy syndrome that is difficult to treat and has high lifetime morbidity. Although standard treatments for IESS typically include hormonal therapy and vigabatrin, treatment options in the Republic of Korea are limited because of the unavailability of adrenocorticotrophic hormones. In this study we aimed to evaluate how children with IESS have been treated over the last few decades in Korea, and to assess their long-term seizures and neurocognitive outcomes.

Methods

This multicenter retrospective study included infants diagnosed with IESS at 6 hospitals between 1994 and 2021, who had a follow-up period of > 2 years. Data on demographics, clinical features, medical history, etiological evaluation, and treatment regimens (including medication duration and dosage, epilepsy surgery, and dietary therapy) were collected. Outcomes were measured in terms of short-term spasms control, subsequent long-term epilepsy, and neurodevelopmental outcomes.

Results

A total of 379 infants with IESS were included. The mean age at the onset of spasms was 7.2 months (range, 1–24 months), and they were followed up for 7.9 years (range, 2–28 years). Etiologies were identified in 64.9% of cohort, with structural (acquired) etiologies being the most prevalent (29.6%). Tuberous sclerosis complex (n = 35), Down syndrome (n = 7), Miller–Dieker syndrome (n = 3), and *CDKL5* (n = 2) were the dominant single-gene causes of genetic IESS. Vigabatrin was the mainstay of treatment, prescribed to 93.9% of the cohort, with 36.4% achieving electroclinical resolution of spasms within 6 months. At the last follow-up, 77.6% of the children were on anti-seizure medications and one-third of them were pharmacoresistant. Approximately 90% of the cohort exhibited intellectual disabilities; of those eligible, 53.9% received special education, with 60% continuing special education into high school.

Conclusions

IESS imposes a substantial burden on children and their families, and many children with this epilepsy require lifelong medical, educational, and social support. Our findings underscore the need for prompt evaluation of etiologies and early treatment; they suggest that a multi-faceted approach is required to support children with IESS and their families.

ABSTRACTS

Topic: Infectious and Inflammatory Diseases/ Neuroimmunology

EPNS25_174 - Specificity of Supportive Features in the 2023 Diagnostic Criteria for MOGAD in Children with Optic Neuritis

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Objectives: Optic neuritis (ON) can be idiopathic or serve as the initial manifestation in children with multiple sclerosis (MS), myelin oligodendrocyte glycoprotein antibody-associated disease (MOGAD) or aquaporin-4 antibody-positive neuromyelitis optica spectrum disorder (AQP4-Ab NMOSD). Distinct clinical and radiological features have been identified to differentiate these conditions. Recent diagnostic criteria for MOGAD currently include additional supportive features, particularly in patients with low positive serum MOG antibodies (MOG-Ab) measured by live cell-based assays, or when using fixed cell-based assays with unavailable titers. This study aims to assess whether the supportive criteria for optic neuritis are specific to patients with MOGAD.

Methods: We included patients under 18 years of age who presented with their first episode of optic neuritis at two tertiary centers between July 2017 and February 2024. All patients were tested for MOG antibodies using a fixed cell-based assay as part of routine clinical care. The cohort included 13 patients with MOGAD, 4 with AQP4-Ab NMOSD, 2 with relapsing-remitting multiple sclerosis, and 4 who were double seronegative. Each patient underwent brain and spine MRI, cerebrospinal fluid testing for oligoclonal bands, and MOG and AQP4 antibody testing as part of their standard care. Neuroimaging was reviewed by two pediatric neuro-radiologists. Descriptive statistics were used to compare the findings between MOGAD and non-MOGAD patients.

Results: Bilateral simultaneous optic neuritis was observed in 5/13 (38%) patients with MOGAD compared to 3/10 (30%) patients with other diagnoses (p=1.0). Longitudinal optic nerve involvement (greater than 50% of the optic nerve length) was seen in 9/13 (69%) MOGAD patients versus 5/10 (50%) non-MOGAD patients (p=0.4). Perineural optic sheath enhancement was present in 12/13 (92%) MOGAD patients compared to 3/10 (30%) in the non-MOGAD group (p=0.006). Optic disc swelling was seen in 7/13 (53%) MOGAD patients versus 4/10 (40%) non-MOGAD patients (p=0.7). All 13 patients with ON-MOGAD exhibited at least one supportive diagnostic feature at onset, compared to 8/10 patients with non-MOGAD. The median number of supportive criteria per patient was higher in the MOGAD group (2 vs. 1.5, p=0.02).

Conclusions: The supportive criteria required for diagnosing MOGAD were present in all patients with MOG-Ab-associated optic neuritis (ON), but were also observed in patients with ON due to other etiologies. Perineural optic sheath enhancement was the only supportive criteria seen more frequently in MOGAD patients. These findings should be taken into account when interpreting borderline MOG antibody results.

ABSTRACTS

Topic: Headache / Migraine

EPNS25_175 - Children and Adolescents attending a Headache Clinic have Severely Reduced Participation - a case-control study

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Objectives

While the impact of headaches on participation has been quantified in general populations through school-based studies, studies on clinical cohorts—where children may face more severe impairments—remain limited. The objective was to assess the impact of headaches on participation in children and adolescents attending a headache clinic compared to controls, aiming to uncover a hidden burden and support early intervention. Participation is quantified as absences from school and other activities, and parental absence from work due to children's headache.

Methods

This cross-sectional, case-control study recruited patients from the Headache Clinic, Department of Pediatrics and Adolescents Medicine, Herlev Hospital, Denmark (October 2018 to April 2021) and controls from primary and secondary schools in the Copenhagen and Zealand area (November 2022 to January 2024). Patients were classified according to the International Classification of Headache Disorders-III. Participation was quantified using the Child and Adolescent Headache Associated Restriction, Disability, Social Handicap and Impaired Participation questionnaire and the Pediatric Migraine Disability Assessment questionnaire.

Results

354 patients (92 with migraine, 109 with TTH, 78 with both migraine and TTH, 22 with secondary, one with cluster, and 52 with unclassified headache) and 131 controls were included. In the past month, patients were absent from school due to headache in 43.1% vs 13.7% ($p<0.001$), missing a mean 1.8 vs 0.3 school days ($p<0.001$) and patients left school early in 31.8% vs 11.5% ($p<0.001$) on 1.2 vs 0.3 ($p<0.001$) days, compared to controls. Absenteeism thus affected 15.0% vs 3.0% of school days in patients compared to controls. Patients were absent from other activities in 74.0% vs 22.9% ($p<0.001$), missing 4.4 vs 0.7 ($p<0.001$) days, compared to controls. Parents of 23.8% vs 9.2% ($p<0.001$) of patients missed work due to their children's headache losing 0.8 vs 0.2 ($p<0.001$) days, compared to controls. Patients with TTH was the most severely affected. Compared to the migraine group, the TTH group had 18.9 vs 3.7 headache days ($p<0.001$), 2.3 vs 1.1 missed school days ($p=$), 1.6 vs 0.9 days left early ($p=$), 5.6 vs 1.8 days missed other activities ($p<0.001$), and 0.4 vs 0.6 parental lost workdays ($p=$). Headache frequency was the strongest risk factor for reduced participation ($p<0.001$).

Conclusions

Headaches cause significantly reduced participation in children and adolescents attending a headache clinic compared to controls. This study emphasizes the necessity of incorporating both an assessment of participation and implementing targeted interventions in the management of childhood headache.

ABSTRACTS

Topic: Neurogenetics

EPNS25_177 - Players in cerebral volume regulation: variants in aquaporin-4 and GPRC5B lead to megalencephalic leukoencephalopathy with subcortical cysts (MLC)

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Objectives

MLC is a leukodystrophy characterized by brain oedema with macrocephaly and a variable degree of motor and cognitive problems as well as epilepsy. Variants in *MLC1* or *GLIALCAM*, encoding proteins involved in astrocyte volume regulation, are the main causes of MLC. In some patients, the genetic cause remains unknown. The purpose of this study was to find the genetic cause in unsolved MLC patients and to further unravel mechanisms of brain volume regulation.

Methods

The study consisted of phenotyping and genetic investigations followed by functional studies. In patients with clinical and radiological signs of MLC, negative for *MLC1* or *GLIALCAM* variants, SNP-arrays, whole exome- and Sanger sequencing were performed. Next, the subcellular localization of the related proteins was determined in cells and in human brain tissue. We investigated functional consequences of the newly identified variants on volume regulation pathways using cell volume measurements, biochemical analysis and electrophysiology.

Results

We identified a homozygous variant in *AQP4*, encoding the water channel aquaporin-4, in two related patients and two different *de novo* heterozygous variants in *GPRC5B*, encoding the orphan G protein-coupled receptor GPRC5B, in three unrelated patients. Both proteins are expressed in astrocytic endfeet, like MLC and GlialCAM. GPRC5B is known to interact with channels involved in astrocyte volume regulation. The *AQP4* variant was found to disrupt aquaporin-4 membrane localization and thereby interfere with the channel function. Cell volume regulation was disrupted in lymphoblasts from patients with the *GRPC5B* variant in a similar way as observed in cells of patients with *MLC1* variants.

Conclusions

Aquaporin-4 and GPRC5B were identified as old and new players in the development of brain oedema. These findings contribute to the growing understanding of brain ion and water homeostasis mechanisms and give direction for treatment strategies for MLC and other conditions involving brain oedema.

ABSTRACTS

Topic: Movement Disorders/ Cerebral Palsy

EPNS25_178 - Caregivers' insights and decision-making on deep brain stimulation in GNAO1-related disorders

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Objectives: Deep brain stimulation (DBS) is an advanced therapeutic intervention for individuals with *GNAO1*-related disorders (*GNAO1*-RD), characterized by severe movement abnormalities such as status dystonicus and dyskinetic crises. Decision-making surrounding DBS is complex and influenced by medical, emotional, and logistical factors. This study aimed to explore patient and caregiver perspectives on the decision-making process, factors influencing outcomes, and family experiences with DBS in *GNAO1*-RD.

Methods: An EU survey was administered to 12 primary caregivers of individuals with genetically confirmed *GNAO1*-RD who had undergone DBS. The survey collected data on demographics, clinical features, decision-making factors, and postoperative experiences. Quantitative data were analyzed descriptively, while qualitative data were thematically analyzed.

Results: The participants included caregivers from 11 countries, with patients undergoing DBS at a median age of 10.7 years and follow-up durations ranging from <1 to 11.7 years. The primary indication for DBS was status dystonicus (9/12). The decision was categorized as urgent in 9/12 cases. Factors influencing the decision included long-term quality of life, DBS effectiveness, prevention of hospitalizations, and surgeon expertise. Postoperatively, 8/12 families reported significant reductions in dyskinetic crises, with improvements observed within days to months. Challenges included inadequate preoperative information, rushed decisions due to medical urgency, and emotional tolls on families.

Conclusions: DBS is a life-saving intervention for GNAO1-RD, yet decision-making is highly complex and emotionally taxing. Enhanced communication, evidence-based guidance, and caregiver support are critical to optimizing outcomes and empowering families during the decision-making process.

ABSTRACTS

Topic: Movement Disorders/ Cerebral Palsy

EPNS25_179 - Dyskinetic crisis in GNAO1-related disorders: Lessons from caregivers' perspectives

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Objectives

GNAO1-related disorders (*GNAO1*-RD) are characterized by a spectrum of developmental delay, epilepsy and movement disorders, including dyskinetic crises. This study aimed to explore the characteristics, management challenges, and impact of dyskinetic crises in children with *GNAO1*-RD, based on parent-reported data

Methods

A cross-sectional EU survey was conducted with 26 parents of children with *GNAO1*-RD across 12 countries. The survey gathered demographic, clinical, and management-related data, with a focus on dyskinetic crises, seizure differentiation, and the overall impact on quality of life.

Results

The mean age of children was 11.43 years (SD=4.51), with a mean genetic diagnosis age of 5.08 years. Dyskinetic crises were currently experienced by 61.5% of children, while 26.9% had current seizures. Parents noted differences in motor patterns, altered consciousness, and response to treatment for differentiating dyskinetic crises from seizures. Dyskinetic crises varied widely in frequency and duration, with triggers including infections and emotions. The dyskinetic crises significantly impacted quality of life, motor function, and emotional well-being, with many children missing educational and social activities. Medications, including benzodiazepines, were rated variably effective; 11 children underwent deep brain stimulation (DBS), with mixed outcomes. Parents reported challenges in managing crises and accessing support services, with notable financial burdens for some families.

Conclusions

Dyskinetic crises in *GNAO1*-RD present complex management challenges, necessitating individualized care strategies. While DBS and medications offer potential benefits, variability in outcomes underscores the need for optimized treatment protocols and accessible resources for affected families. Enhanced healthcare coordination and targeted support services may alleviate disease burden and improve quality of life.

ABSTRACTS

Topic: Neurodevelopmental Disorders / Developmental Neuroscience

EPNS25_180 - Novel GNAO1 variant in α-helical domain reveals alternative mechanism of disease

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Objectives

GNAO1-related disorders (*GNAO1*-RD) are ultra-rare neurological conditions characterized by diverse phenotypes, including movement disorders, developmental delay and epilepsy. The Gαo protein, encoded by *GNAO1*, is composed of three distinct structural regions: the Ras-homology domain (RHD) and the α-helical domain (AHD), separated by a nucleotide-binding cleft, and an N-terminal α-helix (αN). Variants of Gαo located in the RHD have been better characterized, whereas mutations in the AHD remain less understood, complicating understanding their role in the pathology of *GNAO1*-RD. This study aims to investigate a novel *GNAO1* variant (N76K) located in the AHD and its functional implications in *GNAO1*-RD.

Methods

We conducted a comprehensive analysis of a patient presenting with severe symptoms and identified the N76K variant through genetic testing. Functional assays, including bioluminescence resonance energy transfer (BRET) and immunoblotting, were employed to assess protein interactions and signaling dynamics.

Results

The N76K variant exhibited impaired heterotrimer formation, disrupting interactions between Gαo and Gβγ subunits, thus affecting GPCR signaling dynamics. Moreover, N76 is likely critical for holding the Ras-like and α-helical domains together in the nucleotide-bound states and thereby retaining nucleotides in the nucleotide-binding crevice.

Conclusions

The identification of N76K in the α-helical domain underscores the significance of this region in *GNAO1*-RD pathophysiology, revealing a distinct mechanism of action that necessitates tailored therapeutic approaches.

ABSTRACTS

Topic: Neurometabolic Disorders

EPNS25_184 - Epidemiology of X-linked Adrenoleukodystrophy in Denmark: A National Cross-Sectional Study

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Objectives: This study explores the epidemiology of X-linked adrenoleukodystrophy (ALD) in Denmark, comparing incidence rates, genotype, and phenotype distribution with international data. We also investigate age at symptom onset, survival, and conduct a sex-stratified analysis to understand symptom development in female ALD patients.

Methods: This national cross-sectional study collected retrospective data on individuals diagnosed with ALD in Denmark. Inclusion criteria were genetically confirmed ALD and Danish residency, with no age limitations. Data were gathered from Copenhagen University Hospital and other Danish institutions. We contacted all Danish pediatric, neurological, endocrinological, and genetic departments to identify ALD patients and ensured pedigree evaluations for all probands. We used cumulative incidence functions to estimate the risk of developing different ALD phenotypes.

Results: We identified 113 patients (49 males, 64 females) with genetically confirmed ALD. The point prevalence of ALD in Denmark is 1.43 per 100,000 inhabitants (males 0.54; females 0.89). The average birth incidence from 1932-2023 was 1.81/100,000 (males 1.7; females 1.9). We found 34 different, pathogenic variants in *ABCD1*, with c.1679C>T, p.(Pro560Leu) being the most common (21 individuals). Among male patients, 13 (32%) developed cerebral disease, with onset in childhood (46%), adolescence (31%), and adulthood (23%). Symptoms of adrenomyeloneuropathy (AMN) were present in 46% of males and 64% of females. Adrenal insufficiency was observed in 44% of males. Cumulative incidence analysis showed that by age 60, 36% of males developed cerebral ALD, 80% of males developed AMN, and 43% of males had adrenal insufficiency. By age 60, 68% of females had developed AMN. The longest diagnostic delay was found among AMN patients, with an average delay of 8 years for males and 9 years for females.

Conclusions: This study provides an understanding of the epidemiology of ALD in Denmark, revealing a birth incidence comparable to other natural history studies but significantly lower than regions with newborn screening. Our findings underscore the high prevalence of AMN symptoms in both males and females, with up to 80% having developed these symptoms by the age of 60. Notably, the lower-than-expected prevalence of cerebral ALD and adrenal insufficiency, particularly among adults, highlights potential gaps in diagnosis and treatment.

ABSTRACTS

Topic: Neurodevelopmental Disorders / Developmental Neuroscience

EPNS25_185 - Design of a Phase 3 Multicenter Study (BeeLine) to Assess the Efficacy and Safety of Radiprodil, a Targeted Investigational Therapy for Patients With GRIN-related Neurodevelopmental Disorder

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Objectives: Analyses of a Phase 1b study (Honeycomb; EudraCT:2022-000317-14; ClinicalTrials.gov ID: NCT05818943) in GRIN-related neurodevelopmental disorder (NDD) from July 2024 demonstrated that radiprodil, a selective, negative allosteric modulator of GluN2B subunit-containing NMDA receptors, was generally well tolerated and substantially reduced seizure frequency with signs of improvement in behavioral symptoms. We describe the transition of Honeycomb to a double-blind, placebo-controlled, Phase 3 study (BeeLine) to robustly assess the efficacy and safety of radiprodil for eventual registration as a precision treatment targeting the underlying biology of GRIN-related NDD.

Methods: BeeLine is designed to evaluate the efficacy and safety of radiprodil across diverse GRIN phenotypes. Two cohorts of GRIN-related NDD patients (age 1 mo–18 y) will be included: cohort 1: patients with ≥4 countable motor seizures (CMS) in the 28-day pre-randomization period (n≤60) will constitute a randomized qualifying seizure (RQS) cohort; cohort 2: patients with behavioral and other non-seizure symptoms, not meeting the CMS criteria required for the RQS, but meeting other criteria, will constitute a randomized auxiliary (RA) cohort (n≤40). Both cohorts will be randomized (1:1) to radiprodil or placebo. The double-blind maintenance period for the RQS and RA will be 12 and 24 weeks, respectively.

Results: BeeLine includes numerous innovative features to assess radiprodil as a potential targeted disease-modifying treatment for GRIN-related NDD. The primary endpoint is between-group differences in seizure frequency. Additional endpoints include seizure-free days and changes in non-seizure signs, symptoms, and impact using a GRIN-specific clinical global impression scale, being developed using a conceptual model based on caregiver interviews, ABC-2C, Vineland-3, and Peds-QL. Given the favorable effects observed in the Honeycomb analyses, a Bayesian group sequential design will enable interim assessments of overwhelming efficacy leading to potentially expedited development.

Conclusions: The current data suggest the potential for unprecedented efficacy of radiprodil in GRIN-related NDD. The innovative design updates to BeeLine will evaluate changes in disease course induced by radiprodil in patients with diverse clinical phenotypes.

ABSTRACTS

Topic: Neuromuscular Disorders

EPNS25_188 - Evaluating the Validity of the Combined Bedside Test in Diagnosing Juvenile Myasthenia Gravis

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Objective: Myasthenia gravis (MG) is an autoimmune disorder characterized by impaired neuromuscular transmission leading to muscle weakness, including ptosis, and challenges in diagnostic evaluation. Standard confirmatory tests (e.g., anti-AChR, anti-MuSK, RNS, and neostigmine tests) are often limited by varying sensitivity and specificity. The bedside test, incorporating the ice pack test and fatigability test, offers a practical, non-invasive approach. The global incidence of Myasthenia Gravis (MG) has increased, highlighting the critical need for effective diagnostic methods.

This study evaluates the validity of a combined bedside test (the ice pack test and fatigability test) for diagnosing juvenile myasthenia gravis (JMG) in pediatric patients with ptosis.

Methods: This cross-sectional study was conducted at King Chulalongkorn Memorial Hospital, Thailand, from January 2012 to May 2024. The study included pediatric patients (1 month–18 years) presenting with ptosis who underwent at least one of the bedside tests (ice pack or fatigability test), alongside confirmatory tests (anti-AChR, anti-MuSK, RNS, or neostigmine). Data collected included demographics, clinical findings, and test results. Diagnostic efficacy was evaluated using sensitivity, specificity, accuracy, PPV, NPV, likelihood ratios, Fagan Nomogram, Kappa statistics, and McNemar's Chi-Square.

Results: Of 32 patients (47% male, mean age 8 years 10 months) were included. Of these, 28 were diagnosed with JMG, and 4 were controls with alternative diagnoses. Confirmatory tests showed that 73% of JMG patients tested positive for anti-AChR. The combined bedside test has high sensitivity (92.8%) and accuracy (87.5%), but moderate specificity (50%). It significantly outperformed the ice pack test, which had low sensitivity (42.8%) and accuracy (43.8%) (P = 0.0005). The fatigability test had high sensitivity (82%) and PPV (92%) but moderate specificity (50%). Fagan Nomogram analysis shows reduces 16% in the post-test probability for negative results.

Conclusions: The Combined Bedside Test has a high sensitivity (92.8%) and accuracy (87.5%) and is an effective screening tool for diagnosing Juvenile Myasthenia Gravis in children, outperforming the ice pack test alone and providing valuable insights for early detection and management. The fatigability test, with 82% sensitivity, serves as an effective adjunct screening tool. Integrating the Combined Bedside Test into clinical practice could significantly enhance diagnostic accuracy for JMG in children and reduce the need for invasive procedures in pediatric patients.

ABSTRACTS

Topic: Miscellaneous

EPNS25_189 - ILIAD: the ERN-ITHACA federated registry

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Objectives

In 2017, following the EU directive on the application of patient's rights in cross-border healthcare, the European Commission established the European Reference Networks (ERNs). These are pan-European healthcare providers networks that specialize in a set of rare diseases, with the objective of pooling together clinical expertise, knowledge and resources available on rare and complex diseases. ERN ITHACA is the reference network for rare malformative conditions, intellectual disabilities and neurodevelopmental disorders. ERN ITHACA has developed a "meta-registry" called ILIAD, connecting 71 HCPs, databases, and biobanks across the EU for patients with dysmorphic/multiple congenital anomalies syndromes and/or intellectual disability. Through the ERN ITHACA's expert and patient participation network, ILIAD is able to provide an infrastructure for diagnosis, highly specialised multidisciplinary healthcare, evidence-based management, and collection of secure patient data.

Methods

The registry is built on MOLGENIS open-source software, providing flexible rich data structures, user friendly data import and querying, and FAIR interfaces for programmatic data exchange. ILIAD consists of 2 components: a central, web-based registry and a network of linked satellite/client registries forming the ERN ITHACA registry federation. To date, two client installations have been successful and at least six more are ongoing. Data is modelled adhering to international interoperability standards from JRC and EJP-RD.

Results

In addition to the core registry, ILIAD includes thematic sub-registries of patients with biologically proven monogenic or genomic (chromosomal) diagnoses, under the supervision of ERN-based curation teams. ILIAD has adopted a data access policy, for requesting access to the data and the governance of the registry is in place to ensure compliance with applicable legal and regulatory requirements on the use of Personal Data.

Conclusions

We are well underway to share ERN ITHACA patient data, yielding high-quality epidemiological insights and expert consensus statements, informing policy decisions that impact rare disease patients in general and care for ERN ITHACA patients in particular. Please reference this study on the use of Molgenis for rare disease data: van der Velde KJ et al. MOLGENIS research: advanced bioinformatics data software for non-bioinformaticians. Bioinformatics. 2019 Mar 15;35(6):1076-1078. doi:10.1093/bioinformatics/bty742. PMID: 30165396. ERN ITHACA has been funded by the European Union, under the grant agreement number 101156387.

ABSTRACTS

Topic: Movement Disorders/ Cerebral Palsy

EPNS25_190 - Pallidal DBS as a therapeutic option for pediatric DYT-HPCA: insights into Ca2+ and K+ channel dynamics

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Objectives: Biallelic pathogenic variants in the HPCA gene cause DYT-HPCA, a rare autosomal recessive disorder characterized by generalized dystonia and complex motor symptoms. This study aimed to describe the clinical and molecular characteristics of two pediatric individuals with novel HPCA variants and evaluate the effects of globus pallidus internus deep brain stimulation (GPi-DBS) on their movement disorders.

Methods: This is a prospective study. Two sisters with HPCA variants (c.91_98del/p.Tyr31Leufs14) were clinically assessed. Functional studies were conducted on fibroblasts from one of these individuals and a previously reported individual with a different HPCA variant (c.49C>T/p.Arg17), focusing on calcium signaling and potassium channel activation. Statistical analysis was performed using the Student's t-test (for paired or unpaired samples, as appropriate).

Results: GPi-DBS led to significant improvement in dystonia and chorea in one individual, reflected by a 47% reduction in Burke-Fahn-Marsden Dystonia Rating Scale scores. mRNA expression levels for HPCA in both HPCA-mutant cells and HPCA-wild type were similar, as were the levels for the dystonia-related genes CACNA1B and ANO3. Potassium channels related to afterhyperpolarization (KCNQ3, KCNQ5, KCNN1, KCNN3, and KCNN4) were expressed in fibroblasts. Intracellular calcium was increased by stimulating with the calcium ionophore ionomycin, the activation of whole-cell currents in mutant fibroblasts was only slightly lower than in wild-type fibroblasts, with no significant difference between the two. Similar results were obtained when whole-cell currents were activated by the purinergic neurotransmitter ATP, which induced small, similarly sized whole-cell currents. Pronounced depolarisation was observed in both wild-type and mutant fibroblasts, with subtle differences. Potassium channels were inhibited resulting in milder depolarisation and a reduced calcium increase. No significant calcium increase was observed in mutant cells, whereas it remained present in wild-type cells. Basal calcium levels in cells expressing mutant HPCA were slightly higher but not significantly.

Conclusions: To our knowledge, this is the second individual with DYT-HPCA treated with GPi-DBS and the first pediatric case. GPi-DBS is an effective treatment for DYT-HPCA, even in pediatric individuals. Fibroblast analyses showed no significant differences in calcium signaling or potassium channel activation between mutant and wild-type cells. The molecular mechanisms of DYT-HPCA remain elusive. Further research is necessary to improve diagnostic and therapeutic approaches.

ABSTRACTS

Topic: Epilepsy: Medical and Surgical treatment

EPNS25_191 - SUCCESSFULL TREATMENT OF CHILD WITH SCN2A-RELATED DEVELOPMENTAL AND EPILEPTIC ENCEPHALOPATHY WITH APPARENT GAIN-OF-FUNCTION EFFECTS

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Objectives

We report an infant who presented with migrating focal seizures in the neonatal period. She was found to have a mosaic c.4534C>Gp.Pro1512Ala variant in SCN2A. Functional studies on this variant revealed a mixture of gain- and loss-of-function effects.

Methods

A Whole Exome Sequencing was performed through a commercial diagnostic laboratory (SmartGene, Tashkent, Uzbekistan). Whole exome sequencing (WES) as a trio was also performed by SmartGene.

Results

A 6-week-old girl was hospitalized in our department due to experiencing daily seizures in multiple areas, which started on the 5th day after birth. She had no notable personal history. Prior to her admission to our clinic, she had been given Levetiracetam and Phenobarbital within the recommended therapeutic levels but it did not effectively control her seizures. Upon undergoing electroencephalography, bilateral and multifocal epileptiform discharges were observed. Prompt seizure management was achieved using Phenytoin, in accordance with recent literature suggesting the use of sodium channel blockers for SCN2A-related epileptic encephalopathies. The child remained free from seizures but experienced delayed development in motor and cognitive skills. Genetic investigations identified a de novo SCN2A missense pathogenic variant with predicted GoF effect.

Conclusions

This case illustrates the dramatic response to sodium channel blockers suggested an underlying channelopathy.

ABSTRACTS

Topic: Fetal and Neonatal Neurology

EPNS25_192 - Management of neonatal seizures, insights from EPICARE Study Survey

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Objectives: The main objective of this survey is to establish how neonatal seizures are managed across Europe, such as methods of diagnosing seizures, interpretation of results and treatment.

Methods: The survey was created by the European Reference Network for all rare and complex epilepsies (EpiCARE) neonatal seizures and epilepsies working group. The survey was circulated to EpiCARE members, Medical Societies and Meetings, being answered from June 2024 to October 2024. Descriptive and statistical analysis (Chi-squared test) was performed.

Results: In total, 229 responses of 23 European countries were received; after removal of 35 duplicates, 194 surveys were included for analysis. The participating centres are located in: 37 Central Europe, 34 Iberian Peninsula, 29 Germany, 28 Italy, 22 British Isles, 16 Eastern Europe, 15 Western Europe, 8 Nordic Countries and 5 Baltic Countries. The maximum neonatal care support provided by the centres is: regional neonatal intensive care unit (NICU) in 98, NICU in 83, special care nursery in 11 and well neonatal nursery in 2. Most of the centres have more than 100 newborns admitted per year. Nearly all neonatal units have protocols for management and/or treatment of seizures however, there are significant differences between geographic regions. Most centres diagnose seizures using a combination of clinical diagnosis, amplitude integrated electroencephalography (aEEG) and routine EEG without differences between geographic regions. Availability of EEG/aEEG is statistical different across Europe. aEEG is more frequently available followed by routine EEG and continuous EEG monitoring. Continuous EEG monitoring is unavailable in 150 centres, and in the remaining ones, it is only available during working hours. Two-thirds of the centres monitor high risk neonates with aEEG. First line treatment was Phenobarbital in over 90%, while levetiracetam is 2nd choice in over 70%. More than 60% of centres treat electrographic seizures, depending on the seizure burden.

Conclusion: This is the biggest survey about neonatal seizures management ever done in Europe. Most centres have seizure diagnosis/management protocols. Most centres have no access to continuous EEG monitoring. Many centres monitor high risk neonates with aEEG but there are statistical differences between different regional regions. ASM recommendations are adhered but gold standard for diagnosis (full EEG) is less often used. There is an urgent need to improve the diagnostic pathway of neonatal seizures in Europe.

ABSTRACTS

Topic: Epilepsy: Diagnosis and Investigations

EPNS25_193 - Metabolic biomarkers in the cerebrospinal fluid metabolic biomarkers of children with epilepsy: a retrospective cohort study

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Objectives To define the clinical value CSF measurement of biogenic amine, pterins, amino acids, and folates in paediatric onset epilepsies.

Methods Retrospective clinical and biochemical phenotyping of patients with epilepsy who underwent diagnostic CSF measurement of monoamine neurotransmitters, pterins, folates, and amino acids between 2009 and 2022 in a pediatric tertiary centre .

Results The analyzed cohort included 123 patients with epilepsy (mean age at the procedure:4.54±3.65 years). The diagnostic yield for primary neurotransmitter disorders was 1.68% while it was zero for inherited amino acid and folate metabolism disorders.

Patients with higher seizure frequency showed higher levels of CSF homovanillic acid (HVA) and HVA/5-hydroxyindolacetic acid (5HIAA) ratio.

Lower levels of 3-ortomethyldopa (3-OMD) were found in patients with co-occurring neurodevelopmental disorders, and of biopterin, 3-Methoxy-4-hydroxyphenylglycol (3-MHPG) and 5-methyltetrahydrofolate (5-MTHF) in those with movement disorders.

Significantly lower CSF glutamine levels were found in patients under antiseizure medications, polytherapy, and drug resistance.

Patients with relapsing status epilepticus had significantly lower levels of CSF aspartic acid, glycine , leucine , ornithine , valine , and higher levels of CSF serine.

Conclusions CSF examination disclosed differences in the concentrations of various metabolites that might be related to the severity of the epilepsy, the presence of comorbid conditions and medications.

ABSTRACTS

Topic: Neuromuscular Disorders

EPNS25_194 - Muscle biopsy and mitochondrial disease criteria in paediatric patients with neuromuscular phenotypes

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Objectives

The aim of our study is to describe a real-life longitudinal cohort of paediatric patients with neuromuscular manifestations who underwent muscle biopsy as part of their diagnostic evaluation. The goal is to study the role of muscle biopsy in disease diagnostics and identification of mitochondrial dysfunction. We also wanted to examine how the established Nijmegen and modified Walker mitochondrial disease criteria recognized mitochondrial diseases.

Methods

The study was performed retrospectively at the University Hospital, which served as the sole tertiary care center for paediatric neurology in the area. The study included all paediatric patients examined between 1990 and 2022 with undefined neuromuscular symptoms who underwent muscle biopsy. Clinical and laboratory data were collected from medical records, together with all genetic studies. Patients were classified using the Nijmegen and Modified Walker criteria into 'definite,' 'probable,' 'possible,' or 'unlikely' categories.

Results

A total of 219 patients underwent muscle biopsies. Genetic diagnosis was confirmed in 57 patients (26%), with 11 of those (19%) being primary mitochondrial diseases. Mitochondrial DNA defects were found in 9% of diagnosed patients, and nuclear gene defects in 91%. Electron microscopy was performed for 174 patients (79%), with ultrastructural mitochondrial changes observed in 49 patients (28%), 9/11 (81%) with primary mitochondrial disease and 8/46 (17%) with other genetically defined diseases. Ragged-red fibers were found in four patients, of which three with primary mitochondrial disease. OXPHOS measurements were done on 188 patients (86%), revealing decreased enzymatic activity in 48 patients (26%), of which only 13 patients had a genetically defined aetiology (four primary mitochondrial diseases). The Nijmegen and Modified Walker criteria had high specificity (98–100%) but lower sensitivity rates.

Conclusions

This study supports the current recommendations of first-line genetic testing when suspecting mitochondrial disease. However, a significant number of patients with undefined aetiology showed signs of mitochondrial dysfunction. Thus, muscle biopsy and functional studies on patient-derived samples can give useful information on carefully selected patients for the further diagnostic process, especially with variants of uncertain significance. Mitochondrial disease criteria are still valuable tools for clinicians to identify possible mitochondrial diseases.

ABSTRACTS

Topic: Movement Disorders/ Cerebral Palsy

EPNS25_195 - NKX2-1 Related Disorders: Description of the clinical phenotype and genotype through an international registry

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Objectives: This study aims to characterize the clinical and genetic spectrum of NKX2-1-Related Disorders (NKX2-1-RD), identify novel phenotypic features, explore genotype-phenotype correlations, and establish a foundation for future natural history and therapeutic studies.

Methods: We conducted a multicenter, retrospective, observational study. Individuals were recruited via referral physicians, and data were collected using REDCap. Descriptive and statistical analyses were performed.

Results: 68 individuals (37 females, mean age ± SE 16 ± 0.18 years) were included. Neurological symptoms, primarily motor delay, were the most common initial presentation (41 individuals, mean ± SE age of onset 0.87 ± 0,02 years), followed by respiratory symptoms (23 individuals), often manifesting as neonatal respiratory distress syndrome (NRDS). The classical triad (brain-lung-thyroid involvement) was observed in 33 individuals, while 26 had two-system involvement (21 brain-thyroid, 5 brain-lung), and 6, presented with isolated brain symptoms.

Neurodevelopmental delay (NDD) was common, with motor delay predominating (mean age ± SD of gait onset: 29.48 ± 12.33 months). Intellectual disability (ID) was observed in 6 individuals. Late gait onset was associated with more severe NDD and ID. Chorea was the most frequent movement disorder (92.65%), with a mean age ± SD of onset at 2.73 ± 2.91 years. Other motor symptoms included hypotonia (39), dystonia (31), ataxia (23), and myoclonus (22). Mental health conditions were reported in 35% of individuals, with ADHD (18), anxiety (9), and depression (9) being the most frequent.

Hypothyroidism was diagnosed in 82% (mean age ± SE of onset: 4.03 ± 0.22 years). Other endocrinological manifestations were: failure to thrive (11 individuals), growth hormone deficiency (7), and hypogonadotropic hypogonadism (4).

Genetic testing revealed pathogenic variants in 60 individuals, while 8 presented deletions, translocations, or retrotransposon insertions. Half of the variants were de novo. Chorea improved or stabilized in most cases, especially in females, and was more frequent in individuals with mutations than deletions (96.6% vs. 75%, p = 0.067). Myoclonus was significantly associated with anxiety and

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depression. NRDS, present in 24 individuals, was associated with a higher incidence of subsequent respiratory disorders.

Conclusions: This study represents the largest cohort of individuals with NKX2-1-RD reported to date. Symptoms often manifest in early infancy, with neurological features predominating. Despite the broad phenotypic variability, half of the cases exhibit the classical triad. Chorea, a hallmark feature, tends to improve or stabilize over time, particularly in females. These findings enhance our understanding of NKX2-1-RD and provide a foundation for future research.

ABSTRACTS

Topic: Neuromuscular Disorders

EPNS25_196 - Survival Analysis in Untreated Patients with Thymidine Kinase 2 Deficiency (TK2d) Aged ≤12 Years at TK2d Symptom Onset: Findings from the Largest International TK2d Dataset

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Objectives

To report survival outcomes in untreated patients with thymidine kinase 2 deficiency (TK2d) aged ≤12 years at TK2d symptom onset. TK2d is an ultra-rare, autosomal recessive, mitochondrial disease associated with progressive proximal myopathy. Affected patients typically lose the ability to walk, eat and breathe independently. No treatments are approved, so management is limited to supportive care. Understanding survival outcomes in the subgroup of patients with a young age of symptom onset is important, given that they tend to experience rapid disease progression and premature death, often from respiratory failure.

Methods

Unique individuals with TK2d were identified through two literature reviews of published case series, case reports (June 2019; updated 2021) and a retrospective chart review study (NCT05017818) (Integrated Summary of Efficacy–Untreated Patients Database [ISE-UPD]). Kaplan–Meier survival analyses of patients aged ≤12 years at TK2d symptom onset were performed. Patients still alive at last follow-up were censored at their last known age. Patients with no event data, no event date or missing period start/end dates were censored at time point zero.

Results

In total, 117 ISE-UPD patients were aged ≤12 years at TK2d symptom onset (median [quartile (Q)1, Q3] age of TK2d symptom onset: 1.2 [0.5, 2.0] years). Of these, 66 (56.4%) had died (missing: n=10; median [Q1, Q3] age at death: 1.9 [1.0, 3.5] years). Median (95% confidence interval) time from symptom onset to death was 2.6 (1.3, 6.4) years and from birth to death was 4.0 (2.8, 10.0) years (51 patients censored in both analyses).

Conclusions

TK2d is associated with high mortality. Our analysis confirms that patients aged ≤12 years at TK2d symptom onset face a high risk of premature death, with death often occurring in the 3 years after TK2d symptom onset.

UCB funded this study.

ABSTRACTS

Topic: Neuromuscular Disorders

EPNS25_198 - Functional Outcomes in Untreated Patients with Thymidine Kinase 2 Deficiency (TK2d) Aged ≤12 Years at TK2d Symptom Onset: Findings from the Largest International TK2d Dataset

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Objectives

To characterize functional outcomes in untreated patients with thymidine kinase 2 deficiency (TK2d) aged ≤12 years at TK2d symptom onset. TK2d is an ultra-rare, autosomal recessive, mitochondrial disease associated with debilitating, life-threatening proximal myopathy. Management is limited to supportive care (ventilatory/feeding support). Understanding motor function and use of supportive care in the subgroup of patients aged ≤12 years at TK2d symptom onset is important given that they typically experience rapid disease progression, generalized weakness and premature death.

Methods

Unique individuals with TK2d were identified through two literature reviews of published case series, case reports (June 2019; updated 2021) and a retrospective chart review study (NCT05017818) (Integrated Summary of Efficacy [ISE]–Untreated Patients Database [UPD]). ISE-UPD data and pretreatment data (NCT03701568; NCT03845712; NCT05017818) for patients later treated with pyrimidine nucleosides (ISE-pretreatment patients) formed the comprehensive disease course dataset. Developmental motor milestones and ventilatory/feeding support were assessed.

Results

Among patients aged ≤12 years at TK2d symptom onset (N=199), most lost ≥1 motor milestone (ISE-UPD: 20/26 [76.9%], missing/not-at-risk: n=91; ISE-pretreatment: 41/49 [83.7%], missing/not-at-risk: n=33). Only 1/20 ISE-UPD patients (5.0%) and 2/41 ISE-pretreatment patients (4.9%) regained 1 lost milestone. Ventilatory support was used by 50/117 ISE-UPD patients (42.7%; missing: n=44) and 31/82 ISE-pretreatment patients (37.8%; missing: n=29). Feeding tubes were used by 8/117 ISE-UPD patients (6.8%; missing: n=91) and 20/82 ISE-pretreatment patients (24.4%; missing: n=30). Overall, 1 patient (ISE-UPD) discontinued ventilatory support and 1 patient (ISE-pretreatment) discontinued feeding support.

Conclusions

Functional outcomes were comparable between ISE-UPD and ISE-pretreatment groups; most patients aged ≤12 years at TK2d symptom onset experienced loss of motor function, with very infrequent spontaneous milestone regains. These findings, together with sustained ventilatory and feeding support use, highlight the heavy and progressive disease burden in patients aged ≤12 years at TK2d symptom onset.

UCB funded this study.

ABSTRACTS

Topic: Infectious and Inflammatory Diseases/ Neuroimmunology

EPNS25_205 - Neurodevelopmental outcomes in children with Acute Leukoencephalopathy with restricted diffusion- A single center experience from resource limited settings

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Objectives

To prospectively assess the neurodevelopmental outcomes in children with acute leukoencephalopathy with restricted diffusion (ALERD) using standardized scales.

Methods

Prospective, single-center study was conducted over 18 months enrolling children upto 18 years of age with a diagnosis of ALERD. All children were assessed in follow-up using modified Rankin score (mRS), Glasgow Outcome Scale- Extended (GOS-E), Developmental Profile-3 (DP3), Vineland Social Maturity Scale (VSMS), Childhood Psychopathology Measurement Schedule (CPMS), children's sleep habit questionnaire- abbreviated (CSHQ-A), Early Childhood Epilepsy Severity Scale (E-CHESS), neuroimaging and electroencephalography. Quality of life of parents was assessed using WHO-QOL-BREF scale.

Results

We enrolled 23 children (median age of presentation 24 months); majority (52%) were below 2 years of age. Diffuse pattern was observed in 61% and central sparing pattern was in 39%. Mortality rate was 4%. Survivors were followed up for neurodevelopmental assessment (Median duration of follow up: 30 months; range: 3-112 months). Overall neurological outcomes by mRS and GOS-E were severe (30%) and moderate disability (22%), and good recovery (44%). Majority (59%) had global developmental delay on DP-3 scale. VSMS showed 14% mild, 9% moderate, 4% severe and 23% profound intellectual disability. Abnormal sleep habit and psychopathology was recorded in 27% each using CSHQ-A and CPMS scales respectively. Focal epilepsy in 14%, generalized epilepsy in 9% and epileptic spasms in 4% were seen. EEG in children with epilepsy revealed multifocal intermittent epileptiform discharges with frequent generalized discharges in 2 children, left frontotemporal and bilateral frontal discharges in 1 child each. Movement disorders were observed in 55% children: dystonia 36%, cerebellar ataxia 9%, myoclonus 5% and choreoathetoid movement 5%. Follow-up neuroimaging showed diffuse cerebral atrophy in 83%, white matter changes in 30% and persistent diffusion restriction in 17%. Parents reported their quality of life as low in 35%, moderate in 20% and high in 45% by the WHO quality of life scale.

Conclusions

ALERD affects children in the short-term with poor neurodevelopmental outcomes, impaired quality of life and several comorbidities such as poor sleep, epilepsy, behavioral problems, and movement disorders. Hence, children need regular follow-up for early recognition of sequelae and early initiation of rehabilitations, that can improve the overall functioning in the survivors.

ABSTRACTS

Topic: Neuromuscular Disorders

EPNS25_206 - The clinical and genetic characteristics of Duchenne muscular dystrophy patients in Azerbaijan

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Objectives In Azerbaijan, as in many other countries, duchenne muscular dystrophy DMD poses significant challenges for affected individuals and their families. The aim is to present clinical data and identify the mutation spectrum of the DMD gene in a nationwide cohort of DMD patients with the goal of guiding future developments in Azerbaijan.

Methods The research was conducted in the Azerbaijan Medical University neurology department, involving boys with DMD. Assessments involve the evaluation of muscle strength, as well as timed motor performance tests, including the time to stand from a supine position, time to climb four standard stairs,6 minute walking test, The 6-Minute Walk Test, TUG (Timed Up and Go) test. Additionally, the Brooke and Vignos scales for limb function are used. Laboratory approaches involved biochemical evaluation of creatine kinase levels, multiplex ligation-dependent probe amplification (MLPA), and next-generation sequencing (NGS) analysis of the DMD gene. All participants gave written consent to participate in the study. Data were processed using medical statistics methods.

Results 46 male patients, aged between 1 and 26 years (mean age 10 ± 4.7), were recruited. An average age for the disease's onset was 4 years and 3 months. The majority of patients underwent genetic testing based on clinical symptoms and average age at which genetic confirmation was obtained was 8 years and 5 months. At the time of enrollment, 34.8% of patients were dependent on wheelchairs for full-time use. Among the genetic variations in MLPA analysis identified, with 66 % being deletions 19 % duplications and negative results in 7 cases (15, 2 %). To identify point mutations, sequencing was performed on 7 boys with negative MLPA results, revealing point mutations in all of them, including two nonsense, one splicing ,two frameshift and two duplications.

Conclusions In Azerbaijan, as in many countries, DMD remains a significant concern due to its debilitating nature and the lack of widespread awareness and specialized treatment options**.** The initial results show that DMD is diagnosed at a relatively older age in Azerbaijan compared to other countries, emphasizing the need for improved compliance with international DMD care standards.

ABSTRACTS

Topic: Neurometabolic Disorders

EPNS25_208 - Genotypic and phenotypic spectrum of 891 cases of pdha1-related pyruvate dehydrogenase deficiency

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OBJECTIVES: X-linked *PDHA1*-related Pyruvate dehydrogenase complex (PDHc) deficiency causes lactic acidosis and neurological findings, amenable to ketogenic diet/thiamine. This study explores the genotypic and phenotypic spectrum and the natural history to improve counseling.
METHODS: Retrospective study, combining a systematic review of the literature with a multicenter survey. After removing duplicates, all cases were analyzed collectively.
RESULTS: Data from 891 individuals (53% females, 45% unpublished, median age of 6 years) were included. Neonatal (39%) or infantile (37%) presentation was most frequent, with fetal abnormalities seen in 47%. Restricted mean survival time was 10.6 years (95% CI: 9.5-11.8) and median survival 11.2 years (95% CI: 7.8-17.0). Male gender (OR: 6.87, 95% CI: 2.75-17.15), neonatal (OR: 63.26, 95% CI: 7.02-570.13), and infantile (OR: 15.07, 95% CI: 1.78-127.49) presentations, but not genotype, were associated with poor survival. Among 331 different *PDHA1* variants (119 unpublished), missense (50%) and frameshift (29%) were most common, in 75% occurring *de novo*. The most common variant was p.Arg263Gly (n = 68). Frameshift/nonsense variants in males were confined to regions escaping nonsense-mediated decay and were less frequent than in females. Common clinical phenotypes included developmental delay, intellectual disability, muscle hypotonia, abnormal movements, seizures, feeding difficulties, and microcephaly. Neuroimaging findings frequently included basal ganglia, corpus callosum abnormalities, and cerebral atrophy. Gender and age at presentation, but not variant type, correlated with clinical and neuroimaging findings. Independent walking was achieved by 49%, 39% communicated in sentences, and 25% attended regular school. Physicians reported ketogenic (71%) and thiamine (49%) as beneficial.
CONCLUSION: Our study proves several aspects estimated from smaller studies like the equal male:female ratio, and the clinical and neuroradiological findings. This study adds new insights on survival-age at presentation correlations and genotypes (including 119 previously unreported variants). Together these data aid in counselling. The available treatment options warrant early genetic investigations in children with developmental delay.

ABSTRACTS

Topic: Neurogenetics

EPNS25_209 - Hypomelanosis of Ito due to somatic complex MTOR gene variant in one of the monozygotic twins that can only be detected by RNAseq: A mosaic Smith-Kingsmore syndrome case with local overgrowth

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Objectives: Presenting stepwise diagnostic approach of in one of the monozygotic twins with hypomelanosis of Ito clinical picture and localized overgrowth in brain who has a complex variant in an overgrowth syndrome gene,MTOR,that can only be detect by RNAseq of affected tissue while exome sequencing of blood sample was normal.

Methods: Whole exome sequencing (WES) with Twist capture kit and MGI-T7 equipment from blood sample and RNAseq from affected overgrowth tissue of brain sampled after surgical removal

Results: The patient is a 9-year-old girl with a monozygotic healthy twin sister, who began experiencing seizures at the age of 3 months. Due to the refractory nature of her seizures and the identification of focal dysplasia on cranial MRI,she underwent resective epilepsy surgery at the age of 5.However, despite surgical intervention, her seizures persisted, and she also exhibited increasing signs of autism spectrum disorder and intellectual disability, prompting her referral to our clinic at the age of 9.Mild dysmorphic features were detected. Exome sequencing was planned due to resistant epilepsy and focal brain dysplasia and test that was done from blood sample was normal. Re-evaluation by physical examination after this normal result presented “faint and barely visible Blashko lines” that can be visible with mobile phone light was noted.As this is a common feature of mosaicism and technical difficulty of making exome sequencing from paraffinized brain tissue,RNAseq was planned, and it was presented a complex variant including combination of exon skipping in exon 44 and inverted duplication in exon 39 was detected in the mTOR gene.Consequently, the patient was started on treatment with the mTOR pathway inhibitor Sirolimus.Currently, her seizures have been approximately 50% controlled, with noted improvements in autism-related symptoms and increased verbal communication.

Conclusions: Lessons from this complex case were 1) Discordance of clinical features in twins may be a sign of mosaicism 2) clinical features of mosaicism like Blashko lines may be barely visable due to low level of mosaicism 3) localized brain dysplasias must be checked for mosaicism 4)RNAseq is a powerful tool while whole exome sequencing or other genomic tests are not possible in difficult samples like paraffinized tissues. 5)It is highly probable that even if we had been able to perform WES or even whole genome sequencing (WGS) from surgical specimens, we would not have been able to detect this complex mutation. In some cases of complex genetic variants, RNAseq is now a routine diagnostic tool.

ABSTRACTS

Topic: Neurodevelopmental Disorders / Developmental Neuroscience

EPNS25_210 - Etiology and prognosis of developmental and epileptic encephalopathies: genotype-phenotype correlation

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Objectives: Developmental and epileptic encephalopathies(DEEs) are characterized by refractory seizures and frequently recurring epileptic activity with neurodevelopmental delay or regression that usually begin in early life.We aimed to define the relationship between electroclinical features and etiology, as well as the genotype-phenotype correlations and neurodevelopmental comorbidities associated with genetically determined DEEs.

Methods: We evaluated the patients who were presented to the division of pediatric neurology in our university hospital with DEEs when they were between 2017 and 2021 and followed for at least 24months. We examined 136 DEEs children's demographics, neuroimaging, metabolic and genetic findings, treatment strategies, and long-term outcomes. In patients with genetic etiology, chromosome-based and/or next generation sequence based (single gene analysis, epilepsy gene panels and whole-exome sequencing) test results were evaluated retrospectively. The variants identified as clinically relevant were selected. Their pathogenicity was assessed according to the 2015guidelines of the American College of Medical Genetics,and their compatibility with expected clinical findings was evaluated using the OMIM database.The presence of previously reported variants was verified in the Human Gene Mutation Database.Nucleotide changes and protein alterations of the identified variants were documented. If a variant categorized as VUS (Variants of uncertain significance); we systematically reviewed relevant clinical findings to provide context and assist in interpretation.

Results: The age at presentation ranged from 1 to 126 months. MRI commonly revealed white matter involvement, and the most frequent EEG findings were generalized epileptiform activity and hypsarrhythmia. Identified etiologies were genetic causes in 30%,structural causes in 23.5%, and metabolic in 12.5% of the patients. The study identified 35 distinct pathogenic variants across 21 different genes, with the SCN1A gene being the most frequently detected. 60patients were diagnosed with Infantile Epileptic Spasms Syndrome, 11 with Dravet Syndrome, 12with LGS, 5with sleep-activated spike-wave developmental and epileptic encephalopathy, 17with Early Infantile Developmental and Epileptic Encephalopathy, 3with Myoclonic Astatic Epilepsy, and with unclassified developmental and epileptic encephalopathy.Non-ketotic hyperglycinemia was the most prevalent metabolic disorder, and acquired lesions due to hypoxic-ischemic injury were the most common structural cause.The 25 patients had been seizure-free for 24months.

Conclusions: Understanding the various underlying etiologies of DEEs in children, along with their genotypic and phenotypic characteristics, is crucial for early diagnosis and treatment and for developing targeted management strategies.

ABSTRACTS

Topic: Neurometabolic Disorders

EPNS25_212 - Long-term findings of N-acetyl-L-leucine for Niemann-Pick disease type C

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Objectives

The IB1001-301 clinical trial was a Phase III, double-blind, randomized, placebo-controlled trial comparing N-acetyl-L-leucine (NALL) with placebo for the treatment of neurological signs and symptoms in children and adults with Niemann-Pick disease type C (NPC) after a treatment period of 12 weeks. The primary Scale for the Assessment and Rating of Ataxia (SARA) endpoint was reduced -1.97 points with NALL and -0.60 with placebo ($p<0.001$). Extended follow-up data were obtained in an open-label Extension Phase (EP) to evaluate the long-term, neuroprotective effects of NALL for NPC.

Methods

Patients received treatment with orally administered NALL 2-3 times per day in tiers of weight-based dosing. The primary endpoint was the modified 5-domain NPC Clinical Severity Scale (5-Domain NPC-CSS) (range 0-25 points; lower score representing better neurological status). Comparisons were made to the expected annual trajectory of disease decline established in published natural history studies. Exploratory endpoints included the 17-domain NPC-CSS (excluding hearing) and SARA.

Results

54 patients aged 5 to 67 years were treated in the EP. After 12 months, the mean (±SD) change from baseline on the 5-domain NPC-CSS was -0.115 (±2.60) and 1.5±3.1 in the historical cohort (mean difference 1.56; 95% Confidence Interval, 0.31 to 2.92; $p<0.017$), a 108% reduction in annual disease progression. The result of the 17-domain NPC-CSS (exl. hearing) was supportive of the primary analysis and the improvements in neurological status demonstrated in the Parent Study's primary SARA endpoint were sustained over the long-term follow-up. NALL was well-tolerated, and no treatment-related serious AEs occurred.

Conclusions

Children and adults with NPC who were treated with NALL after 1 year showed a statistically and clinically significant reduction in disease progression, consistent with a neuroprotective and disease-modifying effect.

ABSTRACTS

Topic: Neurological Emergencies

EPNS25_213 - Decoding Stroke-Like Episodes in PMM2-CDG: Evidence-Based Insights and Management Strategies from the Largest Cohort Study

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Objectives Phosphomannomutase 2 deficiency (PMM2-CDG) is the most common congenital disorder of glycosylation, often causing chronic neurological symptoms due to cerebellar atrophy and peripheral neuropathy. However, acute neurological complications, including stroke-like episodes (SLE), have been reported in 55% of patients. We analyzed the largest reported PMM2-CDG cohort, offering insights into SLE prevalence and management to better understand SLE characteristics and develop diagnostic algorithms, and evidence-based approaches.

Methods Our multicenter, ambispective study analyzed data from 108 PMM2-CDG patients across nine European centers. Neurological evaluations were conducted following standardized protocols, including validated scales, neuroradiological studies, neurophysiological assessments, and laboratory analyses. Statistical evaluations, including principal component analysis, were performed on data collected in REDCap to identify risk factors and clinical correlations.

Results Of the 108 patients, 25% experienced at least one SLE. Episodes occurred as early as 1.2 years of age and as late as 40 years, with a recurrence rate of 43% (ranging from two to five SLE). Triggers included infections, head trauma (more common in younger patients), or remained unidentified. Clinical characteristics varied by trigger, including relapse timing, symptom duration, and complementary exam findings. Common neurological deficits included motor symptoms and impaired speech, often accompanied by headache and hyperthermia. Video-EEG showed asymmetrical features and slow trace anomalies. Neuroimaging during episodes showed no significant changes beyond baseline anomalies. Benzodiazepines were most effective during acute symptoms. Full recovery was achieved in all cases. Registered preventive strategies were heterogeneous, with some agents showing preliminary positive results. Management protocols varied across centers but included hydration, antipyretics, and antiseizure medication for epilepsy.

Conclusions SLE prevalence appears lower than reported, likely due to underdiagnosis, highlighting the need for increased medical awareness. Evaluation and management of SLE remain inconsistent and lack evidence-based guidelines across hospitals. We propose a detailed evaluation protocol to distinguish presentations, tailor treatment guidelines, and minimize invasive, uninformative tests. A management algorithm customized to triggers and patient characteristics is recommended to improve prognosis.

ABSTRACTS

Topic: Epilepsy: Medical and Surgical treatment

EPNS25_214 - Real-World use of stiripentol in the USA

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Objectives

STIRUS study aimed to gather data on patients prescribed stiripentol since the US marketing authorization in August 2018.

Methods

In this US retrospective, non-interventional, multicenter, chart review, all patients diagnosed with Dravet syndrome (DS) and who had taken stiripentol for at least 3 months in routine practice were eligible. The index date was the start of stiripentol treatment, and patients were followed from this date to their last intake of the medication.

Results

The study included 99 patients from 10 US sites. Median age at first seizure was 5 months, and at DS diagnosis was 15 months. Median age at stiripentol initiation was 6.9 years. At the start of stiripentol treatment, patients were on a median of 3 antiseizure medications, mainly benzodiazepines (clobazam n=81; clonazepam n=11), cannabidiol (n=45), valproate (n=42), fenfluramine (n=24), and levetiracetam (n=23). Mean initial daily dosage of stiripentol was 14 mg/kg/d, then increased to a target dose of 31 mg/kg/d. Mean daily dose at last follow-up visit was 31.8 mg/kg/d.

Following stiripentol initiation, a reduction in seizure frequency was observed and maintained over long-term follow-up, with 38.1% of patients experiencing a marked or mild reduction in seizures in the last 3 months. At baseline, 33.7% of patients had at least one episode of status epilepticus (convulsive seizures lasting >5 minutes), that decreased to 16.3% in the first 3 months of treatment and to 14.9% in the final 3 months. Both a significant decrease in rescue medication use and less emergency room visits were reported, leading to improved quality of life for patients and families/caregivers.

From a safety perspective, 99 adverse effects were reported in 50 patients, with no unexpected or significant adverse reactions observed.

Conclusions

STIRUS provided real-world evidence of DS management in the US. Median age at diagnosis of Dravet syndrome was 1.25 years while it was 5.4 years in 2012, indicating better knowledge of the disease resulting in early diagnosis. The study confirmed stiripentol efficacy in decreasing the frequency of generalized tonic-clonic seizures and the number of status epilepticus, resulting in less hospitalizations, regardless of concomitant clobazam use. No unexpected adverse effects were identified. Somnolence, lethargy and decreased appetite were the most frequent, and may regress when the dose of concomitant antiseizure medications is reduced.

ABSTRACTS

Topic: Epilepsy: Medical and Surgical treatment

EPNS25_215 - Results of a Long-Term Post-Marketing Surveillance Study on Stiripentol Safety and Efficacy in a Large Cohort of Japanese Patients

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Objectives

After its market authorization in Japan (November 2012), a post-marketing surveillance study in all Dravet syndrome (DS) patients that initiated stiripentol (STP) was conducted.

Methods

Data up to 156 weeks after STP initiation were analyzed. STP's safety and effectiveness were prospectively investigated in all DS patients in Japan who were administrated the drug from November 2012 to August 2017. Patients receiving STP for the first time were defined "new patients," while those continuing STP post-domestic clinical studies were defined "continuous patients."

Adverse reactions were reported by treating physicians, who assessed patients' conditions before and after STP initiation. Improvement was rated on a 5-point scale (marked, moderate, mild, unchanged, or worsened) or as undetermined, based on evaluations of seizure frequency (SF), duration, intensity, and daily activities. The percentage change in SF was calculated.

Results

Data were collected in 521 patients, with 520 in the safety analysis set (SAS) and 515 in the effectiveness analysis set (EAS). Adverse drug reactions (ADRs) occurred in 69% of the 520 SAS patients; with the most common being somnolence (37%), decreased appetite (27%), dizziness (13%), weight decreased (9%), and drug level increased (6%). No new safety concerns were identified.

12 deaths were reported: 2 deaths, 2 near drownings, 1 cardiorespiratory arrest, 1 encephalopathy, 1 hypoxic-ischemic encephalopathy, 1 sudden death, 1 status epilepticus, 1 generalised tonic-clonic seizure (TCS), 1 liver disorder, and 1 hepatobiliary cancer.

After 156 weeks or at drug discontinuation, 38% of new patients were markedly or moderately improved, and 60% were at least mildly improved. None of the continuous patients were considered worsened. Median percent change from baseline in TCS and/or clonic seizure (CS) frequency ranged from -46% to -75% after 156 weeks. After 4 weeks of treatment, median percent change in SF was -64% for focal impaired awareness seizures and -61% for generalized myoclonic (MS) and/or generalized atypical absence seizures (AAS). SF gradually decreased, reaching -100% after 57 weeks and 49 weeks of treatment, respectively.

Conclusions

This analysis reports the largest cohort of patients in a real-world setting, followed for 3 years. No new safety concerns were identified, and long-term efficacy of STP in reducing TCS/CS was confirmed. We report efficacy of STP on focal impaired awareness seizures as well as MS/AAS.

ABSTRACTS

Topic: Epilepsy: Medical and Surgical treatment

EPNS25_216 - Review of stiripentol use in Lennox-Gastaut Syndrome

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Objectives

Since the management of Lennox-Gastaut Syndrome (LGS), a severe Developmental and Epileptic Encephalopathy (DEE), remains problematic due to intractable seizures, some physicians use stiripentol (STP) as an alternative. This work aimed at reviewing the use of STP in LGS.

Methods

A Literature search was done (May 2023) in Cochrane Library and PubMed using the terms `stiripentol AND Lennox´, and in the abstract books from relevant meetings (from 2007 onwards) searching firstly 'stiripentol' and then 'Lennox´. The eligibility criteria was the presence of data on STP related to LGS treatment.
Additionally, results of an unpublished exploratory single-blind Phase II trial conducted in the 90's in 4 French centers in inadequately controlled (≥1 seizure/week) LGS patients (2-20 years) were reviewed.

Results

5 references (out of 29 found) were eligible: 3 observational studies [1 meeting abstract], 1 clinical trial, and 1 review. These data, together with some real-world evidence, reported that STP can be an effective and well-tolerated therapeutic option in LGS treatment.
The phase II trial recruited 16 LGS patients. Further to a one-month placebo period, stiripentol was added to the ongoing treatments for 2 months. A significant decrease in the overall seizure frequency was reported (p=0.02), notably tonic-clonic seizures (p=0.01). Additionally, maximal time interval between seizures increased in 13 patients as compared to the baseline period (p=0.01). Regarding safety, one patient discarded the study due to side effects (nausea, vomiting, somnolence). The most frequently reported adverse events were in line with the stiripentol safety profile.

Conclusions

The published evidence and the results of the phase II study suggest a good efficacy and tolerability of STP in treating LGS when used in combination with the current therapy. These preliminary data need to be confirmed in a well-conducted phase III study.

ABSTRACTS

Topic: Epilepsy: Medical and Surgical treatment

EPNS25_217 - Efficacy of Stiripentol Beyond Generalized Tonic-Clonic Seizures: A Retrospective Analysis of Dravet and Non-Dravet Patient Records

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Objectives: Stiripentol (STP) is approved as an add-on therapy with clobazam and valproate for refractory generalized tonic-clonic (GTC) seizures in Dravet syndrome (DS). Its efficacy in other refractory epilepsies is limited, but off-label use has been reported.

Methods: This retrospective, single-center, observational study analysed the efficacy and safety of STP in refractory paediatric epilepsies. Medical records of patients aged ≤15 years with non-Dravet epilepsy or DS who initiated STP treatment between January 2014 and December 2023 were reviewed.

Results: 18 DS and 17 non-DS patients (76.5% of the latter with developmental and epileptic encephalopathy) initiated STP at median ages of 40 [4-179] and 64 [5-180] months, with median doses of 50 [20-100] and 35 [4-100] mg/kg/day (p = 0.032), respectively.

Prior to STP, DS and non-DS patients had been exposed to a median of 4.5 and 9 antiseizure medications (ASMs), respectively (p = 0.002), and were treated with a median of 2 and 3 concomitant ASMs at STP initiation.

After three months of add-on STP, seizures (number, duration, and/or intensity) improved in 76.5% of non-DS and 61.1% of DS patients. Seizure frequency reduced by ≥50% in 44.4% of DS and 58.8% of non-DS patients, and by ≥75% in 38.9% of DS and 41.2% of non-DS patients, with 20% of all patients becoming seizure-free. Efficacy was sustained in 90.9% of DS and 69.2% of non-DS patients for a median of 87 and 13 months, respectively (p = 0.052). The probability of sustained STP efficacy was higher in DS (120 months) than non-DS (16 months; p=0.012). STP reduced all seizure types in both cohorts (i.e., GTC, absence, myoclonic, tonic and focal seizures, and spasms).

STP also improved cognition and Clinical Global Impression scale scores in ~60% of all patients, with sleep improvement in 19.2%. Acute STP treatment resolved status epilepticus in 5 patients within a median of 0.5 days.

Adverse events (AEs), mainly mild-to-moderate, occurred in 44.1% of all patients. Severe AEs were only reported in three DS patients, leading to discontinuation in two cases. Six non-DS patients (35.3%) discontinued ≥1 other ASM after STP initiation.

Conclusions: Add-on STP provides overall improvement in various seizure types for paediatric patients with refractory epilepsy, including syndromes other than DS. It also has positive effects on comorbidities and appears effective in acute treatment of status epilepticus. STP is generally well tolerated.

ABSTRACTS

Topic: Epilepsy: Diagnosis and Investigations

EPNS25_218 - The Risk of Epilepsy following Neonatal Seizures: a Nationwide Register-based Cohort Study

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Objectives The reported risk of childhood epilepsy among children with neonatal seizures varies greatly. Establishing risk factors and characteristics of later epilepsy can guide clinicians toward tailored treatment. We therefore aimed to describe the incidence of epilepsy among children with neonatal seizures, and to identify subpopulations prone to develop epilepsy. We hypothesize that children with neonatal seizures have a greater risk of epilepsy, especially children also diagnosed with neonatal stroke or cerebral malformations.

Methods We performed a nationwide register-based cohort study including all children born in Denmark between 1997–2018. Data were extracted from the Danish Medical Birth Register and the National Patient Register. Epilepsy was defined by a minimum of two registered ICD-10 diagnoses of epilepsy

Results We followed 1,294,377 children and identified 1,998 neonatal survivors with neonatal seizures. The cumulative risk of epilepsy was 20.4% (95% CI 18.5–22.3) among children with neonatal seizures, compared to 1.15% (95% CI 1.12–1.18) among children without. Epilepsy was diagnosed before one year of age in 11.4% of children with neonatal seizures, in an additional 4.5% between one to five years, 3.1% between five to 10 years, and 1.4% between 10 to 22 years. The etiologies of neonatal cerebral infarction, hemorrhage, or malformations (adjusted HR 2.49 (95% CI 1.98–3.14)) and low Apgar score (1.49(1.12–1.98)) were associated with the highest risk of epilepsy, compared to children with seizures of unknown etiology.

Conclusions Epilepsy following neonatal seizures is common and remains a substantial risk throughout childhood. Etiological risk factors are identifiable and relevant when planning appropriate information for parents and follow-up.

ABSTRACTS

Topic: Epilepsy: Diagnosis and Investigations

EPNS25_219 - D'Unseen - Navigating what really matters: Insights from ethnographic research on Dravet Syndrome

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Objectives: This ethnographic investigation aimed to uncover what really matters during the Dravet syndrome (DS) journey, to improve patients' and caregivers' lives, focusing on the experiences faced by all actors in the DS ecosystem.

Methods: Led by a steering committee of 6 European DS experts (neuropediatricians, nurse, neuropsychologist, patient organization members-POs), this research was conducted across France, Italy, Spain, Germany, and the United Kingdom. To explore new and overlooked aspects of daily life with DS to gain a deeper understanding of their experiences, we conducted a two-step approach: macroanalysis through DS expert interviews and literature review. Then ethnographic fieldwork explored individual practices, behaviours, and beliefs via in-depth semi-structured interviews and daily moments observations from families, HCP's, and POs members.

Results: This study included 46 participants and revealed a holistic view of DS, mapping each stakeholder (DS specialists, support care specialists, local institution, POs, extended family and friends, researchers), and their impact on family's journey. The fieldwork allowed a deep understanding of the impact on DS at the macro, meso and micro scale for all stakeholders. We defined an emotional odyssey of life with DS (from first seizure to adulthood) and four parents' postures ("the castaway", "the gatekeeper", "the personal assistant", "the maestro") according to their potential attitudes facing DS and based on four dimensions: control/delegation/novice/expert. The observations highlighted:

- the life-changing moment of the diagnosis, combining emotional shock with practical demands, without the means to implement sustainable changes
- A disconnect throughout the ecosystem of actors in terms of information, amplified by structural and emotional dynamics
- Stigmatizing aspect with seizures as the most isolating aspect
- Absence of a structured rehabilitation pathway amplifying future uncertainty

Conclusions: This ethnographic approach provided real-life perspectives often absent in clinical studies, uncovering critical gaps and actionable opportunities. These insights provide a comprehensive framework for addressing DS complexities, identifying needs, challenges, and strengths at each stage. It will help the clinicians and families to adapt their communication and expectations, and to deliver concrete solutions, ultimately improving the quality of life of the different stakeholders.

ABSTRACTS

Topic: Headache / Migraine

EPNS25_220 - Lifting the burden of headaches in Georgian schools

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Lifting the burden of headaches and QOL in Georgian schools

Abstract

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Introduction: Headache attributed to QOL in adolescents between 12-17 years of age is unknown in Georgia.

Objectives: The aim of our study was to investigate the prevalence of primary headaches and headache-related burden in adolescents in Georgia.

Methods: The study is a cohort combined study with population number 1379 (marginal error 5%). Data was collected from schools in the large cities such as Tbilisi, Kutaisi, Telavi and 9 townships all over the Republic of Georgia. Data are collected according to socio-demographic headache features and headache-related Quality of Life (QOL). In total, there were 1818 students; 438 were absent. The data is analyzed using SPSS. Inferential statistical analysis is used. Data are analyzed via the Pearson-Chi-square test, linear by linear regression, the severity of migraine pain is classified into mild, moderate and severe headache.

Results: 94.9% of adolescents have headaches, 43.90% have migraine, 39.8% have tension-type headache and 0.1% have a combination of both. 1.245% have headaches for more than 15 days per month, 7% report severe overuse of anti-headache medications. QOL is passed into life for myself, life at home, life with friends, school life and loneliness. QOL is significantly lower in adolescents with headaches compared to those without. Both chronic headache and migraine are associated with a significant reduction in QOL. The results of the study show that the higher the frequency of headaches, the lower the quality of life. Also, the longer the headache is, the worse the quality of life (QOL). Chronic migraine has a negative impact on quality of life more than migraine and episodic migraine. Bursting headache (P<05) Chronic migraine has a more negative impact on quality of life than migraine and episodic migraine. Bursting headache was positively associated with quality of life ($p < 05$). The study reveals that chronic headaches are present at a fairly high frequency.

Conclusions: This is the first countrywide school-based study on the prevalence of primary headaches and headache-attributed burden in adolescents in the Republic of Georgia and reveals a significant headache-related burden. These findings are in line with previous studies, which demonstrated a high prevalence of chronic headache in adults. These studies call for the need for a country-wide headache service according to the guidelines of the European Headache Federation.

ABSTRACTS

Topic: Neurorehabiltation

EPNS25_221 - Functional outcomes in children with severe acquired brain injury post rehabilitation

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Objectives

Acquired brain injury (ABI) comprises both traumatic brain injury (TBI) and non-traumatic brain injury (non-TBI). Functional recovery of children post ABI can be varied, with rate of improvement dependent on factors such as type and severity of injury, age and psychosocial factors. This study aims to evaluate the functional outcomes of children with severe ABI enrolled in a structured Neurorehabilitation programme.

Methods

We conducted a retrospective cohort study on children up to 18 years old with severe ABI enrolled in a Neurorehabilitation programme between January 2020 and April 2023. Functional outcomes using Functional Independence Measure for Children (WeeFIM) and European Quality of Life 5 Dimension-Youth (EQ-5D-Y) scores were collected at enrolment to rehabilitation, discharge and every six months for a period of one year. Total WeeFIM score ranges from 18 (complete dependence) to 126 (complete independence). WeeFIM consists of three domains - self-care (ranges from 8 to 56), mobility (ranges from 5 to 35) and cognition (ranges from 5 to 35). EQ-5D-Y scores were recorded using a visual analogue scale from 0 to 100 (100 being the best health status reported). We analysed all patients, and TBI and non-TBI groups separately. The Friedman test was conducted to assess whether there were significant differences in outcome measures across different time points within each group.

Results

Out of 87 patients, 65 (75%) were males with a median age of 8.4 (3.4-14.4) years. 12 had TBI (13%). Median WeeFIM scores for all ABI improved from 18 (18-38.5) at enrolment to 51 (21-76.2) at discharge, 59 (21-109) at six months and 95 (35.7-117.2) at 12 months, $p<0.001$. Median WeeFIM scores of non-TBI patients showed a larger improvement [18 (18-45) at enrolment to 53 (22-78) at discharge to 96.5 (38-118) at 12 months, $p<0.001$] compared to TBI patients [18 (18-18) at enrolment to 29.5 (18.7-56.7) at discharge to 61.5 (40.7-82.2) at 12 months, $p=0.49$]. Mean EQ-5D-Y index for all ABI improved from 73.3±13.3 at enrolment to 77.7±13.4 at six months to 77.8±18.3 at 12 months, $p=0.036$. Mean EQ-5D-Y index of TBI patients showed a larger improvement (74.5±9.0 at enrolment to 84.8±15.6 at six months to 83.5±10.2 at 12 months, $p=0.13$) compared to non-TBI patients (73.1±13.9 at enrolment to 76.4±12.5 at six months to 76.8±19.2 at 12 months, $p=0.15$).

Conclusions

Patients with severe ABI who underwent neurorehabilitation were observed to have continued improvement in functional outcomes over 12 months post diagnosis.

ABSTRACTS

Topic: Neurometabolic Disorders

EPNS25_225 - Interdisciplinary Outpatient Clinic for children with mitochondrial disease- a successful approach to personalized care

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OBJECTIVES: Childhood-onset mitochondrial disorders are rare genetic diseases that often manifest with neurological impairment. To date, pathogenic variants in at least 377 genes across the nuclear and mitochondrial genomes have been linked to mitochondrial disease. The ensuing genetic and clinical complexity of these disorders poses considerable challenges to their diagnosis and management. Nevertheless, despite the current lack of curative treatment, recent advances in next generation sequencing and -omics technologies have laid the foundation for precision mitochondrial medicine through enhanced diagnostic accuracy and greater insight into pathomechanisms.
METHODS: Pediatric patients with genetically proven mitochondrial disease are seen at least annually during an interdisciplinary day-long outpatient clinic. Here they undergo in-depth physiotherapeutic testing, psychological and dietary evaluation, evaluation by a pediatric neurologist and a pediatrician metabolic diseases. This further includes participation in the GENOMIT registry with e.g. completion of the Newcastle Pediatric Mitochondrial Disease Scale (NPMDS) and Quality of Life (QoL) survey, as well as collection of biomarkers (if consented). After multidisciplinary discussion, including biochemists, geneticists, a treatment plan is agreed by the team, discussed with the parents and implemented.
RESULTS: Since the initiation in 2021, 83 pediatric and young adult patients are regularly attending the outpatient clinic at the MetabERN recognized mitochondrial expertise center in Salzburg, 16 patients deceased during follow up. Pathomechanism-based individual treatment strategies with e.g. supplementation of amino acid, ketone bodies, ketogenic diets, nicotinamide riboside or other cofactors, sirolimus etc. were initiated in the majority of patients within a named patient setting. Additionally studies e.g. evaluating the impact of a genetic diagnosis (MitoCOPE) or the adverse events after immunization (MitoVAC) have been conducted and presented in 18 peer-reviewed publications. Caregivers provided very positive feedback on the quality of patient care.
CONCLUSIONS: We highlight the importance of mitochondrial expertise centres in providing the laboratory infrastructure needed to supplement uninformative first line genomic testing with focused and/or further unbiased investigations where needed, as well as coordinating an integrated multidisciplinary model of care that is paramount to the management of pediatric patients affected by mitochondrial diseases. The positive experiences with this outpatient clinic in Salzburg lead to implementation of a comparable structure at the Dr. von Hauner Children's Hospital, Department of Pediatric Neurology and Developmental Medicine, Munich, Germany starting in early 2025.

ABSTRACTS

Topic: Neurometabolic Disorders

EPNS25_226 - Assessment of cognitive function in CLN3 patients: application of the Vineland Adaptive Behavior Scale

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Objectives

CLN3 disease manifests in early school age with vision loss, followed by seizures and progressive psychomotor regression. Monitoring cognitive decline is crucial to evaluate efficacy of new therapies. However, standard neuropsychological tests lack test batteries suitable for individuals with visual impairments. The Vineland Adaptive Behavior Scale (Vineland-3) is a psychometric tool that evaluates an individual's adaptive functioning via standardized caregiver interviews and is therefore applicable in visually impaired patients.

Methods

14 CLN3 patients (ages 8-17 years, male n=4, female n=10) were tested using the Vineland-3 with a total of 27 assessments in 1-3 follow-up exams per patient. Disease progression was categorized using an established CLN3 disease staging system which categorises four disease stages according to the onset of vision loss, epilepsy, and motor decline regardless of cognitive function levels. The analysis focused on three primary domains - communication, socialization, and daily living skills - along with their respective subdomains and the overall adaptive behavior composite score.

Results

The mean score for the communication domain was 63.4 in patients at disease stage 1 (n=6), 40.9 at stage 2 (n=8), and 30 at stage 3 (n=1). Similarly, the mean score for the socialization domain declined from 81.3 (stage 1) to 59.7 (stage 2) and 63 (stage 3). The daily living domain showed the most significant decline, with mean scores of 69.6 (stage 1), 46.3 (stage 2), and 26 (stage 3). Analysis of the three subdomains within each main domain, as well as the global adaptive behavior composite score (mean scores: 67.2 for stage 1, 44.4 for stage 2, and 34 for stage 3), also revealed a consistent decline across all three disease stages.

Conclusions

In conclusion, application of the Vineland-3 allows to assess cognitive function of CLN3 patients regardless of their progressive vision loss and supports the categorization of patients into different disease stages.

ABSTRACTS

Topic: Neurometabolic Disorders

EPNS25_227 - Inter-rater reliability of the Hamburg iCRS scale: quantitative scoring of disease progression in a cohort of infantile CLN1 patients

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Objectives

Neuronal ceroid-lipofuscinosis type 1 (CLN1) disease is caused by deficiency of the lysosomal enzyme palmitoyl-protein thioesterase 1 (PPT1). The infantile phenotype in CLN1 represents the most rapidly progressive form among all NCL phenotypes. First symptom is early developmental delay. Patients do not achieve major developmental milestones. Therefore, established NCL rating scales are not applicable. The Hamburg iCRS (infantile clinical rating scale) is a novel clinical rating scale for the longitudinal and quantitative description of disease progression in infantile phenotypes. In this study, we assessed inter-rater reliability of this scale to ensure reproducibility of the items and consistency between multiple raters with different clinical background.

Methods

The patient cohort comprised of 14 CLN1 patients with infantile phenotype (male = 10, female = 4). The Hamburg iCRS contains the following rating items: three main functional domains (gross motor function, fine motor function, and expressive language) and six subcategories (communication/interaction, visual attention, irritability/agitation, seizures, sleep and feeding). To assess inter-rater reliability, two raters (one pediatric consultant, one pediatric resident) performed longitudinal ratings independently and solely based on instruction provided in a rater manual. Cohen's Kappa was used as a measure of agreement between raters.

Results

Strong agreement among raters was defined as a Kappa value ≥0.80. All three main functional domains showed almost perfect agreement with Kappa values of 0.94, 0.83, and 0.80. Five out of six subcategories showed equally strong agreement. Only the subcategory agitation & irritability had lower Kappa values of 0.62. Here, ratings of the less experienced rater tended to be lower in score reflecting higher severity.

Conclusions

The high inter-rater reliability demonstrates that the Hamburg iCRS is a valuable tool for evaluating the therapeutic efficacy of experimental treatments for infantile CLN1 disease and is well-suited for multicenter application in future clinical trials.

ABSTRACTS

Topic: Movement Disorders/ Cerebral Palsy

EPNS25_229 - Phenotypic and genetic characterization of G protein-coupled receptor pathway genes in individuals with neurodevelopmental disorders.

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Objectives: This study aims to comprehensively characterize the clinical and genetic profiles of individuals with neurodevelopmental disorders associated with mutations in G protein-coupled receptor (GPCR) pathway genes, seeking to identify shared phenotypic traits, highlight key genetic findings, and explore their implications for diagnosis and management.

Methods: This retrospective, observational, multicenter, international study analyzed clinical and genetic data from individuals with confirmed neurodevelopmental disorders. Data collection focused on clinical presentation, neurodevelopmental domains, imaging findings, and family history.

Results: Clinical data were collected from 13 individuals, of whom 54% were male. Most diagnoses were made through clinical exome sequencing (CES, 46.2%), followed by whole exome sequencing (WES, 30.8%). Genetic variants identified included seven in GNB1, two in ADCY5, and one each in GNB2, GNB5, GNAL, and GNAI1. Consanguinity was reported in only one individual. The mean current age is 11.5 years, with a range from 1 to 39 years. Developmental delay was the most common initial symptom, present in six individuals, while other presentations included difficulties in breastfeeding (two individuals), hypertonia (one individual), cervical dystonia (one individual), and epilepsy (one individual). The most affected domain was language, with 10 individuals impacted, five of whom never developed speech. Motor impairments were noted in nine individuals, with four unable to walk independently. Cognitive assessments revealed four individuals with normal or borderline intelligence, four with mild intellectual disability (ID), two with moderate ID, and three with severe ID. Only one individual exhibited autism spectrum disorder (ASD). Eleven individuals displayed no dysmorphic features, while five had epilepsy, and MRI abnormalities were observed in four individuals. Two individuals in the cohort have died.

Conclusions: Neurodevelopmental disorders linked to GPCR pathway gene variants represent a clinically heterogeneous group characterized by developmental delays, epilepsy, and movement disorders, significantly impacting quality of life. This is an ongoing study, and we aim to recruit more individuals to expand the cohort, enabling a more comprehensive phenotypic classification and identification of inter-gene differences. Additionally, we plan to complement this work with functional studies to elucidate the molecular mechanisms underlying these disorders, advancing diagnostic accuracy and enabling personalized therapeutic strategies.

ABSTRACTS

Topic: Neurogenetics

EPNS25_231 - The Future of Genetic Testing for Global Developmental Delay in Early Childhood

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Objectives

Children with Global Developmental Delay (GDD) present phenotypic and genetic heterogeneity as well as a multifactorial etiology in which the correct diagnosis is often a challenge.

An early diagnosis is key to improve the clinical outcome and prevent further complications. Unfortunately, despite the variety of diagnostic tests available, for many this odyssey will ultimately be futile and many remain without a genetic diagnosis.

Although few cases require precise monitoring and therapy, obtaining a correct genetic diagnosis remains essential for clinical care and for the well-being of the patient and family (emotional relief and access to resources and support).

The aim is to emphasize the importance of the establishment of a well-defined referral route for the patients with GDD, as well as implementing an adequate protocol for clinical diagnosis and genetic testing.

Methods

Prospective cohort study enrolled patients aged 12 to 60 months with GDD from January, 2022, to January 2023 from a regional hospital with GDD and few minor associated signs.

Results

The study encompassed 63 patients with GDD, most of them with no signs or few signs associated. Following the guidelines it was asked microarray (positive in 12 patients) and test for Fragile X Syndrome (positive in one case).

For the rest of the patients without a diagnosis, a Clinical Exome Sequencing (CES) was requested, which was positive in 8 patients.

In some cases it was need a deep study to find the genetic diagnoses. The first step was phenotyping and clinical reassessment of the patient. After this, the different steps will include completing the study, reanalyzing previous studies, evaluating Variants of Uncertain Significance (VUS), reevaluating the data with different bioinformatics algorithms or analyzing Genes of Uncertain Significance (GUS).

Conclusions

Some patients present phenotypic signs associated with developmental delay that may suggest the presence of a syndromic genetic disorder but the majority of the patients do not present signs or present only few minor signs associated with GDD. Even in the case of the syndromic forms, the clinical signs are not always obvious enough to allow a simple diagnosis.

In conclusions, when there is no clinical suggestive diagnosis for a specific genetic test, it may be not enough to follow the actual consensus guidelines and it would be interesting to review the need of a new guideline to include other studies such as Phelan-McDermid Syndrome, which is recommended to be studied in all children with GDD.

ABSTRACTS

Topic: Epilepsy: Medical and Surgical treatment

EPNS25_232 - Analysis of initial seizure characteristics in patients with infantile onset genetic epilepsy

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Objectives

The present study aimed to investigate the initial clinical features of infantile-onset genetic epilepsy and compare initial seizure variables and responses to sodium channel blockers between *SCN1A* and non-*SCN1A* group.

Methods

We selected 122 patients, comprising 58 patients with *SCN1A* mutations and 64 patients with mutations in other than *SCN1A*, from our institutional database.

Results

Patients identified in the *SCN1A* group tended to present with fever, prolonged seizure duration, and hemiclonic seizure semiology. Clustering of seizures was found more frequently in patients from the non-*SCN1A* group. However, an overlap of seizure variables and seizure type in both groups was also noted. While sodium channel blockers aggravated seizures in more than half of the patients (21/29, 72.4 %) in the *SCN1A* group, the opposite tendency toward a favorable response to sodium channel blockers (19/30, 63.3 %) was found in those in the non-*SCN1A* group. Notably, no patient showed seizure aggravation after the use of sodium channel blockers in the non-*SCN1A* group.

Conclusions

This study highlights the need for comprehensive comparative research to guide the management of infantile onset genetic epilepsy patients.

ABSTRACTS

Topic: Epilepsy: Diagnosis and Investigations

EPNS25_234 - Development of an in vitro platform for preclinical investigations on Progressive Myoclonic Epilepsy Type 1 (EPM1)

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Objectives

Progressive myoclonic epilepsy type 1 (EPM1) is an autosomal recessive disorder caused by mutations in the cystatin B (CSTB) gene and is also known as Unverricht Lundborg Disease (ULD). Affected individuals have tonic-clonic seizures, stimulus-sensitive and action-activated myoclonus, myoclonus during sleep, and dysarthria. CSTB functions as an intracellular thiol protease inhibitor. Also, it plays a key role in brain development and regulates mitochondrial function, apoptosis, cell migration, and differentiation. Recent studies have shown that EPM1 patients and EPM1 knockout mice have GABAergic neuron impairment. Our study investigates the role of CSTB in regulating GABAergic neuron functions in patient-derived cells.

Methods

Induced pluripotent stem cells (iPSCs) were generated from EPM1 patients' dermal fibroblasts and differentiated to GABAergic neurons by forced expression of Ascl1 and Dlx2. Validation of cell identity has been performed with quantitative PCR and immunocytochemistry-based methods including western blot and flow cytometry. Different molecular techniques were used to characterize the normal and patient cell lines.

Results

CSTB expression is significantly reduced in the patient iPSCs when compared to control cells. Preliminary data suggests low AKT levels, alterations in mitochondrial function, decreased proliferation, and an increased tendency to undergo apoptosis in mutant cells. In addition. Cell cycle defects were seen in the patient's cells. In GABAergic neurons, reduced GABAergic marker expression is detected in the patient neurons after differentiation.

Conclusions

The patient-derived neurons recapitulate features seen in EPM1 patients and provide a tool to study the role of GABAergic neurons in EPM1 disease progression.

ABSTRACTS

Topic: Cerebrovascular Disorders

EPNS25_235 - Cerebrovascular Events in Pediatric Neurology Practice: Two Years of Experience in Tertiary Children Hospital

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Objectives: Stroke is cerebral damage and neurological findings that occur as a result of sudden blockage or rupture of cerebral arteries or veins. The incidence of childhood stroke is known to be approximately 2 per 100,000 person-years. But clinical data are quite limited on children. In this study, we aimed to share our stroke experience.

Methods: We retrospectively analyzed the data of patients followed up for cerebrovascular events in our center between January 2023 and December 2024. Patients were evaluated in terms of age, gender, place of application and complaint, family history, laboratory and neuroimaging features, treatment and treatment response, modified Rankin scale (mRS) scores, and etiology.

Results: A total of 29 patients were included. The mean age of the cases was 9.37 years. The majority of cases (69%) were male. 18 patients (62%) had ischemic stroke, 9 patients (31%) had hemorrhagic stroke, and 2 patients (6%) had venous thrombosis. The most common complaints were headache, vomiting, hemiparesis, seizures, unconsciousness, cerebellar findings, respectively. The mean time from the onset of complaints to presentation to a health facility was 31 hours. When we examined the patients' medical history, 17% (n=5) had a history of cardiac surgery and 10% (n=3) had epilepsy. The median D-dimer level at first admission was 2320 ug/L**.** %79 of the patients (n=23) were admitted to intensive care. Arterial dissection was detected in 3 patients, all of whom had a history of trauma. The most commonly affected vessels were middle cerebral artery (MCA) and posterior inferior cerebellar artery (PICA). The rate of patients who underwent surgery was 31% (n=9). It was found that 80% of the patients who received medical treatment were treated with only low molecular weight heparin (LMWH) and 20% were treated with both LMWH and aspirin. A sequelae-free recovery rate of 62% was detected. The mean pedNIHSS score used in arterial ischemic stroke cases older than 2 years of age was found to be 13.3. Cardiac diseases and head trauma were found to be the most common causes. Complete recovery was not observed in 91% of patients with a Pediatric (mRS) score ≥4 at presentation.

Conclusions: Childhood cerebrovascular disorders are important causes of morbidity. Pediatric stroke is among the top 10 causes of death in pediatrics. We demonstrated that clinical symptoms, diffusion MRI and d-dimer levels are important for diagnosing and treating childhood stroke.

ABSTRACTS

Topic: Neurometabolic Disorders

EPNS25_237 - Cognitive and Intellecutal Functioning in Vanishing White Matter and Metachromatic Leukodystrophy Patients: A Prospective Study

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Objectives Vanishing White Matter (VWM) and Metachromatic Leukodystrophy (MLD) are leukodystrophy subtypes characterized by neurological deterioration. Manifestations include mood changes, cognitive decline, motor dysfunction, and early death. A previous systematic review on leukodystrophies and cognitive and intellectual functioning (submitted) revealed that childhood-onset leukodystrophies result in more profound cognitive and intellectual deficits than adult-onset forms. It also emphasized the importance of considering disease stage and progression in relation to cognitive and intellectual deficits. The review also identified substantial knowledge gaps, for example in understanding how the cognitive domains are affected in more common specific leukodystrophies like VWM disease and MLD. The current study aims to build on the findings of the systematic review by investigating neuropsychological and intellectual functioning in patients with VWM and MLD. Using a standardized neuropsychological test battery, we seek to establish a detailed cognitive and intellectual profile for these patient groups.

Methods This prospective study evaluated 10 adult MLD, 4 childhood VWM and 6 adult VWM patients with genetically confirmed diagnoses. Each patient underwent extensive neuropsychological testing using a standardized test battery that assessed the key domains information processing speed, memory, language, executive functioning, attention and social cognition. Additionally, IQ was determined with standardized intellectual testing. This standardized approach was designed to address knowledge gaps by enabling direct comparisons between the two leukodystrophies and between patients at different stages of disease progression.

Results The neuropsychological and intellectual data of the MLD and VWM patients is currently being analyzed. Detailed results will be available soon.

Conclusions Building on the findings of the recent systematic review, the current study addresses critical gaps in leukodystrophy research by providing a detailed, standardized assessment of cognitive and intellectual functioning in VWM and MLD. The results will inform future longitudinal studies and contribute to the development of sensitive, disease-specific outcome measures to improve patient care and therapeutic trials.

ABSTRACTS

Topic: Neurogenetics

EPNS25_239 - Investigating the Role of the CCT7 A502V Mutation in Neurodegenerative Disorders: Insights from Computational and Functional Enrichment Analyses

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Objectives: Neurodegenerative diseases (NDs) involve progressive neuronal loss and dysfunction of the central nervous system, with poorly understood genetic and molecular mechanisms. CCT7, a key component of the TRiC chaperonin complex, aids in protein folding, especially for cytoskeletal proteins. A missense mutation in the *CCT7* gene (A502V) was found in two siblings with early-onset neurodevelopmental delay and epilepsy. This variant, listed as a "Variant of Unknown Significance" in the UniProt database, has no established link to neurodevelopmental disorders. This study aimed to investigate the hypothesis that the A502V mutation disrupts CCT7 function and contributes to impaired neurological development.

Methods: Bioinformatic tools, including SIFT, were used to predict the effects of the A502V mutation on CCT7 function. Structural modeling with the MolMol program was used to assess the impact of the mutation on protein structure, stability, and its role within the TRiC complex. STRING functional enrichment analysis and Cytoscape pathway intersection analysis were used to identify pathways involving CCT7 and their overlap with neurodegenerative disease pathways.

Results: SIFT analysis classified the A502V mutation as "Tolerated" (score: 0.30), potentially not significantly impairing protein function. However, the high conservation of the affected residue (score: 0.92) suggests its structural and functional importance. Structural modeling revealed a large central cavity in CCT7, critical for folding target proteins like actin and tubulin. While the mutation, located in an α-helix, did not disrupt the helical structure, it may affect interactions within the TRiC complex, involving 621 predicted interacting partners. STRING-based enrichment analysis highlighted critical biological processes including protein folding and stabilization, positive regulation of protein-related pathways, and cellular components like chaperonin-containing complex. Key molecular functions identified included ATP-dependent chaperone activity and protein-binding interactions. Pathway analyses also revealed links to neurodegenerative disease pathways involving proteins, such as PPP2R2B, HSPB8, PPP5C, and GBA.

Conclusions: This study used computational methods to assess the impact of the A502V variant on CCT7. While predicted to be "Tolerated," the mutation's conservation and potential disruption of TRiC complex interactions suggest that further investigation is needed. STRING analysis highlighted CCT7's role in protein folding and its association with neurodegenerative pathways. These findings provide insight into the mechanisms linking CCT7 dysfunction to neurodevelopmental and neurodegenerative disorders. Future work will include generating recombinant plasmid vectors for wild-type and mutant *CCT7* to perform functional and proteomic analyses.

ABSTRACTS

Topic: Neurogenetics

EPNS25_240 - A Nationwide Survey of Hypomyelinating Leukodystrophies in Japan; Advancing Genetic Epidemiology and Comprehensive Clinical Profiles

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Objectives: Hypomyelinating leukodystrophies (HLDs) are genetically diverse disorders caused by central nervous system hypomyelination, leading to motor and intellectual disabilities and sometimes multi-organ involvement. Previous epidemiological studies on HLDs have limitations due to selection biases, incomplete population coverage, and pre-genomic era data. This study aims to delineate and update the epidemiological, clinical, genetic, and radiological landscapes of HLDs using a comprehensive population-based approach.

Methods: We conducted a two-nationwide cross-sectional survey in Japan, targeting all medical facilities with at least one board-certified pediatric neurologist. Patients' demographic characteristics, genetic diagnoses, clinical features, and radiological findings were collected. Descriptive statistics, heatmaps, and hierarchical clustering analyzed frequencies of clinicoradiological features, natural history, and subtype relationships.

Results: The primary and secondary surveys achieved 54.7% (519/948 facilities) and 75.4% (199/264 cases) recovery rates, identifying 190 unique patients. Among the patients, 173 (91%) had a confirmed genetic diagnosis. The most common HLD was PLP1-related disorders (41%), followed by MCT8 deficiency (12%), 18q deletion syndrome (9%), TUBB4A-related hypomyelination with atrophy of the basal ganglia and cerebellum (7%), POLR3-related leukodystrophy (5%), and Cockayne syndrome (5%). Of the 78 PLP1-related disorders, duplication was the most frequent mutation type (54%), followed by missense (12%), exon3B/intron3 (9%), null (5%), and splice site (5%). The nationwide estimate was 340 patients (95% CI: 280–410), with an incidence of 1.2 per 100,000 live births and a prevalence of 1.1 per 100,000 among those under 20 years old. Heatmap and clustering analyses revealed distinct clinical and radiological patterns across HLD subtypes, confirming known features and identifying significant diagnostic clues (e.g., nystagmus, dystonia, ataxia, facial dysmorphia). Notably, pyramidal signs were rare in 18q deletion syndrome, underscoring its unique profile. Regarding regression patterns and interventions, motor regression in PLP1-duplication typically began in the second decade, later than in other HLDs. PLP1-null and exon3B/intron3 mutations require fewer medical interventions but more orthopedic surgeries. Additionally, an early diagnostic role for automated auditory brainstem response was observed in PLP1-duplication and missense mutations.

Conclusions: This nationwide survey provides a robust overview of HLDs in Japan by integrating epidemiological, genetic, clinical, and natural history data and enables more apparent genotype-phenotype correlations. These findings support earlier diagnosis, tailored patient management, and future research toward developing HLD therapies.

ABSTRACTS

Topic: Headache / Migraine

EPNS25_243 - Effect of Alpha-Lactalbumin and Sodium Butyrate in pediatric primary headache: insights into Quality of Life, clinical outcomes, and laboratory findings

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Objectives

To evaluate the effect of Alpha-lactalbumin (ALAC) and Sodium butyrate (NaBu) in reducing the frequency or intensity of headache episodes of at least 25% compared to standard treatment. A secondary interest was the correlation between change in microbiome and systemic inflammatory status, sleep quality, and QoL.

Methods

This prospective open-label study included patients <18 years with primary headache and treated for at least 12 weeks with standard therapy (T0). Participants received ALAC and NaBu for another 12 weeks (T12). Blood tests, serum cytokine (ELISA) and microbiota profiling, and validated questionnaires assessing QoL and sleep were administered at T0 and T12. The collected data were entered into an electronic database. The results obtained were analyzed using statistical software, employing a paired-sample t-test or the Wilcoxon ranked test for non-parametric alternatives.

Results

We enrolled 56 patients (64% female, mean age 11.7 years), 46% of whom had migraine and 43% tension-type headache. Forty-two patients (75%) completed the study at T12. Response rate was 80%. The median headache frequency decreased from 5 to 3 episodes/month, median duration was reduced from 4 to 2 hours, and VAS-intensity dropped from 7 to 4/10 ($p < 0.005$). Significant improvements were obtained in QoL and sleep quality. Although no significant changes were detected in the serum levels of key cytokines (IL-2, IL-6, IL-10, IL-1ß, PAI1, CGRP, CCK, MPO, and VIP), median SOD concentrations increased and NPY levels decreased significantly after treatment ($p < 0.005$). There was no difference at T12 in terms of microbiome variability in identified species, but examining the relative abundances of both genera and species, Bifidobacteria and Lactobacilli showed a significant increase, consistently with the treatment provided

Conclusions

Growing evidence of the role of the gut-brain axis and intestinal microbiota in the pathophysiology of primary headache suggests new treatment strategies. In patients with primary headache and receiving standard therapy, treatment with ALAC and NaBu reduced headache frequency, intensity and duration, and improved sleep and quality of life. Finally, serum SOD and NPY might act as potential biomarkers for treatment response.

ABSTRACTS

Topic: Neurodevelopmental Disorders / Developmental Neuroscience

EPNS25_244 - Effects of cerebellar transcranial direct current stimulation (ctDCS) in very preterm born young adults

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Objectives :Very preterm-born young adults have an increased risk for developmental disorders and aberrant brain development with neurological deficits. Cerebellar transcranial direct current stimulation (ctDCS) is becoming increasingly important as an additional tool in the treatment of neurological disorders. This study investigates whether the excitability of the cerebellar cortex is disturbed in formerly very preterm-born (VPB) young adults due to aberrant brain development and whether this can be positively influenced by means of ctDCS.

Methods: The presumed effects of ctDCS on the excitability of the cerebellum were measured using cerebellar brain inhibition (CBI). CBI is an electrophysiological measure of the strength of the connection between the cerebellar cortex and the motor cortex. ANOVA analysis was performed with the measurement factors polarity of ctDCS (anodal/cathodal/sham), time course (before/up to 2 hours after stimulation) and the inter-subject factor very preterm-born vs. control.

Results: A total of 40 subjects were studied, including 20 (VPB) young adults without neurological deficits and 20 sex-and age-matched term-born controls. CtDCS in anodal and cathodal polarity both influenced CBI significantly by means of reduced CBI measures compared to sham stimulation. There were no significant differences concerning ctDCS polarity (anodal/cathodal), time course (before/up to 2 hours after stimulation) and the inter-subject factor VPB patients vs. controls.

Conclusions: Excitability of the cerebellar cortex could be influences by ctDCS measured by CBI in VPB young adults as well as controls with anodal and cathodal polarity. Both polarities reduced CBI without showing group differences. In this highly selected group of VPB young adults the cerebello-thalamo-cortical-pathway seems to be preserved as a complex neuronal network.

ABSTRACTS

International evidence-based consensus on the management of gastrointestinal Topic: Epilepsy: Diagnosis and Investigations

EPNS25_246 - The Assessment of Neuromotor Maturity in Patients Diagnosed with Self Limited Focal Epilepsies of Childhood: Case – Control Study

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Objectives. Epilepsy is a chronic disorder which can cause cognitive and behavioral problems by affecting the central nervous system. In this study, it is aimed to evaluate the maturation of the intellectual and neuromotor development of the patients who are diagnosed with 'Self-limited Focal Epilepsies of Childhood', which are known to have favorable prognosis by the clinicians.
Methods. For the present study, we evaluated 30 patients who are between 6-12 years old and diagnosed with Self-limited Focal Epilepsies of Childhood (SeLFE) and for the control group, 30 children who are similar in age and without known neurological disorders were included. WISC-R Test was used for the assessment of the intelligence level, and INPP Screening Test, that basically evaluates balance, the ability to organize dissociated movements of the right/left halves of the body, residual primitive reflexes and postural reactions, was utilized for the assessment of neuromotor maturity of these children.
Results. In WISC-R Test, SeLFE group had statistically significantly lower scores than the control group. Upon analyzing the test results of INPP Screening Test; a total of 8 participants, 4 from each; patient and control groups of 30 people, had abnormal scores. WISC-R performance scores of the patients who had abnormal scores in INPP screening test (n = 4) were significantly lower at the border when compared with all participants who had normal scores in INPP screening test. The participants, who had low scores from WISC-R verbal and performance parts both , also showed delayed neuromotor maturation findings.
Conclusions. Our study is the first clinical study to use the INPP Screening Test to assess neuromotor maturation in patients diagnosed with epilepsy. More clinical researches are needed to find out if the clinical context of 'Self-limited Focal Epilepsies of Childhood' is truly favorable, especially in neuromotor maturity. INPP screening test provides substantial insights about brain maturation. However, many other studies should be conducted on larger groups of patients for the standardization of this test.

ABSTRACTS

Topic: Miscellaneous

EPNS25_247 - Analysis of the Persistence of Neurological Symptoms in Children with post-COVID-19 syndrome: A Systematic Review and Meta-Analysis

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Objectives

Since the onset of COVID-19 pandemic, the literature has focused on defining Long COVID or post-COVID-19 syndrome (PCS). Current studies highlight a high prevalence of neurological manifestations, including headache, "brain fog," sleep disturbances, altered smell and/or taste, fatigue, and mood disorders. This study aims to evaluate duration, prevalence, progression, and risk factors associated with neurological symptoms in pediatric patients with PCS.

Methods

A systematic review with meta-analysis was conducted using articles from PubMed, Web of Science, Scopus, and EMBASE. Inclusion criteria were observational studies, retrospective and prospective, on pediatric patients (below 18 years) with confirmed PCS and neurological symptoms, a minimum follow-up of 3 months, in studies published after 2020. Study eligibility was assessed using the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines; the Population Intervention Comparison Outcome (PICO) principle; and validated risk of bias tools.

Results

A total of 219 articles were reviewed, of which 10 met the inclusion criteria and PRISMA guidelines. The studied population included 200,365 children (58.45% male). Predominant neurological symptoms during the acute phase of COVID-19 infection were headache (48.3%), fatigue (19.1%), sleep disturbances (18.3%), and altered smell/taste (16.9%). At 6 months, olfactory/taste dysfunction decreased to 4.8%, while fatigue significantly increased to 30.9%. Headache (19.5%) and sleep disturbances (7.5%) also slightly decreased at 6 months. Few studies reported follow-up at 12 and 24 months, and none at 36 months or beyond, making it challenging to determine long-term prevalence of PCS-related neurological symptoms. Some studies identified possible risk factors, such as sociodemographic characteristics, comorbidities, increasing age, and mental disorders. The risk of bias analysis highlighted significant selection and outcome biases, especially in case series, complicating meta-analyses.

Conclusions

This review provides an initial estimate of the duration of neurological symptoms in pediatric PCS, which are highly heterogeneous in presentation and severity. Headache, fatigue, and mood disturbances are the most persistent symptoms, while smell and taste alterations decrease over time. Limitations prevented addressing all outcomes. Further research is needed to study symptom evolution and targeted interventions.

ABSTRACTS

Topic: Neuromuscular Disorders

EPNS25_248 - The real-world long term effects of nusinersen in Spinal Muscular Atrophy: safety, efficacy, and systemic impact of universally available therapy in Poland

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Objectives

Spinal muscular atrophy (SMA) is a progressive degenerative disorder characterized by muscle weakness and atrophy. It is caused by inactivating mutations in the survival motor neuron 1 (*SMN1*) gene leading to irreversible loss of motoneurons. It was the leading monogenic cause of infantile mortality until 2016, when the first disease-modifying therapy, nusinersen, was approved. In Poland nusinersen is available from 2019 within government-funded SMA therapy access program, which offers universal treatment coverage. The aim of this study was to present the real-world data of nusinersen treatment in the whole spectrum of SMA patients.

Methods

This cohort study utilized data from the Polish national SMA treatment registry, including 887 patients receiving nusinersen under standardized protocols. In order to present long-term data, only the patients who started treatment between 2019 and 2021 were included. Participants were enrolled from accredited centers following genetic confirmation of SMA. There were no exclusion criteria except for contraindications for lumbar punctures. Baseline characteristics, including SMN2 copy number and motor function (measured by CHOP-INTEND and HFMSE scales), were recorded. Efficacy was evaluated over 2 years in the whole cohort. The primary outcomes were changes in CHOP-INTEND and HFMSE scores.

Results

Of the 887 participants (52% male, children and adults, mean age at qualification: 19 years), 24% had SMA1, 24% SMA2, and 52% SMA3. Given that there was no newborn screening for SMA available until 2021, there were only 4 presymptomatic cases (0.5%) in the cohort. Motor functions improved significantly across all SMA types and stages, irrespective of the baseline motor function, age and number copies of SMN2 gene. SMA1 patients showed CHOP-INTEND gains from 0 to 15 points by month 19 ($p < 0.001$). SMA2 and SMA3 patients exhibited HFMSE improvements to 6.1 and 6.8 points, respectively ($p < 0.001$). Younger age at treatment initiation, absence of ventilation dependence, and higher *SMN2* copy numbers were associated with better outcomes. Delayed treatment initiation and worse baseline motor function was associated with poorer response. In 2021, as a result of the success of treatment, Poland implemented the newborn screening program for SMA.

Conclusions

The findings highlight nusinersen broad efficacy in improving motor function across the SMA spectrum, including advanced cases. Poland's program demonstrates the feasibility of integrating high-cost therapies into public healthcare systems, emphasizing early diagnosis, equitable access, and multidisciplinary care. These results underscore the importance of timely intervention and structured follow-up to optimize treatment outcomes in SMA.

ABSTRACTS

Topic: Neuro-Oncology

EPNS25_250 - Selumetinib Improves Cognitive Function and Modulates Brain Connectivity in NF1 Patients : A Longitudinal Study

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Objectives

Neurofibromatosis type 1 (NF1) is associated with cognitive dysfunction, which significantly impacts an individual's overall health. Selumetinib, a MEK inhibitor, has been shown to alleviate plexiform neurofibromas and improve neurocognitive abilities. This study aimed to evaluate changes in neurocognitive function and functional brain connectivity following selumetinib treatment in patients with NF1.

Methods

A cohort of 86 patients with NF1 (aged 4 to 45) was enrolled in a clinical trial investigating the effects of selumetinib on plexiform neurofibromas. Participants underwent functional magnetic resonance imaging (fMRI) scans and neurocognitive evaluations at baseline (pre-treatment), at one year, and at two years of follow-up. Functional MRI data were analyzed using the CONN toolbox, and functional network analyses were performed. For the neurocognitive assessment, age-appropriate Korean versions of the Wechsler Intelligence Scale were utilized. We then examined the relationship between changes in intelligence scores over two years and concurrent differences in functional connectivity in these patients.

Results

Among the 86 patients (53 males, 33 females), the average age at enrollment was 16.1 years. After one year of selumetinib treatment, both Full Scale IQ (FSIQ) and Processing Speed Index (PSI) had increased significantly ($P < 0.05$). At the two-year follow-up, FSIQ, Verbal Comprehension Index (VCI), Perceptual Reasoning Index (PRI), and PSI all showed significant improvements ($P < 0.05$), whereas the Working Memory Index (WMI) did not. Paired t-test analyses of changes in brain network correlation strength from baseline to 24 months revealed that the negative correlation between the Default Mode Network (DMN) and the Salience Network was significantly attenuated ($P < 0.05$), as was the negative correlation between the DMN and the Dorsal Attention Network ($P < 0.05$). No significant correlation was found between changes in Wechsler Intelligence Scale scores over time and changes in network correlation.

Conclusions

Selumetinib treatment in NF1 patients led to significant improvements in neurocognitive function. This study highlights the potential of selumetinib to enhance cognitive function and modulate brain connectivity in NF1 patients. Further research is warranted to explore the long-term effects and underlying mechanisms of these changes.

ABSTRACTS

Topic: Cerebrovascular Disorders

EPNS25_252 - Blood Pressure Profile and Evolution in Pediatric Moyamoya Disease: A Longitudinal Analysis and Revascularization Impact

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Objectives

Moyamoya is a chronic progressive cerebral arteriopathy and is one of the most important causes of recurrent stroke in children and young adults. Hypertension is often co-diagnosed in patients with moyamoya. The aim of this study was to report prevalence of hypertension in patients with pediatric-onset moyamoya and identify its clinical and neuroimaging associations.

Methods

Patients with pediatric-onset moyamoya followed at a tertiary center were included. Blood pressure (BP) was documented retrospectively at moyamoya diagnosis and was measured prospectively under stable conditions during clinical follow-up visits. BP above the 90th percentile was referred to as high BP. High BP was further categorized as elevated BP, Stage 1, and Stage 2 Hypertension.

Results

A total of 44 patients (54.4% female) were included, with a mean age of 14.6 ±6.2 years. The median age at moyamoya diagnosis was 6.95 years (IQR 4.1, 10.3). Median clinical follow-up duration was 47 months (range: 12–180 months). Thirty (68.1%) patients underwent revascularization surgeries. High BP was detected in 16 patients (36.3%), at a mean age of 9.95 years (±5.26), at a median of 1.65 years (IQR 0.3, 6.4) after moyamoya diagnosis. Among them, Stage 1 and Stage 2 hypertension were each identified in 6/16 patients (37.5%). One patient was diagnosed with midaortic syndrome, while the remaining patients did not exhibit extracranial detectable medium-large vessel vasculopathy. Patients with high BP showed significant associations with bilateral moyamoya (p=0.006), clinical stroke (p=0.038), higher composite cerebrovascular stenosis scores at last follow-up (p=0.003) and a greater number of revascularization surgeries (p=0.012). At study conclusion, blood pressure improved in 8/16 patients (50%), with all improvements occurring in patients who underwent revascularization surgery (8/13, 61.5%).

Conclusions

Approximately one-third of children with moyamoya exhibit high BP, often associated with a more severe cerebrovascular steno-occlusive disease. Revascularization surgery appears to have a beneficial impact on BP in this population. Further research is warranted to explore the mechanisms behind hypertension in children with moyamoya and to identify optimal management strategies.

ABSTRACTS

Topic: Cerebrovascular Disorders

EPNS25_253 - Headache in Children and Young Adults with Cerebral Cavernous Malformations - Clinical, Neuro-imaging and Genetic Determinants

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Objectives

Cerebral cavernous malformations (CCMs) are low-flow vascular anomalies of the central nervous system (CNS) which may be associated with neurological symptoms, including seizures and focal deficits. Although headaches are recognized in CCMs patients, their prevalence and associations remain poorly characterized. This study aimed to evaluate the prevalence of headaches in children and adults with CCMs and to identify associated clinical, genetic, and neuroimaging determinants.

Methods

A cross-sectional study on children and their first-degree adult relatives diagnosed with CCMs, performed a tertiary referral pediatric center (November 2021- December 2024). Clinical, genetic, and neuroimaging parameters were recorded. Headache was defined as the occurrence of at least two distinct episodes within a three-month period. Validated tools including HIT-6, MIDAS/PED-MIDAS, and PEDQL were used to assess headache severity, disability, and quality of life.

Results

Sixty-three patients were included [47.6% females, median age- 16.03 years, range- 3-66 years, 35 (55.5%) with familial CCMs]. Overall, 37 (58.7%) participants reported headache. Adults reported headaches more frequently than children (56.8% vs. 43.2%, $p<0.05$, OR: 0.271), with headache patients showing higher median age (20.7 vs. 12.8 years, $p= 0.019$). Patients with headache were more likely to present with headache as a presenting symptom of the CCMs (78.8% vs 47.1%, $p= 0.023$, OR: 4.179, CI: 1.178–14.824). T1-weighted MRI hyperintensity within the CCMs was associated with debilitating headaches (grade IV MIDAS, $P=0.023$). No significant associations were observed between headache and gender, positive genetic diagnosis, epilepsy, history of symptomatic bleeding, lesion number, or location.

Conclusions

Headaches are common in patients with CCMs, increasing with age but are unrelated to lesion burden. T1-Hyperintensity within the CCMs is associated with headache severity, potentially serving as an imaging biomarker for identifying patients at risk of debilitating headaches.

ABSTRACTS

Topic: Neuromuscular Disorders

EPNS25_254 - Comparison of Combination Therapy with Nusinersen and Onasemnogene Abeparvovec Versus Nusinersen Monotherapy in Spinal Muscular Atrophy Patients: A Multicenter Retrospective Study

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Objectives: Currently, there is no systematic approach to classify the various combination treatment options for patients with spinal muscular atrophy (SMA) receiving disease-modifying therapies (DMTs) or to clarify potential benefit-risk differences between treatment regimens. This study aimed to compare SMA patients with 2 SMN2 copies who received combination therapy to SMA patients with 2 SMN2 copies who received nusinersen (NS) monotherapy.

Methods: We conducted a retrospective analysis of SMA patients followed across five centers since 2017. Combination therapy was defined as concurrent use of NS and Onasemnogene Abeparvovec (OA) within the treatment period. Group A comprised patients with two copies of *SMN2* who received combination therapy, while the control group (Group B) included patients with two copies of *SMN2* who received NS monotherapy.

Results: The study included 40 SMA patients with 2 copies of SMN2 receiving combination therapy and 43 patients receiving NS monotherapy (Group B). Patients had two copies of *SMN2* (Group A) were 23.0 months (SD: 14.59, min:4-max:64 months) at OA treatment. The median age at treatment initiation was 4.25 months in GroupA and 5 months in Group B. Follow-up durations were 42.95 months for GroupA and 34.42 months for GroupB.Three patients in GroupA and two patients in GroupB achieved independent stepping, while only one patient (in GroupA) achieved independent walking. There were no significant differences between the groups in final CHOP-INTEND scores, motor function, or feeding route requirements. However, the need for respiratory support was significantly lower in the combination therapy cohort(p:0.02).

Conclusions: While combination therapy with OA and NS did not show a significant advantage over NS monotherapy in terms of motor function outcomes, it was associated with a reduced need for respiratory support. This finding suggests a potential benefit of combination therapy in respiratory function preservation. However, given the small number of patients receiving OA within the optimal treatment window and the retrospective nature of the study, further prospective research and standardized guidelines are needed to better assess the long-term efficacy and safety of combination therapy in SMA patients.

ABSTRACTS

Topic: Epilepsy: Medical and Surgical treatment

EPNS25_255 - "Let's talk about sex"-ual and reproductive health in paediatric patients with epilepsy

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Objectives: A pregnant woman with epilepsy is 10 times more likely to die during pregnancy or childbirth than those without epilepsy. Some of these deaths are preventable with improved education. In paediatrics, we are ideally placed to address issues around sexual and reproductive health (SRH) before young women and girls may become pregnant. There is little guidance on how/when this should be done and how children and young people (CYP) want to receive this information.

We sought to understand clinician knowledge around these issues and establish how National Institute for Health and Clinical Excellence (NICE) guidelines were being applied to clinical practice in the West Midlands (United Kingdom) to identify service provision gaps, with the intention of improving mortality in women with epilepsy in our region and beyond.

Methods: We conducted a service evaluation on how information relating to contraception and sexual health, planning of pregnancy, pregnancy and post-partum health was currently provided to CYP and healthcare professional confidence in providing it. A questionnaire was devised based on the NICE Guidelines "Epilepsies in children, young people and adults" expected standards and circulated to general paediatricians, specialist nurses and neurologists in the West Midlands. Two focus-groups were held with CYP and women living with epilepsy. A training day was organised as an intervention and questionnaire repeated.

Results: Results: Our initial questionnaire (n=58 respondents) revealed only 1/3 of healthcare professionals were confident in managing epilepsy in female CYP of child-bearing age. 44% felt confident about discussing contraception but only 10% felt confident in recommending and 3% in prescribing contraception. Discussions around contraception and pregnancy were not frequently held during clinic (echoed in our focus groups). 100% respondents felt education was lacking, and 100% welcomed further training. Through providing an education day a repeat survey (n=17) showed that 100% individuals had improved knowledge and skills to approaching SRH in epilepsy management.

Conclusions: We identified a service provision gap in providing information and education on SRH for CYP with epilepsy. This is also echoed from feedback from service users. By providing a focused educational programme this service gap can be addressed.

ABSTRACTS

Topic: Neuropsychiatric Disorders / Functional Neurological Disorders

EPNS25_257 - Treatment of food neophobia in children using therapeutic nutrition

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Objectives: Food neophobia in children causes various deficiencies, which impede the processes of neuroplasticity and reduce the rehabilitation potential of children with neurological disorders. This study aimed to observe the effects that the collagen hydrolyzate intake has on children with protein-energy malnutrition and food neophobia.

Methods: Prospective data evaluation of electroencephalography (EEG) with coherent analysis, biochemical blood analysis, and parent polling of 71 patients aged 4 to 8 years. The patients, all with prolonged food neophobia (2 years and more), protein deficiency, a strong preference for foods rich in carbohydrates, and delays in mental and speech development, were divided into the treatment (n=36) and control (n=35) groups. The treatment group ingested a hydrolyzed form of collagen that contained a wide range of amino acids, macro- and microelements. The intake was 8-10 grams of the product in the morning before food for 3 months. To avoid aversion among children, seven flavor options were offered. The control group underwent a standard treatment with nutritionists and psychologists.

Results: Out of the treatment group, protein levels higher than 60 g/L were registered in 31 patients (86,1%), compared to 11 (31,4%) in the control group, indicating a statistically significant difference ($p<0,05$). Normal ferritin and glycohemoglobin presence in blood was observed more frequently in the treatment group. The EEG tests showed no significant difference. In the treatment group, an increase in the coherence of the interhemispheric connections in the frontal lobe (FP1-FP2; F3-F4) was seen. The Polling data showed that the children that ingested collagen started eating better (100%), had fewer objections to food (80%), and began eating protein at will after 10 days (72%). In the control group, 48% of patients demonstrated improvements in eating behavior.

Conclusions: Collagen hydrolyzate intake by children with food neophobia and protein deficiency raises protein levels in the blood and correlates with a better eating behavior. The organoleptic properties and the simplicity of consumption of the product can help overcome the set opposition to certain foods in children with neurodeficit and food neophobia.

ABSTRACTS

Topic: Epilepsy: Diagnosis and Investigations

EPNS25_258 - Low-level mosaic scn2a variant causing early infantile onset epileptic encephalopathy: characterization using heterologous cell expression and neurons from IPSC cells

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Objectives: *SCN2A* encodes for the Nav1.2 channel, located on chromosome 2q24.3. Nav1.2 is one of the most relevant neuronal sodium channels and it is expressed in excitatory and glutamatergic neuron [Menezes et al, 2020], with a fundamental role in the initiation and conduction of action potentials [Meisler et al, 2021]. Haploinsufficiency in the *SCN2A* gene is involved in a wide range of epileptic phenotypes [Oyrer et al, 2018]. Pathogenic *SCN2A* variants are generally *de novo* germline mutations and no cases of mosaicism have been described, except for a case where paternal germline mosaicism resulted in developmental and epileptic encephalopathy (DEE) in half siblings [Zerem et al, 2014].

Methods: Two patients with seizure onset within the first three days of life and resistant to multiple anti-seizure medications (including sodium channel blockers) were subjected to next-generation sequencing (NGS) from blood. The analysis identified a *SCN2A*: c.4976C >T; p. Ala1659Val with a low-level mosaicism of 15%, confirmed on both patients' fibroblasts. The p.Ala1659Val variant was inserted in a stabilized SCN2A plasmid by site-directed mutagenesis. Expression and functional characterization of the p.Ala1659Val variant were performed in Hek293 cells by western blotting, confocal microscopy, and patch clamp. Patients' fibroblasts were cultured to reprogram them into induced pluripotent stem cells (iPSCs).

Results: No effect of the p.Ala1659Val variant on channel expression was noted, whilst a reduction of the peak current and a shift of half activation voltage towards more negative values was observed thus confirming that the selected variant is detrimental to the brain's electrophysiological function. Then to get iPSC clones derived from patients, fibroblasts were transduced with Sendai Virus to induce pluripotency. Around 50 iPSC clones were obtained. Each clone was characterized to discern between wild-type (WT) and heterozygous ones. The best clones, both WT and mutated, will be differentiated into glutamatergic neurons through neurogenin protocol to test them on MicroElectrode Assay (MEA). Mutated and isogenic neurons will be plated alone and with different grades of mosaicism on MEA and will serve to investigate the impact of sodium channel mosaicisms on brain function.

Conclusions: This study provides valuable insights into the *SCN2A* p.Ala1659Val variant's functional consequences, highlighting the utility of heterologous cell and iPSC-derived neuronal models in understanding complex neurological disorders.

ABSTRACTS

Topic: Infectious and Inflammatory Diseases/ Neuroimmunology

EPNS25_259 - Pediatric Rheumatologic Diseases Initially Presenting with Neurological Symptoms

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Objectives

Rheumatological diseases are a group of autoimmune and inflammatory diseases that can affect many organs and systems. Neurological system involvement in rheumatological diseases may include psychiatric symptoms, headache, encephalopathy, cranial nerve symptoms, seizures, myelopathy, radiculopathy or peripheral neuropathy. Although neurological involvement findings in rheumatological diseases are known; rheumatological diagnoses do not come to mind first in patients presenting with neurological complaints. In this study, it was aimed to draw attention to this situation by examining patients who were diagnosed with rheumatology despite presenting with neurological findings.

Methods

Demographic characteristics, clinical data, laboratory and imaging findings of patients aged 0-18 years who applied to the pediatric neurology clinic with neurological findings and were diagnosed with rheumatological diseases were retrospectively examined.

Results

A total of 8 patients who presented with neurological findings and were diagnosed with rheumatological diseases were identified. The patients' ages ranged from 6 to 15 years. Motor, sensory and cerebellar findings, encephalitis and headache were the initial complaints. Laboratory tests, electrophysiological tests and neuroimaging were performed on the patients according to their findings. When these patients were examined, it was seen that 1 was diagnosed with systemic lupus erythematosus, 4 with Sjögren's disease, 2 with Behçet's disease and 1 with central nervous system primary vasculitis.

Conclusions

Rheumatologic diseases should be considered when making a differential diagnosis in patients presenting with neurological findings. Patients will be discussed with their clinical, laboratory and imaging findings.

ABSTRACTS

Topic: Epilepsy: Diagnosis and Investigations

EPNS25_260 - Pattern Sensitivity in Pediatric Epilepsy and Non-Epileptic Controls: A Clinical and EEG-Based Analysis

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Objectives

In daily life, individuals frequently encounter pattern-related visuals such as ties, roller blinds, pedestrian crossing stripes, or stimulating designs in children's video games. These visuals may cause nausea, vomiting, dizziness, vision blackouts, and even seizures in both epilepsy patients and those without epilepsy. Although testing for pattern sensitivity during EEG evaluations is recommended in the follow-up of epilepsy patients, it is often not performed in many centers due to various reasons. This study aimed to determine the frequency of pattern sensitivity in individuals without epilepsy and in epilepsy patients according to subtypes. Additionally, it sought to identify which types of epilepsy and other factors pose a higher risk in this regard.

Methods

The study included patients aged 5–18 years who underwent EEG evaluations for epilepsy or suspected epilepsy. In addition to routine EEG procedures, photic stimulation, and hyperventilation, the patients were shown a series of 10 different black-and-white interlaced images for 10 seconds each, totaling 100 seconds. During this time, clinical complaints (e.g., dizziness, nausea, vision blackouts) and the effects on EEG were recorded.

Results

The ongoing study has thus far evaluated a group of patients with a mean age of 13.1 ± 3.62 years, of whom 53.8% were male. EEG abnormalities induced by pattern stimulation were observed in 9.3% of the control group and 12.7% of the epilepsy group. Clinically, complaints were recorded in 13% of the total patient group.

Conclusions

This study is one of the few to focus on epilepsy subtypes within a broad pediatric population. Compared to the existing literature, we identified a higher frequency of pattern sensitivity.

ABSTRACTS

Topic: Neuropsychiatric Disorders / Functional Neurological Disorders

EPNS25_265 - Characteristics of Neuropsychological Profiles Depending on Intelligence Level as Objective Markers for ADHD Diagnosis

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Objectives

ADHD is a neurodevelopmental disorder characterized by various cognitive features, which can differ based on a patient's intelligence level. This study aims to analyze the IQ profiles of ADHD patients with superior (above 110), normal (90-110), borderline (70-89) intelligence levels. The goal is to identify objective markers that can assist in more precise ADHD diagnosis by considering cognitive characteristics associated with different intelligence categories.

Methods

The study included 121 ADHD patients with an IQ of 70 or above, diagnosed according to DSM-5 criteria between April 2018 and June 2024, with IQ assessments conducted using the WISC-V. Patients were categorized into superior, normal, borderline groups. Key subscales such as verbal comprehension, visual-spatial reasoning, working memory, processing speed, and the cognitive efficiency index were analyzed. Statistical analyses were conducted using ANOVA and correlation tests to evaluate differences between groups

Results

The average age of the patients was 8.19±1.88 years, with a male-to-female ratio of 3.03:1 and an average IQ of 92.75±14.01. Significant differences in IQ profiles were found based on intelligence levels. Patients with superior and normal intelligence showed substantial deficits in working memory and processing speed, leading to lower cognitive efficiency. In contrast, the borderline group displayed a more uniform pattern across indices.

Conclusions

This study suggests the necessity of considering IQ profile patterns based on intelligence levels as objective markers in the diagnosis of ADHD. These findings will enable more precise and objective assessments in the ADHD diagnostic process and serve as a foundation for personalized treatment.

ABSTRACTS

Topic: Neurodevelopmental Disorders / Developmental Neuroscience

EPNS25_266 - Analysis of Next Generation Sequencing (NGS) Gene Panel Test of Patients With Developmental Disorders Including Autism Spectrum Disorders

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Objectives

The prevalence of autism spectrum disorder (ASD) has been on the rise in recent years, with a significant increase in the number of diagnosed cases. According to a 2020 report by the US Centers for Disease Control and Prevention (CDC), 1 in 36 individuals is affected by ASD. This growing prevalence has spurred significant interest in understanding the underlying causes of ASD, which are often linked to genetic factors. Research has shown that between 40% to 80% of ASD cases have genetic abnormalities, and up to 45% of these cases can be identified through genetic testing. In light of this, the primary objective of this study was to determine the rate of positive results and the specific types of mutations detected using next-generation sequencing (NGS) gene panel tests in patients with developmental disorders, particularly focusing on ASD and global developmental disorder (GDD).

Methods

The study was conducted among a cohort of 1,547 patients diagnosed with developmental disorders who visited our hospital between March 1, 2021, and December 31, 2024. Of these patients, 99 underwent NGS gene panel tests. The patients included 74 with ASD, 16 with GDD, and 9 with intellectual disability (ID). The genetic test results of these patients were thoroughly analyzed to identify potential mutations linked to their developmental disorders.

Results

The results showed that out of the 99 patients who underwent NGS testing, pathogenic mutations were detected in 1 patient, likely pathogenic mutations in 5 patients, and variants of uncertain significance (VUS) in 53 patients. Additionally, 40 patients showed normal genetic results. Some of the VUS-related genes, such as CNTNAP2, RELN, CACNA1C, GRIN2B, and SHANK2, are strongly associated with ASD. These findings underscore the complexity of interpreting genetic results in patients with developmental disorders, as many of the VUS-related genes may still require further investigation to determine their clinical significance. In this context, family testing may provide valuable insights into whether these variants are truly pathogenic.

Conclusions

The study identified pathogenic or likely pathogenic mutations in 6 patients (8.0%). A significant proportion of patients, 42.6%, had variants of uncertain significance, particularly among those with ASD. These results emphasize the need for continued genetic and family-based analyses to fully understand the role of these variants and their potential impact on clinical outcomes. Further research is necessary to clarify the clinical relevance of these findings and improve diagnostic approaches for individuals with ASD and other developmental disorders.

ABSTRACTS

Topic: Infectious and Inflammatory Diseases/ Neuroimmunology

EPNS25_267 - Bacterial meningitis associated cerebral vasculitis and infarcts– a case series

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Objectives

Bacterial meningitis is a severe infectious condition associated with high morbidity and mortality. Cerebral vasculitis is a serious complication of bacterial meningitis that can lead to cerebral infarcts, further increasing the risk of poor outcomes. Currently, no treatment guidelines or safety and efficacy studies exist for managing cerebral vasculitis in this context, particularly in children.

Methods

We present a brief case series of pediatric patients hospitalized with bacterial meningitis complicated by cerebral infarcts secondary to cerebral vasculitis. Streptococcus pneumoniae and Staphylococcus aureus were the primary causative pathogens. Cerebral magnetic resonance imaging (MRI) revealed multifocal ischemic brain lesions and extensive large-vessel vasculopathy.

Results

Based on expert opinion and a presumed inflammatory mechanism, a treatment regimen of five days of pulse intravenous methylprednisolone followed by an oral prednisone taper was added to initial heparin therapy. Patients demonstrated clinical and radiographic neurological improvement without adverse events. All patients continue rehabilitation with ongoing recovery.

Conclusions

Cerebral vasculitis is a serious complication of bacterial meningitis that can result in stroke, leading to significant morbidity and mortality. It should be suspected in patients with meningitis who, after an initial response to antimicrobial therapy, develop recurrent fever, elevated inflammatory markers, persistent decreased consciousness, or new focal neurological deficits. The combination of pulse intravenous methylprednisolone and intravenous heparin represents a novel therapeutic approach that warrants further investigation.

ABSTRACTS

Topic: Movement Disorders/ Cerebral Palsy

EPNS25_268 - Exploring potential genetic pathways in Ataxic Cerebral Palsy

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Objectives

Cerebral Palsy (CP) concerns a group of permanent disorders of movement and posture caused by non-progressive disturbances in the developing brain. Ataxic-CP (aCP) is a rare and deviant subtype (≈5% of CP cases) often associated with hypotonia. Abnormal cerebellar development and pathogenic missense variants involved in Early Onset Ataxia (EOA) are associated with aCP, raising doubts about this diagnostic CP-entity. In this work we explore and compare the underlying genetic pathways involved in the concept of aCP and EOA.

Methods

We compared known EOA genes (n=154) with genes linked to cerebellar hypoplasia and neonatal hypotonia (n=617), that were conceptually defined as representative for aCP. To elucidate shared biological pathways between EOA and aCP we performed an integrated functional enrichment analysis. Biological pathways were considered significantly enriched when $\alpha = < 0.01$.

Results

We identified 40 shared genes between aCP and EOA. The shared top pathways were specifically involved in cellular morphogenesis and development. Notably, typical EOA pathways such as lipid metabolic processes were also significantly enriched in the aCP analysis. Ciliary and cell cycle processes in early development were overrepresented in aCP compared to EOA, whereas repair mechanism pathways were more prevalent in EOA.

Conclusions

The shared biological pathways suggest aCP could be attributable to the developmental part of the EOA pathogenetic spectrum. The involvement of metabolic pathways in aCP points to potential underlying genetic etiologies. Therefore, our findings support integrating genetic testing into routine care for aCP children.

ABSTRACTS

Topic: Headache / Migraine

EPNS25_271 - Headache attributed to rhinosinusitis in pediatric patients: clinical insights and diagnostic implications

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Objectives

Headache attributed to rhinosinusitis (HRS) is relatively uncommon in pediatric patients and is frequently misdiagnosed as a primary headache disorder. This study was conducted to identify the clinical characteristics of HRS (bacterial rhinosinusitis (BRS) and non-BRS) and determine the appropriate treatment for headaches.

Methods

We retrospectively reviewed the medical records of 1,777 patients who presented with headache and underwent neuroimaging at two centers between January 2014 and December 2023.

Results

Of the 1,777 patients, 203 (11.3%) were diagnosed with HRS (47 with BRS and 90 with non-BRS). The proportion of males was significantly higher in the BRS group (76.6% vs. 57.8%, $p = 0.029$). A comparison of clinical characteristics between the BRS and non-BRS groups revealed significantly higher frequencies of respiratory symptoms in the BRS group ($p < 0.001$) and blurred vision in the non-BRS group $p = 0.034$). The BRS group demonstrated the involvement of a greater number of sinuses and more frequent use of therapies, including antibiotics and antihistamines ($p < 0.001$ for both).

Conclusions

Recognizing the clinical characteristics of BRS and non-BRS is important for the accurate diagnosis and optimal management of pain in pediatric patients with headache, as alleviating headaches significantly affects both the quality of life and academic performance.

ABSTRACTS

Topic: Epilepsy: Medical and Surgical treatment

EPNS25_273 - Ictal Autonomic Signs in Children with Drug-resistant Focal Epilepsy

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Objectives: This study investigated the frequency and types of autonomic symptoms during seizures in children with drug-resistant focal epilepsy.

Methods: Peri-ictal autonomic symptoms were evaluated in children with drug-resistant focal epilepsy who underwent video-EEG monitoring between January 2013 and January 2025. Data on demographics, epilepsy characteristics (age at seizure onset, seizure classification, etiology, interictal and ictal EEG, MRI, PET, SPECT, epilepsy surgery, and seizure outcomes) were reviewed.

Results: A total of 184 seizures from 45 patients (24 males, 53.3%), aged 2-212 months (mean 119.87 ± 64 months), were analyzed. Epilepsy etiology was structural in 34 patients (75.6%), unknown in 5 (11.1%), genetic in 4 (8.9%), metabolic and immune in one patient each (2.2%). Structural causes included cortical developmental malformations (16 patients, 47.1%), tumors (13, 38.3%), hippocampal sclerosis (2, 5.9%), perinatal insult (2, 5.9%), and porencephalic cyst (1, 2.9%). Interictal EEG showed focal abnormalities in 35 patients (77.8%), multifocal in 4 (8.9%), bilateral diffuse in 2 (4.4%), and was normal in 4. Ictal EEG was non-lateralizing in 26 patients (57.8%), localizing in 15 (33.3%), and lateralizing in 3 (6.7%); no scalpEEG changes were observed in one patient. Seizure classification included focal impaired awareness seizures with non-motor-onset (20 patients, 44.4%), motor-onset (16, 35.6%), and focal aware seizures with non-motor-onset (9, 20%). Multiple autonomic signs/symptoms were present in 27 patients (60%). The most frequent autonomic features were tachycardia (27 patients, 60%), nausea/vomiting/emesis (18, 40%), and hyperventilation (14, 31.1%). Less common findings included hypersalivation (7, 15.6%) and flashing (6,13.3 %). Other less frequent autonomic features included cyanosis, coughing, epigastric elevation/abdominal pain, perictal water drinking, ictal bradycardia, ictal spitting, pallor, hypoventilation, ictal urgency, lacrimation, and hyperhidrosis. Asystole, belching/gassing, respiratory arrest, piloerection, ictal defecation request, and ictal erection were not observed. Ten patients (22.2%) underwent resective epilepsy surgery and 2 underwent VNS. Mean age at surgery was 105 ± 54.5 months, with a mean postoperative follow-up of 45.3 ± 33.8 months, 8 patients (66.7%) achieved seizure freedom.

Conclusions: The epileptic networks are closely linked to the autonomic nervous system. Tachycardia, nausea/vomiting/emesis, and hyperventilation were the most frequently observed autonomic findings in this cohort. Ictal autonomic changes may provide diagnostic information about seizure onset zones and may have therapeutic implications particularly regarding SUDEP and may guide evaluation for epilepsy surgery.

ABSTRACTS

Topic: Neurodevelopmental Disorders / Developmental Neuroscience

EPNS25_274 - Excessive crying in very preterm infants: A temporary phenomenon or an early indicator for developmental behavioral and emotional problems?

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Objectives

Regulatory problems (RPs), including excessive crying (EC), sleeping, and feeding difficulties, occur in 5-20% of infants. Whether these problems serve as an early indicator of behavioral and emotional problems in childhood remains unclear. Preterm infants are found at increased risk to develop RPs, including EC, and problems with behavioral and emotional regulation.

This study aims to explore the relationship between crying behavior and the occurrence of behavioral and emotional problems during the first two years of life in a cohort of high-risk very preterm infants.

Methods

This prospective observational study included 329 high-risk very preterm infants, born before 30 weeks gestation and/or with a birthweight of less than 1000g. Parents reported crying behavior (hours/day) at 3 and 6 months corrected age and behavioral/emotional outcomes were assessed using the Brief-Infant-Toddler Social and Emotional Assessment (BITSEA) at 12 months and Child Behavioral Checklist (CBCL) at 24 months. Univariable and multivariable linear regression analyses evaluated associations between crying, perinatal risk factors, and behavioral outcomes. Covariates included birthweight, gestational age, sex, 5-minute APGAR scores, presence of bronchopulmonary dysplasia and maternal trait anxiety measured using the State and Trait Anxiety Inventory.

Results

Out of 329 infants (56% male, mean gestational age 28 weeks), 42 infants exhibited EC (≥ 3 hours/day) at 3 months. The mean total CBCL T-score was 49.7 and mean BITSEA problem and competence scale scores were 11.4 and 13.3, respectively. Univariable analysis showed an association between crying behavior at 3 months and higher BITSEA problem scores (ß=0.970; 95% CI [0.244; 1.697]; *p=0.*009), which was no longer significant in the multivariable model. No associations were observed between crying behavior at 3 or 6 months and CBCL scores. Maternal trait anxiety was significantly associated with scores on the BITSEA problem scale (ß= 0.356; 95% CI [0.214; 0.498] *p* =0.001) and internalizing CBCL T-scores (ß=0.394; 95% CI [0.079; 0.709]; *p* =0.015).

Conclusions

No association was found between crying behavior and emotional or behavioral outcomes in high-risk preterm infants within the first two years of life, offering reassurance to parents. Further research is needed to explore the potential impact of EC on other developmental domains.

ABSTRACTS

Topic: Neuropsychiatric Disorders / Functional Neurological Disorders

EPNS25_275 - Effects of the COVID-19 pandemic: an epidemiological analysis of brazilian hospitalization for pediatric neurotic disorders from 2019 to 2023

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Objectives: To analyse the epidemiological data of hospitalizations for pediatric neurotic disorders such as generalized anxiety, panic syndrome and social phobia in Brazil from the years 2019 to 2023.

Methods: The retrospective study was based on secondary data from DATASUS, the Department of Information and Informatics of the Unified Health System of Brazil. The ICD analyzed was of “Neurotic disorders, stress-related disorders and somatoform disorders", and the variables used were: year, age of patient, number of hospitalizations, average cost per hospitalization and average stay of the patient.

Results: The total number of hospitalizations for neurotic disorders in patients from 0 to 19 years old was 2.922. Per year, from 2019 to 2023, the number of hospitalizations was: 536, 420, 484, 711 and 771 and the age with the most hospital admissions ranged from 15 to 19 years old, with 1.666 cases. The average cost of hospitalization was 458 reais (75 dollars), and the average stay of these pediatric patients was 4,64 days in the hospital.

Conclusions: From 2019 to 2020, there was a 21.6% fall on the number of pediatric hospitalizations for neurotic disorders. An hypothesis of that would be the global health context of the COVID-19 pandemic, which overloaded the health system in Brazil and made it less possible for other medical conditions (such as neurotic disorders) to receive the proper attention and hospital space. However, in the year of 2022, after the pandemic, it's noticeable that the hospitalizations increased 46.9% if compared to 2021 and 32.6% if compared with the pre-pandemic context of 2019. This way, it is possible to infer that the pandemic context (mainly with the social distancing affecting the pediatric population, that so needs to develop emotional and social skills during this period of life) affected brazilians from 0 to 19 years old, making they more susceptible to anxiety, fear and social phobia. Finally, it is necessary for the Brazilian health system, as well as other systems around the world, to further investigate this epidemiological scenario and try to come up with solutions that minimizes damage for this population and allows children to live healthier and with fewer hospitalizations for neurotic disorders, stress-related disorders and somatoform disorders.

ABSTRACTS

Topic: Neurogenetics

EPNS25_276 - Smith-Kingsmore syndrome associated with stroke: expansion of the phenotype

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Objectives: Smith-Kingsmore syndrome (SKS) is an ultrarare genetic disorder caused by pathogenic gain-of-function heterozygous variants in the *MTOR* gene. SKS is characterised by macrocephaly, epilepsy, developmental delay, dysmorphic craniofacial and skeletal abnormalities. We describe 3 unrelated females with SKS due to de novo *MTOR* variants, and unusual novel features.
Methods: Data was collected retrospectively (across 2 different centers) following the expressed written consent of the patient and/or parents involved in their care.
Results: Individual 1 was born at 34+5 weeks gestation, with congenital macrocephaly. She required supplemental respiratory support from birth. On day 2, she developed neonatal seizures. MRI brain showed acute left MCA infarct (managed conservatively), and posterior callosal dysgenesis, ventriculomegaly and right frontal cortical malformation in keeping with SKS. She developed hyperinsulinemic hypoglycaemia requiring diazoxide. VSD, ASD and respiratory complications (supplemental oxygen until 7 weeks, OSA and laryngomalacia) were noted. Trio exome revealed *MTOR* variant pGlu2419Lys.
Individual 2, born at 35 weeks gestation presented with macrosomia, macrocephaly, ventriculomegaly, partial callosal agenesis and cardiac anomalies. Overgrowth gene panel revealed *MTOR* variant p.Thr1977Ile. At age 2 years she developed status epilepticus and ventilator dependence and was found to have diffuse alveolar haemorrhages, multifocal cerebral infarcts (MRI) and cerebral vasculitis [proximal narrowing of ACAs, MCAs, PCAs) with positive laboratory investigations for c-ANCA (1:80), ANA (1:640), anti-Histone (11.7), anti-dsDNA, and ENA]. She was treated with steroids, rituximab, and sirolimus (mTOR inhibitor). Sirolimus is continued indefinitely for activating *MTOR* variant, with excellent seizure control.
Individual 3 presented with pre-natal cardiomegaly, macrosomia and macrocephaly. By early childhood, she was profoundly delayed and had characteristic clinical features of SKS (frontal bossing, hypertelorism, café-au-lait spots, intermittent breakthrough seizures and ventriculomegaly (mild) on MRI. Trio exome identified novel *MTOR* variant p.Ser2215Thr.
Conclusions: This case series describes unusual novel features of SKS including stroke, diffuse and CNS vasculitis, while also adding to its molecular spectrum. It raises interesting questions about disease pathways involved in *MTOR*-related SKS, and empiric use of precision therapy.

ABSTRACTS

Topic: Neurorehabiltation

EPNS25_277 - Rhizotomy procedures in Brazil from 2019 to 2023: a global reference

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Objectives: Describe and analyse the data of rhizotomy procedures done by the brazilian Unified Health System from the years 2019, 2020, 2021, 2022 and 2023.

Methods: This study is retrospective and was formulated on data collected secondarily from DATASUS, brazilian Department of Information and Informatics of the Unified Health System. The data refers to rhizotomy procedures of three categories: percutaneous rhizotomy with balloon, percutaneous rhizotomy by radiofrequency and open microsurgical rhizotomy. The variables used were: year of procedure, number of procedures, average cost of the hospitalization and average hospital stay for the rhizotomy.

Results: From 2019 to 2023, 8.241 rhizotomies were performed in the Brazilian Unified Health System (representing 0.01% of all the hospital procedures made during the same time period), with the following division through the years: 1.882, 1.173, 1.325, 1.771, and, in 2023, 2.090. Also, the average cost per hospitalization for the procedure was 1465 reais (240 dollars) and the average stay of these hospitalizations was 1,2 days.

Conclusions: It is possible to infer that the global pandemic of COVID-19 impacted the rhizotomy procedures performed in Brazil, since, from 2019 to 2020, there was a fall of 37.6% in the number of those hospital procedures. This probably happened because the overload of Brazil's health system trying to fight the COVID-19 virus redirected medical and financial resources from other procedures such as the rhizotomy to the pandemic. After 2020 and 2021, it is possible to observe that the number of procedures in 2022 didn't reach the pre-pandemic context of 2019, having stayed 5.8% behind the expected. Nonetheless, in 2023, the number of rhizotomies is the highest in 5 years, 11% bigger than in 2019 and 35.9% bigger than the average number of procedures in the previous four years. This recent increase in the number of rhizotomies, together with the low number of days that a patient remains in the hospital for the procedure, demonstrates Brazil's progress in this area and its commitment with a well-performed procedure available for more people who need it. The historical and medical literature shows the country as both a pioneer on rhizotomy procedures and the current home for rhizotomy specialized centers, which, added with the recent epidemiological data collected on this study, shows Brazil as a global reference on rhizotomy.

ABSTRACTS

Topic: Epilepsy: Diagnosis and Investigations

EPNS25_278 - Characteristics and evolution of paediatric patients with status epilepticus

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Objectives

The purpose of this study was to ascertain the clinical characteristics of paediatric patients that presented with status epilepticus as their first seizure manifestation, and to know the evolution of said patients after the event.

Methods

This is a descriptive retrospective study. We identified every patient in our centre that presented with status epilepticus (convulsive or non-convulsive) in a 14-year period. Demographic and clinical information was obtained with authorization from the Medical Research Ethics Committee and recorded in an anonymized database. Statistical analysis was carried out with Microsoft Excel® software.

Results

We identified 101 patients during the 14-year period who presented with status epilepticus during the first year of epilepsy onset or at debut, according to International League Against Epilepsy (ILAE) definitions. 60% of the patients were male, and the mean age of debut was at 51 months old. Aetiological diagnosis was reached in 65.3% of the patients, genetic and structural causes being the most frequent, representing 23% of the total each. Infectious causes followed, being responsible for 19% of status epilepticus. The most common electroclinical syndrome was Dravet syndrome, diagnosed in 10% of the patients. During follow up, 92% presented further seizures, of which 49.4% were refractory. 45% met the criteria for epileptic encephalopathy. This was most common in patients with genetic causes, as 78% of those developed epileptic encephalopathy. Twelve patients received ketogenic diet, and epilepsy surgery was performed on 3 of them, but none during the status epilepticus. One patient received electroconvulsive therapy with good outcome.

Conclusions

Status epilepticus is a severe clinical condition in the paediatric patient, with long-term repercussions in a great number of patients. In our study, most patients presented with further seizures, and almost half of them developed a refractory epilepsy. Cognitive impairment in patients with status epilepticus is not uncommon in the long term, especially in patients with genetic or structural aetiology.

ABSTRACTS

Topic: Epilepsy: Medical and Surgical treatment

EPNS25_279 - Preventive therapeutic strategies in TSC-associated epilepsy in past and ongoing clinical trials

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Objectives

Tuberous sclerosis complex (TSC) is associated with high risk of drug-resistant epilepsy. A search for more effective therapies led to the use of ASM at early stages of epileptogenesis, before the onset of clinical seizures. During the last decade several trials aimed to prevent epilepsy in TSC have been performed or initiated. Our work presents the analysis of the results of completed studies and designs of the ongoing trials.

Methods

Four studies aiming to prevent epilepsy in TSC were found in the literature and in the clinical trial database (clinicaltrials.gov). Two studies: EPISTOP (NCT02098759) and PREVeNT (NCT02849457) have been completed and the results have been published. Two studies: ViRAP (NCT04987463) and TSC-STEPS (NCT05104983) are still ongoing. Additionally, an EPISTOP-IDEAL study aimed to re-analyse the data using innovative statistical methodology.

Results

Both EPISTOP and PREVeNT studies aimed to compare the effect of preventive treatment with vigabatrin versus standard of care treatment (after the onset of seizures) on epilepsy and neurodevelopmental outcomes in infants with TSC using EEG as a biomarker for epilepsy prediction. For some outcome measures, both studies yielded similar results and conclusions. For example, both studies showed the disease-modifying effect of pre-emptive vigabatrin on infantile spasms associated with TSC. None of children treated preventively in the EPISTOP trial (0%) and 20.6% in the PREVeNT study developed infantile spasms, whereas in the standard treatment groups infantile spasms were seen in 40% and 44.4% of patients in the EPISTOP and PREVENT study, respectively. Both trials also failed to show a benefit of preventive vigabatrin on the neuropsychiatric outcome at the age of 2 years. However, the overall neurodevelopmental outcome of TSC children at the age of 2 years was significantly better in both studies than in any previously reported cohort. Only EPISTOP study showed that preemptive vigabatrin reduced the risk of seizures in TSC infants. The study designs and the composition of participants might have contributed to that difference.

The authors also present current status of the two ongoing studies with mTOR inhibitors in neonates and young infants with TSC – ViRaP and TSC-STEPS.

Conclusions

Preventive trials in TSC showed that the disease modification is feasible in epilepsy. They also demonstrated the added value of the collaboration between different study teams.

ABSTRACTS

Topic: Neurogenetics

EPNS25_280 - Expanding the Clinical and Genetic Spectrum of FIG4 Mutations: Identification of a Novel Pathogenic Variant in a Case Series

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Objectives

The *FIG4* gene encodes a phosphoinositide phosphatase crucial for vesicle trafficking. In animal models, deficiency disrupts lysosomal storage and causes spongiform neurodegeneration. In humans, complete loss of *FIG4* causes Yunis-Varon syndrome (YVS), a severe multisystem disorder with Central Nervous System (CNS) dysmyelination, skeletal defects and early death. Partial loss-of-function variants cause peripheral nervous system (PNS) demyelination in Charcot-Marie-Tooth disease type 4J (CMT4J). Intermediate phenotypes with both CNS and PNS involvement have been reported. This study expands the phenotypic spectrum of *FIG4* mutations.

Methods

A retrospective case series of 4 patients with *FIG4* mutations from two tertiary centres. Clinical, radiological and genetic data were compared.

Results

All but one patient were born to non-consanguineous parents; two were first cousins. One family had a history of stillbirth with skeletal dysplasia. Most were born healthy at term, except for one born preterm at 31 weeks. Two pregnancies were complicated by poor growth and reduced foetal movements.

Patients presented between 7 weeks and 17 months with central hypotonia, global developmental delay and feeding issues. Motor and speech delay were universal. Three developed dystonia and spasticity, three had bulbar dysfunction, and two had visual defects due to macular dysfunction. Both male patients had undescended testes. Three died prematurely: two from respiratory failure and one from sudden unexplained causes. Post-mortem in one showed prominent neurodegeneration with spongiosis. Neurometabolic tests were mostly normal. MRI in three patients showed bilateral, symmetrical T2 hyperintensity of thalamic nuclei with laminar sparing, facilitated diffusion, and symmetric inferior olivary hypertrophy, pallido-nigral and white matter changes along dentato-rubro-olivary pathway. A similar MRI phenotype was seen in the other patient with thalamic sparing and extensive white matter signal changes.

Genetic analysis confirmed compound heterozygous or homozygous *FIG4* variants in all patients. A recurrent variant of unknown significance (c.1108T>C; p(Ser370Pro)) was found in three cases and reclassified as likely pathogenic.

Conclusions

Testing for *FIG4* variants should be considered in patients with central hypotonia, developmental delay, and characteristic neuroradiological and histopathological findings to enable early diagnosis and inform reproductive counselling.

ABSTRACTS

Topic: Epilepsy: Medical and Surgical treatment

EPNS25_281 - Vagal Nerve Stimulation (VNS) Parameters for Clinical Response in Pediatric Epilepsy

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Objectives

Vagal nerve stimulation (VNS) is a well-known non-pharmacologic treatment option for patients with drug-resistant epilepsy.The objective of this study was to determine the effective dose and titration time to achieve effective VNS treatment in pediatric epilepsy patients

Methods

The demographic parameters of the patients were analyzed retrospectively, and a generalized linear mixed model (GLKM) was constructed to determine the relationship between basic stimulation parameters and seizure frequency and clinical response.

Results

Among the 30 patients who participated in the study, a significant majority of 23 (76.6%) exhibited a more than 50% reduction in seizure frequency.A subsequent analysis of factors such as epilepsy duration and age at implantation revealed no statistically significant differences in the response to VNS treatment among pediatric patients.For patients undergoing treatment, the target output current was set at 1.5 mA and 10% duty cycle by the GLCM. The findings indicated that these effects were independent of the titration time of treatment ($p<0.001$).Patients who continued treatment for a longer duration exhibited a higher probability of responding to treatment, and this effect was more pronounced when the target output current and duty cycle (independent of titration time) were achieved from the dosage settings ($p=0.032$).

Conclusions

In the present study, it was ascertained that the probability of response to treatment in pediatric refractory epilepsy patients is contingent upon target outflow current and duty cycle. It was observed that the efficacy rate of treatment was low in patients who did not achieve seizure success despite reaching the target outflow current and duty cycle.

ABSTRACTS

Topic: Neuromuscular Disorders

EPNS25_283 - Juvenile myasthenia gravis and associated disorders -10-year experience of a single centre

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Objectives: Juvenile myasthenia gravis (JMG) is the most common autoimmune postsynaptic disorder of the neuromuscular junctions (NMJ) in pediatrics. JMG may be associated with acquired presynaptic defects including neuromyotonia and Morvan syndrome related to voltage-gated potassium channel complex (VGKC) and anti-contactin-associated protein-like 2 (CASPR2) beside other mostly autoimmune disorders. We present long term assessment, complications and variability of clinical course, treatment response and outcome of pediatric patients with JMG.

Methods: 14 patients with JMG at the age 7-18 years were studied. Electromyography (EMG), neurography, repetitive nerve stimulation (RNS), anti-acetylcholine receptor antibodies (AChR) anti-muscle-specific kinase (anti-MuSK) antibodies test, brain and spinal magnetic resonance imaging (MRI), autoimmune encephalitis panel voltage-gated potassium channel complex (VGKC) anti-contactin-associated protein-like 2 (CASPR2) and Leucin rich glioma inactivated 1(LGI1) antibodies test were performed**.**

Results: 13/14 patients relapsed at least on 2 occasions, of which 13 were girls and 1 boy. Onset of JMG at the age of 6-17 years, on average was > 11 years, anti-AChR antibodies were positive (+) in 11/14, seronegative JMG in 1/14, anti-MuSK antibodies + in 2/14, decremental response was 5-30 %. Frequent relapses (>3) in 11/14 patients, thymectomy was performed in 5/14 (8-19 years) in 3 transsternal in 2 video-assisted thoracoscopic, duration of remission range 2 weeks-16 years, severe active uncontrolled disease, resistant to therapy in 1/14, plasmapheresis (PF) performed in 2/14, chronic therapy: rituximab, i.v. gamma globulins (IVIG), PF (chronic for 2 years). Associated diseases were present in 5/14: autoimmune thyroiditis, sacroileitis 2/14, neuromyotonia, JMG and autoimmune encephalitis (Morvan syndrome) and positive anti VGKC and CASPR2 antibodies in 1/14, successful treatment outcome in 12/14 in pharmacological remission only 1/14 at the age 18 y in total remission.

Conclusions: The clinical presentation of JMG is very heterogeneous, therapy is generally effective, however complete remissions are rare, clinical course is usually mild to moderate with favourable outcome. Severe clinical course with short remission periods (< 3 weeks) refractory on the first and the second line immunotherapy requires immunomodulatory therapy, additional controlled clinical trials of new therapeutic approaches as well as clinical guidelines are needed. JMG may be associated with acquired presynaptic defects of NMJ. Retesting of serostatus and genetic testing is mandatory in seronegative patients with JMG and suspected congenital myasthenic syndrome (CMS).

ABSTRACTS

Topic: Movement Disorders/ Cerebral Palsy

EPNS25_285 - Quality of life of cerebral palsy - concerns of children/adolescents and their caregivers

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Objectives

To characterize the quality of life of children/adolescents with cerebral palsy and their caregivers, using questionnaires.

Methods

Observational, cross-sectional study, performed between September 1, 2023, and February 28, 2024 (6 months) of pediatric patients with cerebral palsy aged between 4–12 years followed in Neuropediatric hospital appointment. The study involved sending questionnaires to the children/adolescents with cerebral palsy and their caregivers, with questions addressing the perception of those children/adolescents regarding their friends/family, participation in activities, communication, health, adapted devices, pain, discomfort, access to services, family health, happiness and concern. The statistical analysis was made using IBM SPSS v.25.

Results

Of the 31 cerebral palsy eligible patients, 28 caregivers agreed to answer the questionnaire, and 4 children/adolescents were cognitively able to do that.

The caregiver questionnaire was about children/adolescents with median age of 7.3 years (range 3.5–10.6 years), IQR 4.8–9.0 years, 60.7% male, 92.9% with spastic cerebral palsy.

In a scale of 1 (very sad) to 9 (very happy), caregivers classified the way their children/adolescents feel about their relationship with friends/family with median 7.6, ability to participate in activities 7.3, ability to communicate 7.7, health 6.8, adapted devices 7.0, access to services 6.9, family health 6.0, happiness 9.0. From 1 (no pain) to 9 (much pain), pain 2.9. From 1 (never) to 5 (always), concern about the future 1.0.

Regarding the questionnaire answered by children/adolescents, from 1 (very sad) to 9 (very happy), the relationship with friends/family was classified with median of 8.6, ability to communicate 8.2, health 8.8, happiness 9.0, From 1 (never) to 5 (always), concern about the future 1.5.

Caregivers' answers correlated 100% with those of children/adolescents regarding communication and happiness, but no correlation was found between caregivers and children/adolescents' answers regarding the relationship with friends/family, perception of own health and concerns about the future.

Conclusions

Caregivers' perception about family health is worse than children/adolescents' happiness. The ability of children/adolescents to relate with friends/family, participate in activities and communicate is perceived better than health and access to services.

ABSTRACTS

Topic: Movement Disorders/ Cerebral Palsy

EPNS25_286 - Hypokinetic movement disorder: early parkinsonism in children

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Objectives: Hypokinetic movement disorder is rare in pediatrics. Parkinsonism is a broad term that manifests with motor signs: rigidity, bradykinesia, tremor, and speech, psychiatric and cognitive disturbances. Early parkinsonism includes the juvenile Parkinson's disease (PD), and secondary parkinsonism caused by various disorders. Patients with early parkinsonism of different etiology, clinical course and outcome are presented.

Methods: Five children age 18 months- 12 years at the onset of clinical symptoms, were assessed between 5-15 years, and investigated using next-generation sequencing (NGS), dopamine transporter single-photon emission tomography (SPECT DAT I123), brain magnetic resonance imaging (MRI), metabolic test, lumbar puncture and cerebrospinal fluid examination**.**

Results: A boy with normal motor and speech-language neurodevelopment until the age of three, manifested first with frequent falls, without signs of cognitive regression. On examination global hypokinesia, tremor provoked by stress and fever, hyperreflexia, dysarthria and frequent speech arrests with focal dystonia. SPECT DAT I123 showed reduced number of dopamine transporters and an atrophic thalamus. Compound heterozygous missense and nonsense variant in the new gene were detected as the cause of the juvenile Parkinson's disease (PD). Four children with secondary parkinsonism are presented. Boy at the age of 12 non-ambulant, with parkinsonism, dystonia and signs of corticospinal tract involvement and recurrent necrotizing encephalitis since the age of 18 months and heterozygote missense variant in RANBP2 gene. A 7-year-old boy with dystonia and parkinsonism caused by an *ATP1A3* gene variant associated with epilepsy. A 7-year-old boy with Leigh syndrome developed parkinsonism after a cerebral coma during a respiratory infection, and a 12-year-old boy with SCN8A-related developmental and epileptic encephalopathy, parkinsonism and degeneration of the basal ganglia and brainstem on MRI.

Conclusions: In patients with early parkinsonism, including juvenile PD, due to the overlap of clinical signs with other movement disorders, delay in diagnosis is not rare. DAT I123 SPECT together with NGS may enable appropriate diagnosis of early parkinsonism. Early parkinsonism, both juvenile PD and secondary parkinsonism of genetic etiology, usually manifest by a favorable response to low dose L-dopa therapy with carbidopa.

ABSTRACTS

Topic: Neurometabolic Disorders

EPNS25_287 - Niemann Pick C disease: 25yrs of experience from a tertiary metabolic centre – what do neurologists need to know in a changing diagnostic era?

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Objectives

To review clinical presentation and routes to diagnosis of children and young people with Niemann Pick Type C (NPC).

Methods

Retrospective case-note review of patients with NPC who have received care at a tertiary paediatric metabolic centre over the last 25years. Data on clinical presentation and investigations leading to diagnosis were collected.

Results

52 patients were identified; 29 female and 23 male, the oldest child was born in 2000. 24 patients are known to have died, six transferred to other centres. Age at diagnosis ranged from birth to 16y. 50% had a hepatic presentation with prolonged jaundice +/- liver dysfunction and/or hepatosplenomegaly. This patient group received diagnosis earlier than those with a neurological presentation. In six patients, a molecular diagnosis was not achieved, or a variant of unknown significance created diagnostic uncertainty. Eleven patients had a typical disease course but experienced a delay in diagnosis, in part, due to a lack of physician awareness of NPC. Two patients had an atypical presentation characterised by abrupt seizure onset in the absence of clinically obvious saccade impairment or ataxia.

Conclusions

NPC is a rare condition with a broad range of clinical phenotypes and presentations. Use of molecular diagnostics is complicated by the high prevalence of deep intronic variants; relying on genetic testing risks delays to accessing therapy. Patients who have hepatic presentations are more likely to receive an earlier diagnosis. The available therapies, which can be disease modifying, are only indicated for those with neurological symptoms so there is a greater rationale for identifying these patients quickly. Novel biochemical methods can support diagnosis rapidly and reduce the diagnostic odyssey for families, however we must improve clinical recognition of the range of clinical features of NPC to achieve this.

ABSTRACTS

Topic: Neurometabolic Disorders

EPNS25_288 - Infantile neuronopathic Gaucher disease: phenotypic spectrum and genotype:phenotype correlation from review of 250 cases

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Objectives

To describe the phenotypic spectrum of infantile (type 2) neuronopathic gaucher disease and highlight potential genotype:phenotype correlations which can be observed when patients are subclassified by nature and timing of clinical presentation.

Methods

This study had three component parts; 1 – A case-series of thirteen patients referred to a single UK centre from across Europe; 2 – Collection of additional patient cases from referring clinicians and from historical UK databases; 3 – Review of the published literature to identify additional reported cases since 1990. Literature search used pubmed searching for the following key terms "gaucher type 2", "neonatal gaucher", "infantile gaucher", "perinatal lethal gaucher", "type II", "neuronopathic gaucher" and "neuropathic gaucher". Cases were included if data was provided on genotype and/or clinical presentation.

Results

The data presented here of the combined case-series (n=13), historical unpublished cases (n=51) and published literature (n=186) provides a cohort of 250 patients. Of these, genotype data was available for 223 cases, phenotype data was available for 227 patients and thus both genotype and phenotype data was available for 200 patients. Patients could be phenotypically categorised into one of four subcategories (neonatal inflammatory, neonatal neuronopathic, early infantile neuronopathic, late infantile neuronpathic) on the basis of age and type of clinical presentation. 150 distinct genotypes were seen across the cohort, with 31 genotypes occuring more than once. In the most frequently occuring genotypes, patients also segregated phenotypically.

Conclusions

We have provided the largest single review of patients with gaucher type 2 offering both a clinical and genetic analysis. We have shown it is possible to identify genotype:phenotype correlations using a novel but simple clinical categorisation of patients at point of presentation. This system offers a platform for future clinical studies and genotype:phenotype analysis. We hope it can be utilised to identify the most appropriate candidates for therapeutic interventions and clinical trials.

ABSTRACTS

Topic: Epilepsy: Diagnosis and Investigations

EPNS25_289 - Predicting the Progression of Patients with SeLECTS Diagnosis to EE-SWAS with Artificial Intelligence

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Objectives: Some patients with self-limited epilepsy with centrotemporal spikes (SeLECTS) may progress to recurrent seizures, and epileptic encephalopathy with spike-wave activation in sleep (EE-SWAS). In this study, we aim to develop an Artificial Intelligence aided tool that will help us predict the prognosis of patients, seizure recurrence, and progression to EE-SWAS using resting-state electroencephalogram (EEG) data. Predicting these patients in advance will assist clinicians in making treatment arrangements and ensure close patient follow-up.

Methods: The study group consisted of 28 patients who progressed to EE-SWAS during a 5-year follow-up period. There were also 24 patients in the control group with a good prognosis. Electrode outputs obtained from 19 EEG channels were used for each sample. We studied electrodes targeting centrotemporal regions. MNE-Python and MATLAB applications were used to transfer EEG signals to the Machine Learning (ML) environment. First, samples were taken from the EEG signals at a frequency of 200 Hz before applying the Maxwell filter. After processing, general statistical features (standard deviation, variance, Hjorth parameters, etc.) and power spectral density features were extracted separately from each determined channel. A total of 36 features were extracted from each channel, and in total, 468 features were obtained. Using the Relief feature selection method, the most-significant 30 features were included in the classification. In terms of ML, 3-layered Artificial Neural Network (ANN), Support Vector Machine (SVM), and Random Forest algorithms were used, and 5-fold cross-validation was applied as a generalization method.

Results: Among the methods, the SVM achieved the highest classification accuracy of 0.83 (the method we developed determined the prognosis of the patients with 83% accuracy). The ANN method achieved 0.78 accuracy. The K nearest neighbor method showed the lowest performance, with 0.75 accuracy.

Conclusions: When the classification performances were evaluated, it was found that the SVM provided a high classification performance, which could compete with the results obtained in the literature. Considering these results, the use of ML approaches may facilitate the diagnosis and treatment of patients diagnosed with SeLECTS. In subsequent studies, different algorithms will be tested to detect artifactual regions in EEG signals and the performance of deep learning approaches for classification will be examined.

ABSTRACTS

Topic: Neurogenetics

EPNS25_291 - Paroxysmal Post-Traumatic Pain: Diagnosing CMT Type 2B with RAB7A Variant

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Objectives: To describe a case of an adolescent presenting with paroxysmal pain in one limb following trauma to the same area. A targeted genetic test confirmed a pathogenic RAB7A missense variant described as a cause of Charcot-Marie-Tooth (CMT) type 2B.

Methods: A 15-year-old male presented with intermittent paroxysmal pain described as sharp pain localized to the outer aspect of the left leg. The pain began after a sports-related trauma to the same leg and worsened with activity but improved with rest or distraction. Despite the paroxysmal discomfort, the pain was mild, tolerable, and did not require analgesics. Neurological examination revealed no deficits. The sensory examination was normal for pain, temperature, touch, position and vibration across all limbs. Reflexes, strength, and coordination were intact, and gait was normal. The patient's father had a confirmed diagnosis of Charcot-Marie-Tooth (CMT) type 2B due to a pathogenic RAB7A variant and presented with foot ulcers 5 years ago. A targeted genetic test for the RAB7A gene was requested for the patient after obtaining informed consent.

Results: The genetic analysis confirmed a pathogenic missense variant in the RAB7A gene, consistent with CMT type 2B. Despite the genetic diagnosis, the patient exhibited no neurological deficits, and the paroxysmal pain remained localized and mechanical**.**

Conclusions

This case emphasizes the importance of a thorough clinical history, including family history. RAB7A has been identified as a cause of CMT type 2B, a form of inherited neuropathy often characterized by sensory loss and variable motor involvement. Paroxysmal post-traumatic sensory pain may represent an early symptom of RAB7A neuropathy. Close follow-up is required to monitor symptom progression and guide management strategies.

ABSTRACTS

Topic: Epilepsy: Medical and Surgical treatment

EPNS25_292 - Comparative safety and effectiveness of Laser Interstitial Thermal Therapy versus endoscopic treatment in pediatric patients with epilepsy caused by hypothalamic hamartoma – A single-center experience

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Objectives

This study aims to compare safety and effectiveness of Magnetic Resonance Guided Laser Interstitial Thermal Therapy (MRg-LITT, LITT) and endoscopic treatment in treating pediatric patients with epilepsy syndrome caused by hypothalamic hamartoma.

Methods

A retrospective analysis was conducted on patients who underwent surgery for hypothalamic hamartoma between 2005 and 2024. Demographics, medical history, seizure onset age and semiology, Delalande classification of hamartomas, surgery and recovery time, perioperative and long-term complications were analyzed. Seizure outcome was measured in Engel and ILAE score. Statistical analysis was performed using analysis of variance to compare surgery time, postoperative recovery time, and frequency of seizure-free outcomes between patients undergoing LITT or endoscopic surgery. The follow-up period ranged from 1 to 18.8 years.

Results

The cohort included 18 patients (14 males, 4 females), divided into two groups: 7 treated with LITT and 11 with endoscopic treatment. All patients had gelastic seizures, in 9 out of 18 (50%) other types of seizures were present. In the endoscopic group, electrolyte disturbances were the most prevalent perioperative complication, occurring in 6 out of 11 (54.6%) interventions; others included hyperphagia and short-term memory deficits. Both groups experienced transient hormonal disturbances and headache. One out of seven LITT interventions resulted in permanent neurological deficit – discrete right-sided paresis. Mean surgery time was significantly shorter, at 4.2±0.5 hours in LITT group compared to 1.7±0.6 hours in the group with endoscopic approach ($p<0.05$). The hospital stay was shorter in MRg-LITT group (3.8±1.8 days versus 7.4±2 days, $p<0.05$). Complete seizure remission (Engel class I and ILAE score 1) was achieved in 85.7% (6/7) of patients in the LITT group versus 45.5% (5/11) in endoscopy group.

Conclusions

LITT, as minimally-invasive approach, demonstrates greater effectiveness than endoscopic technique in surgical management of epilepsy associated with hypothalamic hamartoma in children. In addition, it provides fewer complications and shorter recovery time after surgery.

ABSTRACTS

Topic: Epilepsy: Diagnosis and Investigations

EPNS25_293 - Infantile epileptic spasms syndrome associated with UDP-glucose-6-dehydrogenase deficiency

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Objectives: We present the clinical and molecular features of 3-month-girl with DEE associated with a pathogenic variant in the UGDH gene. This gene encodes a protein that converts uridine diphosphate (UDP)-glucose into UDP-glucuronate, which plays a crucial role in the biosynthesis of glycosaminoglycans, essential components of the connective tissue and extracellular matrix. Here we present to ultra rare disorder leads to early onset severe infantile epileptic spasm syndrome.

Methods: Three-month girl, presented with epileptic spasms, characterized by limb extension, and occurring in clusters most commonly upon awakening. The EEG showed a disorganized pattern consistent with hypsarrhythmia. Infantile epileptic spasms syndrome was diagnosed.

Results: A homozygous pathogenic variant in the UGDH gene, NM_003359.4 (c.554C>T – p.185I) reported at whole exome sequencing analysis.

Conclusions: In our knowledge, this patient is the first reported in Türkiye, contributing to the description of the clinical spectrum of UGDH gene alterations. Notably, UGDH is not included in the commercial panels for DEE and clinical exome sequencing, emphasizing the need for WES in these cases. Consequently, UGDH-related DEE may be underdiagnosed.

ABSTRACTS

Topic: Epilepsy: Diagnosis and Investigations

EPNS25_295 - Effect of 3 Hz spike-and-wave discharge on sleep spindle density in childhood absence epilepsy

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Objectives

Childhood absence epilepsy (CAE) is a common form of childhood epilepsy, characterized by frequent, brief episodes of generalized absence seizures. The diagnosis of CAE is accompanied by 3-Hz spike-and-wave discharges on EEG, which are thought to reflect abnormal thalamocortical oscillations. Sleep spindles, which are rhythmic oscillations in the 12–16 Hz frequency range, play a crucial role in cognitive functions such as memory consolidation and synaptic plasticity. The study is aims to analysis the effect of 3-Hz spike-and-wave discharges in sleep spindle density in children with CAE.

Methods

The authors retrospectively reviewed the medical records of patients who were diagnosed with CAE at Soonchunghyang university hospital. Patients who were diagnosed with CAE. The average montage waking and sleep EEGs recorded in the international 10-20 system were analyzed. The Epochs on NREM stage 2 were used, and we extract 13Hz, 14Hz, 15Hz sleep spindle on C3-average channel to analysis the sleep spindle density using the python package lunapi (https://zzz.bwh.harvard.edu/luna/). The analysis of covariance was performed, adjusting for potential confounders such as the use of anti-seizure medication and age. Since the small study populations, we selected statistically significant *P*-value as below 0.1.

Results

This study group enrolled patients for the analysis. The pSSW group had 11 subjects (mean age 8.3 ± 2.2 year-old, 9 girls) in the nSSW group had 3 patients (mean age 7.9 ± 0.5 year-old, 3 girls). A total of 7 patient was treated with anti-seizure medication(ASM) and most common ASM was lamotrigine. There were no differences in sleep spindle density regarding on ASM usage (1.04 ± 0.56 vs 1.04 ±0.56, *P*=0.95), whereas nSSW group has higher spindle density than the pSSW group (1.8 ± 0.43 vs 1.01 ±0.56, *P*=0.07) after adjusting age and ASM covariance.

Conclusions

This study investigated the impact of 3-Hz spike-and-wave discharges on sleep spindle density in children with CAE. The findings revealed that there was no significant difference in sleep spindle density associated with the use of ASM. However, the presence of 3-Hz spike-and-wave discharges was associated with significantly reduced sleep spindle density compared to the absence of spike and slow discharges. These results suggest that 3-Hz spike-and-wave discharges may impair the generation or regulation of sleep spindles, which could have implications for cognitive functions, such as memory and synaptic plasticity, in children with CAE. Further research with larger sample sizes is warranted to confirm these findings and explore their potential clinical implications.

ABSTRACTS

Topic: Movement Disorders/ Cerebral Palsy

EPNS25_297 - Efficacy of repetitive transcranial magnetic stimulation in children and adolescents with generalized dystonia: a randomized sham-controlled trial

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Objectives

Repetitive transcranial magnetic stimulation (rTMS) may modulate aberrant cortico-basal ganglia circuitry and may be harnessed for dystonia management. The primary objective of this study was to estimate the proportion of children with generalized dystonia showing ≥20% reduction in severity on Burke-Fahn-Marsden-Dystonia-Rating-Scale motor (BFMDRS-M) scores with adjunct rTMS at 12 ± 1 weeks compared to sham stimulation.

Methods

This was a double-blind, randomized sham-controlled trial (CTRI/2022/01/039806). Children (5-18 years) with non-progressive generalized dystonia with BFMDRS-M score ≥40 were enrolled. After a 4-week observation period participants were randomized to rTMS or sham groups. Allocation concealment was ensured. Antidystonia medications were kept unchanged throughout the study. Magventure model X100 with Magoption, figure-of-8 coil, 87 mm was used for rTMS. Resting Motor threshold (RMT) was calculated at left motor cortex or contralateral to most affected side. The intervention consisted of two cycles of rTMS (10 and 5 days each) four weeks apart. Inhibitory rTMS (1 Hertz): 1500 stimuli at 90% RMT; duration 45-minutes was delivered at the premotor cortex (2.5 cm anterior to hot spot using 10-20 system). Sham group received placebo stimulation with a similar protocol. Statistical analysis was performed using two-sample t-tests, Chi-square and Wilcoxon rank-sum (Mann-Whitney) tests.

Results

Fifty-five children were screened and 44 were enrolled (23-rTMS; 21-sham). Eleven children had non-lesional dystonia (7-rTMS; 4-sham) and 33 had structural lesions (16- rTMS;17-sham). Baseline characteristics were comparable. Mean age(years) was 8.7±3.4 (rTMS) and 8.3±2.6(sham). Mean BFMDRS-M score at baseline was 69.9 ± 19.3 (rTMS) and 75.7 ± 20.5 (sham). Compliance rates were 22/23 (rTMS) and 19/21 (sham). On intention-to-treat analysis, 39% (9/23) participants in rTMS group achieved ≥20% improvement in BFMDRS-M scores, compared to none in sham group [P=0.0013]. The median (IQR) percentage change in scores at follow-up was 10 (0–24) in rTMS and 3.8 (0–7.4) in sham group [P=0.016]. On Subgroup analysis, 71% (5/7) children with non-lesional dystonia compared to 25% (4/16) with lesional dystonia [P=0.028] showed ≥20% improvement with rTMS. No major adverse events were observed.

Conclusions

rTMS may reduce dystonia severity in a proportion of children with generalized dystonia. Children with non-structural etiology may respond better to this modality.

ABSTRACTS

Topic: Epilepsy: Diagnosis and Investigations

EPNS25_298 - Epilepsy in children with multiple sclerosis.

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Objectives

To analyze the prevalence, age of onset, and types of epileptic seizures in patients with pediatric multiple sclerosis (MS). To evaluate the effectiveness of anticonvulsant therapy.

Methods

An observational cross-sectional retrospective cohort study of 90 patients (29 boys, 61 girls) with pediatric MS over 9 years of follow-up (period from 2015 to 2023) was conducted. The duration of the disease ranged from 1 to 12 years [IQR: 2; 6].

Results

4 patients had epileptic seizures (4.4%), it was female in 100%, remitting MS was also in 100%. Epileptic seizures began after the diagnosis of MS in 50% (2 patients) of cases. This was not a manifestation of a clinical exacerbation. In 50% (2 patients) of cases, epileptic seizures began before the onset of MS symptoms. Foci of demyelination were already present during the MRI examination in 1 of them. The average age of onset of MS with epilepsy was 14.0 years [IQR: 13.0; 15.0]. The average age of MS onset without epilepsy was 14.0 years [IQR: 12.0; 16.0]. The EDSS score at the onset of MS in patients with epilepsy was 1.5 [IQR: 1.0; 2.0], in patients without epilepsy – 1.5 [IQR: 1.0; 2.0]. The EDSS score at the last visit in patients with MS and epilepsy was 2.0 [IQR: 1.5; 3.0], in patients with MS without epilepsy – 1.5 [IQR: 1.0; 1.5]. Epilepsy was focal in 75% of cases (3 patients), generalize in 25% (1 patient). There was no epileptic status or pharmacoresistant course in any case. In all cases, remission was achieved with the use of a single anticonvulsant drug.

Conclusions

Epilepsy in pediatric MS is more common than in the general population. Epileptic seizures may be a clinical manifestation of MS. Epileptic seizures in MS are more often focal. It is well treated with anticonvulsant medications.

ABSTRACTS

Topic: Neuromuscular Disorders

EPNS25_299 - Dual Activation of Osteoblastogenesis and Neurogenesis by Heat-Killed Enterococcus faecium in Parkinson's Disease

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Objectives

Parkinson's disease (PD) is defined by neurodegeneration, muscle atrophy, and bone deterioration, largely due to dopamine depletion. This study evaluates the therapeutic potential of heat-killed *Enterococcus faecium* FBL1 (HEF) in mitigating PD-related dysfunction through osteoblastogenesis and neurogenesis pathways.

Methods

A PD mouse model was set up using 1-methyl-4-phenyl-1,2,3,6-tetrahydropyridine (MPTP), followed by supplementation with HEF (10^9 or 10^{10} CFU/mL). Behavioral tests (rotarod, grip strength, wire hanging, forced swimming) assessed motor function. RNA sequencing and enrichment analyses identified gene expression changes and pathway activities. Histological and protein analysis quantified α-synuclein aggregation and osteoblastogenesis and neurogenesis pathway activities.

Results

In the rotarod test, MPTP-treated mice exhibited a significant reduction in walking time, 4.1 times lower than that of the normal group. However, treatment with HDF notably improved the retention time, with a dose-dependent increase, compared to MPTP group. Wire-hanging test showed enhanced muscle strength, as HEF-treated mice demonstrated a 2.1- and 3.3-fold increase in the latency to fall at low and high doses, respectively, when compared to MPTP group. Grip strength and forced swim test, further supported the findings of neuromuscular recovery and reduced immobility in the HEF treated mice. The α-synuclein aggregation in the brain and muscle induced by MPTP were attenuated by HEF. Volcano plot analysis of muscle tissue revealed that MPTP treatment caused significant dysregulation, with 142 upregulated and 163 downregulated genes, including the downregulation of Wnt signaling-related genes Astn1 and Frat2, which are involved in neurogenesis and muscle regeneration. Conversely, the osteogenesis-related gene Pbx1 was upregulated by HEF, compared to MPTP treated group. Treatment with HEF also restored gene expression, notably increasing Tnxb, essential for tissue integrity, and Gsn, involved in various biological processes, compared with MPTP. Key markers of skeletal muscle differentiation (Myf5, MyoG, Myh1), osteoblastogenesis (Bmp2, Bmp4, SMAD1/5/8, RUNX2), and neurogenesis (Wnt3a, β-catenin, TCF1, LEF1) were downregulated in MPTP-induced PD but restored by HEF. Inflammatory markers (TNF-α, iNOS, and NF-κB) were significantly elevated in the MPTP group. However, these levels were reduced by HEF in a dose-dependently.

Conclusions

This study highlights the pivotal role of osteoblastogenic (BMP/SMAD signaling) and neurogenic (Wnt signaling) pathways in maintaining muscle and bone homeostasis in PD. HEF offers a novel therapeutic approach targeting the BMP/SMAD and Wnt signaling pathways to mitigate muscle and bone degeneration in patients with PD.

ABSTRACTS

Topic: Neurogenetics

EPNS25_301 - Novel insights to how MAEA loss impairs DNA repair and replication and leads to developmental delay; 7 cases presenting in childhood

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Objectives

Ubiquitin E3 ligases play crucial roles in the DNA damage response (DDR) by modulating spatio-temporal turnover, cellular localization, activation and interactions of key DNA repair and replication proteins. This study seeks to uncover the function of an E3 ubiquitin ligase called MAEA in the DDR, as well as its role in a neurological phenotype and developmental delay observed in children affected by a variant in in the gene.

Methods

We performed a CRISPR-Cas9 screen focused on ubiquitin E3 ligases and related proteins. By using camptothecin, a DNA damage- and replication stress-inducing topoisomerase I poison, we identified the CTLH E3 ubiquitin ligase complex — and particularly its core subunit, MAEA — a novel player in homologous recombination and DNA replication. Furthermore, we identified 7 children (3 male and 4 female, aged 4-16 years) bearing putative loss-of-function MAEA variants who present with nonsyndromic global developmental delay.

Results

Molecular and cellular phenotyping with replication inhibitors and other S-phase-toxic drugs revealed MAEA and other CTLH complex members play a role in homologous recombination. DNA fiber assays demonstrated that MAEA loss and the patient variants confer severe DNA repair and replication deficiencies. Finally, we identify that MAEA null cells struggle to form RAD51 foci when challenged with IR or camptothecin, indicating the point at which MAEA may function in homologous recombination and DNA repair.

Conclusions

We propose a model wherein MAEA loss prevents efficient RAD51 loading and leads to impaired homologous recombination and DNA replication. Without RAD51, replication forks are unprotected and fork restart is difficult, as observed in our data. This may explain the developmental delay observed in our cohort. In sum, MAEA is a novel DNA replication and repair regulator with the potential to guide both diagnostic and therapeutic approaches in patients.

ABSTRACTS

Topic: Neurometabolic Disorders

EPNS25_302 - EIF2B5 gene augmentation therapy improves molecular and clinical signs in a murine model of vanishing white matter

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Objectives: Vanishing white matter (VWM) is an autosomal recessive neurological disorder mostly affecting children. It is characterized by degeneration of central nervous system (CNS) white matter resulting in progressive ataxia, spasticity, and cognitive decline. Additionally, patients often experience episodes of rapid decline triggered by stressors like fever or minor head trauma, leading to significant disability and premature death. This disorder is caused by mutations in the genes encoding the α-ε subunits of eukaryotic translation initiation factor 2B (eIF2B), which impair its functionality. There is no curative treatment available for VWM.
This study aimed to utilize adeno-associated virus (AAV) vector-based gene therapy to express human *EIF2B5* coding sequences, thereby restoring eIF2B activity within the CNS and mitigating disease symptoms in a murine model of VWM (*Eif2b5*$^{R191H/R191H}$, i.e. VWM mice).

Methods: Healthy control and VWM mice were treated with either a placebo or AAV vectors via intracerebroventricular injection at postnatal day 0. AAV vectors with high CNS tropism were used, containing a constitutive promoter driving either human *EIF2B5* or mouse *Eif2b5* transgenes. Additionally, a bicistronic vector expressing both human *EIF2B5* and green fluorescent protein (GFP) was utilized to evaluate AAV biodistribution across the brain and among different cell types. Treatment effects on molecular and clinical outcomes were assessed using quantitative PCR for vector copy number (VCN) analysis, Western blotting, flow cytometry, immunofluorescence and locomotor function tests.

Results: Both human *EIF2B5* and mouse *Eif2b5* AAV vector groups showed significant clinical improvements compared to saline-treated control VWM mice. Biodistribution analysis revealed higher VCN and eIF2Bε protein levels in anterior brain regions compared to posterior regions. VCN of FACS-sorted astrocytes and immunofluorescence analyses indicated preferential transduction of astrocytes. Flow cytometry of whole-brain isolated single cells showed transduction of approximately 10% of total astrocytes.

Conclusions: This preclinical study demonstrated robust improvements of clinical signs in VWM mice and partial restoration of cellular function, by primarily targeting astrocytes. The long-lasting improvement of clinical symptoms underscores the potential of CNS-directed AAV-based gene augmentation for treating severe disabilities associated with pathogenic *EIF2B5* variants in VWM patients.

ABSTRACTS

Topic: Epilepsy: Diagnosis and Investigations

EPNS25_303 - The EpiLing-Tool- a new diagnostic tool to identify dissociative seizures by taking the patient´s history

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Objectives

Studies have shown that conversation analysis (CA) of doctor-patient-encounters can help to differentiate between epileptic seizures (ES) and dissociative seizures (DS).In a translational approach we aimed to develop a reliable, non-instrumental diagnostic tool for the distinction between ES and DS in pediatric patients that takes the individual`s seizure description into account. We hence familiarized clinicians with linguistic features contributing to either diagnosis in order to enable them to perform CA-based analysis on doctor-patient encounters.

Methods

We analyzed 80 recorded doctor-patient-encounters with young seizure patients (aged 6.1 to 17.9 years, mean 13.9 years). Conversations followed a guideline emphasizing the importance of non-directive conversation and open invitations for patients to talk. Based on the acquired data we created a scoring table - the EpiLing-Tool - presenting two sets of eight items, either favoring a diagnosis of ES or DS by focusing on the depiction of individual seizure perception, attitude towards the seizure, seizure interruption strategies and the course of the conversation. We performed two one-day-training sessions in which clinicians blinded to the medical diagnosis used the EpiLing-Tool on recordings of patient interviews. In the first session 50 participants rated 11 recordings, in the second ten recordings were rated by 25 participants

Results

An average of 30.7 EpiLing-Tools (range 9 to 49) were completed for every recording per patient. In the eight patients with DS, the correct diagnostic conclusion was documented in 205 of 236 ratings using the EpiLing-Tool (sensitivity 86.9%). In the ES group the correct scoring result was identified in 364 of 409 (sensitivity 89.0%). The EpiLing-Tool`s sensitivity in this group did not differ between the five patients with focal ES (sensitivity 88.6%), and the eight patients with generalized ES (sensitivity 89.2%).

Conclusions

The EpiLing-Tool is a simple to administer, cost-effective and promising scoring table that can help clinicians to recognize DS when they first take the history of children and adolescents with seizures. CAVE: Ad hoc use could lead to false results! Doctors without linguistic training should take part in a training course.

ABSTRACTS

Topic: Neurometabolic Disorders

EPNS25_304 - Living with pyruvate dehydrogenase complex (PDHc) deficiency in Sweden: Parent experiences

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Objectives: The objective of the study was to gain a comprehensive understanding of the experiences of parents of individuals with pyruvate dehydrogenase complex (PDHc) deficiency in Sweden.

Methods: Semi-structured interviews were conducted via telephone or videoconferencing with parents of 32/46 living patients (70% of total population in Sweden; median age 14 years) with PDHc deficiency. Data was recorded, transcribed and analysed using thematic analysis.

Results: Thematic analysis resulted in nine main themes: Journey to Diagnosis and Aftermath, Ketogenic diet as key, What helps? What hinders? A different life, Impact on parents, Impact on siblings, Uncertain future, and Milder cognitive difficulties. The journey to diagnosis was often complex but diagnosis brought relief and treatment. The ketogenic diet requires effort, but parents believe that it ultimately helps their child. Support for families comes in the form of supportive school personnel, respite care and other affected families. However, caregivers often face barriers in the form of a lack of integrated care and authorities who do not understand their child's needs, resulting in parents needing to coordinate healthcare and battling with authorities for supports. Having a child with PDHc deficiency creates a different lifepath. Some parents come to acceptance of their situation but feel that no one fully understands. Parents often experience a negative impact on their mental health and sleep and their careers. Siblings can also be negatively affected but they may also take more responsibility and mature quicker than peers. Parents perceive the future as uncertain as they worry about their child's mortality, transition to adult healthcare. Parents of children with a milder phenotype perceive that their child's condition is often hidden, and that their child is not supported as well they might be.

Conclusions: The responses of parents highlight the wide-ranging impact of PDHc deficiency on the family. Parents see the ketogenic diet as key to their child's wellbeing and could identify good examples of provision in school and the health sectors. However, parents often lack the support and must take responsibility themselves to coordinate their child's care. Parental sleep and mental health is often negatively affected. Collaboration between medical, disability and educational services and a more responsive social care system is essential in provision of care of individuals with PDHc deficiency.

ABSTRACTS

Topic: Epilepsy: Diagnosis and Investigations

EPNS25_306 - Understanding and Modeling the Dravet Syndrome Diagnostic Pathway: DS'coverED Study Results

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Objectives: Dravet syndrome (DS), a rare developmental and epileptic encephalopathy, is often diagnosed with delays that hinder timely therapeutic interventions. The DS'coverED study aimed to understand the diagnostic pathway for infants with DS, evaluate its duration, and identify opportunities to improve the diagnostic timeline.

Methods: A European Steering Committee including eight neuropediatricians and one European Dravet Syndrome Federation representative designed an online survey sent to pediatric neurology centers across Europe. The survey included 12 questions about physicians' practice and 25 questions addressing patients' diagnostic journey, from seizure onset to diagnosis and DS-specific anti-seizure medication (ASM) initiation, including stiripentol, fenfluramine and cannabidiol. One question allowed physicians to propose suggestions to optimize the diagnostic timeline.

Results: Fifty-three physicians shared their practices, and 45 patient profiles were completed. Among respondents, 85% work at university hospitals and 53% have over 15 years of DS experience. DS diagnosis was confirmed to families after genetic test results in 94% of cases. Patients' diagnostic journey included the following milestones (mean patient age): first seizure (5.9 months), consultation with a neuropediatrician with experience in DS (13.4 months), genetic test prescription (14 months), DS mentioned to family (16.8 months), genetic test results (18.6 months), formal DS diagnosis announcement (19 months), and DS-specific ASM initiation (26.7 months).
Two significant delays were identified:
- 7 months (standard deviation (SD): 12 months) to consult a DS specialist from seizure onset. This may be attributed to delayed referral to expert centers and limited DS awareness among non-specialists.
- 8 months (SD: 12 months) between formal diagnosis announcement and initiation of DS-specific ASM. Contributing factors include patient age, seizure frequency and duration, availability of DS-specific drugs at diagnosis, and physician confidence in prescribing these treatments.

Conclusions: These insights provide a framework for addressing DS diagnosis delays and highlight the need for practical measures. Improving access to expert centers, raising awareness of DS clinical features and benefits of early initiation of DS-specific ASMs could improve patient management and quality of life.

ABSTRACTS

Topic: Epilepsy: Diagnosis and Investigations

EPNS25_307 - Genetic test outcome in Infantile Epileptic Spasms Syndrome: A single centre study

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Objectives: Infantile spasms are a type of epileptic seizure which presents between 1 month to 2 years of age. There is evidence that early recognition and investigations towards aetiological diagnosis leads to precision treatment and may improve neurodevelopmental outcome. We conducted an audit of infants presenting with infantile spasms to analyse whether the diagnostic pathway was followed and if investigations were done to look for aetiology.

Methods: Data was obtained from 14 infants after auditing outpatient clinic letters and inpatient clinical notes retrospectively over a 5-year period (2019-2024). The parameters explored were a) Diagnosis of Infantile Spasms for treatment b) Whether investigations were performed in given time frame c) Aetiology

Results: All 14 infants had classic seizure descriptions. 4 (28.5%) infants were treated based on event semiology alone whereas the remaining 10 (71.4%) were treated based on clinical and EEG findings of hypsarrhythmia (classic/modified) or epileptic encephalopathy. 12/14 (85.7%) had an EEG within 24 hours and 2/14 (14.3%) within 48 hours. 11/14 (78.5%) had an MRI brain within 7 days; 1 was in tertiary centre, 1 had a month prior to seizure onset and 1 had the MRI after 15 days due to an existing genetic diagnosis. Aetiology was determined in 9 (64.2%) infants. Genetic causes were identified in 6 (42.8%), of which 3 were positive microarray 1p36 deletion, 10p15.3,16p11.2 microdeletions and the other 3 were positive genome sequencing for TUB1, TLK2 and CDKL5 pathogenic variants. 1 had hypoxic-ischaemic encephalopathy, 1 had brain injury following in-utero Parechovirus encephalitis and 1 had multi focal cortical dysplasia. 1 with 1p36 deletion had corpus callosum thinning with cerebral atrophy and 1 with lissencephaly on MRI was positive for TUB1 pathogenic variant. All 14 infants had a negative metabolic screen.

Conclusions: Majority of the cohort were treated based on clinical and EEG findings. Most infants had an EEG and MRI brain within the timeframe of 24 hours and 7 days respectively. Although a small cohort, a significant percentage had an aetiological diagnosis. Genetic cause (42.8%) was highest compared to infective, hypoxic and structural ones. The analysis suggests that genetics is the principal test that identified aetiology in infants after presentation with seizures.

ABSTRACTS

Topic: Neurodevelopmental Disorders / Developmental Neuroscience

EPNS25_308 - The prevalence of developmental delay and neurodevelopmental disorders in a large cohort of patients with achondroplasia

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Objectives: This project aims to better understand the rates of developmental delay and neurodevelopmental disorders in patients with achondroplasia. Achondroplasia is the most common genetic cause of short stature world-wide and is associated with a range of skeletal abnormalities and resultant chronic sequalae. Due to anthropomorphic differences, the developmental profile in achondroplasia is known be unique, particularly in the area of gross motor skills, with skills such as independent sitting and walking often being achieved later than other children. Achondroplasia it is not thought to be associated with neurodevelopmental abnormalities. It is noteworthy however that other conditions caused by variants in same gene (*FGFR3*) are associated with higher rates of neurodevelopmental abnormalities. There is also increasing anecdotal evidence of higher rates of neurodevelopmental disorders in achondroplasia patients. This relationship is however poorly explored and warrants further assessment.

Methods: Retrospective developmental milestones and neurodevelopmental data was collected from all individuals with a diagnosis of achondroplasia seen by the Achondroplasia MDT service. Data regarding additional procedures and diagnosis was also collected. Developmental data was compared to the gold standard achondroplasia development charts (*Ireland et al.*), using the 90th percentile cut-off for delays. Neurodevelopmental disorder rate, in particular Autism, ADHD and Special Education Needs in this cohort was compared to population prevalence.

Results: In this study, data from 240 children with achondroplasia was included. In total 52 children (21.6%) had a delay in one or more developmental domains with respect to achondroplasia milestones. Looking at specific milestones (Independent walking and first word), the proportion greater than the 90th centile cut-off for delay was not statistically different to that seen in the Australian cohort assessed by Ireland *et al.* When assessing neurodevelopmental disorders, statistically higher rates of autism (Bonferroni corrected p=0.0032) were seen in this cohort when compared to population prevalence. When assessing the rates of special education needs, the cohort as a whole did not have higher rates of special education needs compared to population prevalence. When specifically assessing those with a developmental delay there was a higher rate of long term special education needs when compared to population prevalence (Bonferroni corrected p=0.031).

Conclusions: This large cohort provides valuable insights into the extent of developmental delay and neurodiversity in achondroplasia patients. It offers further evidence of increased neurodevelopmental disorders, particularly autism, and highlights a potential link between early developmental delays and long-term special education needs in Achondroplasia patients.

ABSTRACTS

Topic: Neurodevelopmental Disorders / Developmental Neuroscience

EPNS25_309 - Comparison of NLRP3 and RANK-RANKL-OPG Pathway-Related Gene Expression Levels in Children with Autism Spectrum Disorder, Their Typically Developing Siblings and Healthy Control

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Objectives
It has been thought that increased proinflammatory cytokines may be associated with behavioral and cognitive problems seen in autism spectrum disorder (ASD). We aimed to evaluate the gene expression levels of NLRP-3 and OPG-RANKL-RANK inflammasome pathways in children with ASD, their typically developing siblings, and healthy control and the correlation between gene expression levels and severity of autism core findings in ASD.

Methods

Fifty children aged ≥3-18 years who were diagnosed with ASD were included in the study group- AC group. A total of 50 typically developing children (34 were siblings of the study cases- HSAC group and 16 healthy control- HC group) aged ≥3-18 years were included as the control group. The expression levels of interleukin beta, caspase 1, NLRP3, NLRP1, TNFRSF11B, TNFRSF11A and TNFSF11 genes located in the OPG-RANKL-RANK pathway were measured. The severity of autism core findings was determined by the CARS test, Turkish School Age Language Development Test (TODİL), Turkish Early Language Development Test (TEDİL) and Turkish Communication Development Inventory (TİGE) scores, and the scores obtained from these tests were correlated with gene expression levels.

Results

No statistically significant difference was found between the expression levels of 7 genes in the AC, HSAC and HC groups and correlation between gene expression levels and severity of autism core symptoms.

Conclusions

Although there is no evidence that the NLRP-3 and OPG-RANKL-RANK inflammasome pathways are active in ASD cases between ≥3-18 years, studies evaluating the role of these pathways in neuroinflammation in earlier periods of life are needed.

ABSTRACTS

Topic: Neuro-Oncology

EPNS25_310 - Acute CNS Complications of Chemotherapy in Children with Oncological Diseases

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Objectives

The Aim of the study is to investigate the frequency and clinical manifestations of acute CNS complications in children with oncological diseases undergoing chemotherapy.

Methods

A retrospective study was conducted on 396 children treated with chemotherapy between 2013 and 2023. Oncological diagnoses included: acute lymphoblastic leukemia 92 (23.2%); malignant lymphomas 69 (17.4%); bone tumors (osteosarcoma and Ewing sarcoma) 58 (14.6%); brain tumors 43 (10.9%), neuroblastoma 37 (9.3%), nephroblastoma 18 (4.5%), germ cell tumors 18 (4.5%), soft tissue sarcomas 17 (4.3%), and other rare malignancies 28 (7%). Clinical examination, biochemical tests, CNS imaging (CT, MRI angiography), cerebrospinal fluid analysis, virological and serological tests, prothrombotic factor analysis, metabolic, genetic, immunological tests, and EEG were used

Results

CNS complications were observed in 21 patients (5.3%). Diagnoses included acute lymphoblastic leukemia (n=10), acute myeloid leukemia (n=2), non-Hodgkin lymphoma (n=3), CNS tumors (n=3), and extracranial solid tumors (n=4). Specific complications included PRES-6 (1.5%), intracranial hemorrhage-2 (0.5%), venous sinus thrombosis with hemorrhage-1 (0.25%), fungal infection-3 (0.75%), meningitis of unspecified etiology- 1 (0.25%), generalized CMV infection-1 (0.25%), holoxan encephalopathy-2 (0.5%), post-radiation encephalopathy-2 (0.5%), and autoimmune encephalitis-3 (0.75%).

Conclusions

A comprehensive understanding of CNS neurotoxicity in pediatric oncology patients facilitates prevention and proper management, improving survival and quality of life. Acute CNS complications from chemotherapy present diverse clinical and neuroimaging features, with PRES being the most common and generally having a favorable prognosis. CNS fungal infections and hemorrhages were associated with the poorest outcomes. Overlapping complications often complicate diagnosis and treatment, necessitating a multidisciplinary approach for effective management.

ABSTRACTS

Topic: Cerebrovascular Disorders

EPNS25_311 - Recurrent arterial ischemic stroke in pediatric patients

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Objectives: to analyze the frequency and causes of recurrent arterial ischemic stroke (AIS) in pediatric patients.

Methods: 127 pediatric patients with AIS were analyzed. The average age at the time of AIS development was 7 [IQR: 6.2; 9.5] years; the average age at the time of analysis – 13 [IQR: 11.7; 15.8] years. Recurrent AIS occurred in 24 (18.9%) patients: 16 (66.7%) boys and 8 (33.3%) girls.

Results: 10 (41.7%) patients had recurrent AIS within 30 days from the first case, and 14 (58.3%) patients had recurrent AIS later than 30 days from the first case. There were the following etiological factors of AIS in patients with recurrences: prothrombotic abnormalities – in 6 (25%) patients, arteriopathy – in 8 (33.3%), infectious diseases – in 4 (16.7%), cardiogenic pathology – in 3 (12.5%), hypoplasia of cerebral vessels – in 2 (8.3%), other etiological factors – in 5 (20.8%). 4 patients had 2 etiological factors.

The following reasons are likely to have led to the recurrent AIS: insufficient dose of antithrombotic drugs or not taking them after the first case of AIS was indicated in 19 (79.2%) patients; the delayed surgical treatment in moyamoya disease – in 3 (12.5%) people; insufficient dose of antithrombotic drugs and/or delayed X-ray endovascular occlusion of the patent foramen ovale – in 2 (8.3%) patients.

Recurrent AIS was more common in patients with moyamoya disease rather than other etiological factors ($p_{Chi\text{-}square}$=0.004, OR=6.5 [95% CI: 1.6; 26.5]); in patients with insufficient dose of antithrombotic drugs or not taking them after the first case of AIS ($p_{Chi\text{-}square}$=0.000, OR=0.04 [95% CI: 0.01: 0.32].

We have developed a prognostic model for predicting recurrent AIS in children, including such independent factors as age (p=0.026, OR=1.01, [95% CI: 1.00-1.02]), taking antithrombotic treatment after the first case of AIS (p=0.000, OR=0.09, [95% CI: 0.02-0.34]) and moyamoya disease (p=0.002, OR=15.78, [95% CI: 2.71; 92.03]), (AUC=0.85±0.036 [95% CI: 0.78; 0.92]). The sensitivity and specificity of the developed prognostic model at a cut-off grade of 22.6% were 83.3% and 81.6% respectively.

Conclusions: the main factors for recurrent AIS in pediatric patients are an insufficient dose of antithrombotic drugs, failure to take them after the first case of AIS, and moyamoya disease.

ABSTRACTS

Topic: Neurogenetics

EPNS25_312 - Deciphering genetic diagnosis in paediatric epilepsy disorders

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Objectives: Pediatric epilepsies are heterogenous group of multifaced and complex disorders. Timely diagnosis and proper management strategies are crucial for adequate therapeutic treatment, better prognosis and outcome. Genetics plays an important role in approximately 30-50% of epilepsy cases. Implementation of next-generation-sequencing (NGS)-based tools, such as WES (whole exome sequencing), WGS (whole genome sequencing) as diagnostic tool, reduces a 'trial-and-error' approach to disease treatment.

Methods: We examined, forty-nine infants and children, aged younger than 18 years with unexplained epilepsy clinical features and suspected genetic etiology. The patients were tested and diagnosed by a neurologist and/or pediatrician and clinical data was represented. Features like: intellectual disability (mild, severe), developmental skills and supports needed, craniofacial malformations, motor function, movement disorder, cerebral palsy and others phenotype features, were noted. Whole exome sequencing was applied on 22 patients and 27 patients were examined through whole genome sequencing. Individual bioinformatics analysis and interpretation of the data were performed based on every patient clinical phenotype.

Results: We identified pathogenic variants in 24 out of 49 patients and achieved diagnostic yield of 49%. Twenty-four percents of the patients (17/49) remained undiagnosed and re-analysis of the data after one year, was recommended. The genetic background and etiology of the seizures remained unknown in 16% (8/49) of the patients. Most of the identified variants were in genes associated with ultra rare disorders with early-onset of the seizures and low (less than 1-9/1 000 000) or no prevalence in Orphanet. Some of the identified disorders were: CDKL5 deficiency disorder, Rett syndrome, Smith-Kingsmore syndrome, Juberg-Marsidi syndrome, GRIN2B encephalopathy and others.

Conclusions: From diagnostic point of view, there is no single test that can diagnose all epilepsy disorders, but WES and WGS enables to analyze more than one thousand distinct genes, associated with the pathogenesis of epilepsy. The diagnostic yield in our cohort was 49% and the present study has shown that about half of our patients with unknown etiology have a very clear genetic background. Discovering the genetic etiology of the disorders, established substantial impact of both diagnostic clarity and therapeutic guidance in our patients, it allowed prevention in the families and a long-term prognosis and outcome.

ABSTRACTS

Topic: Neuromuscular Disorders

EPNS25_313 - International evidence-based consensus on the management of gastrointestinal adverse events related to the use of risdiplam in patients with spinal muscular atrophy: methodology

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On behalf of the SMA Delphi Panel

Objectives

The selective survival motor neuron-2 mRNA-splicing modifier, risdiplam, is the first oral treatment approved in Europe and the USA for the treatment of patients with spinal muscular atrophy (SMA). In pivotal trials, risdiplam has been shown to improve motor function in infants with SMA type I and patients aged 2–25 years with SMA types II or III for up to 48 months. Risdiplam is well-tolerated, with the most frequently reported adverse events (AEs; in ≥5% of patients) including fever, diarrhoea and rash. Although trial data have shown that treatment-related diarrhoea does not lead to discontinuation, instances of pausing risdiplam treatment to resolve diarrhoea have been reported in clinical practice. Best practice recommendations for the management of gastrointestinal (GI) AEs experienced in patients with SMA treated with risdiplam are lacking. Owing to the treatment benefit offered by risdiplam, there is a need to consider recommendations for the management of potential GI AEs.

Methods

To address this need, an international panel of experts were recruited to participate in a modified Delphi consensus process. The Delphi panel steering committee gathered to discuss clinical management approaches to GI AEs related to the use of risdiplam in patients with SMA. The outcomes of these discussions and a targeted literature review informed the generation of draft consensus statements concerning the clinical management of GI AEs related to the use of risdiplam. The statements will be taken through up to three rounds of voting, during which panel members will vote anonymously on each statement (6-point Likert scale). Statements that fail to reach a pre-defined consensus threshold will be revised based on expert feedback and carried through to the next round of voting. Statements will be considered final if they meet the pre-defined consensus threshold in any voting round. A non-voting patient advisory panel comprising patients, representatives from patient advisory groups, and expert patients will review each statement and provide their feedback to the patient expert serving on the Delphi consensus panel.

Results

The voting process is ongoing, and the finalized consensus statements will be presented.

Conclusions

It is hoped that the statements generated using this modified Delphi consensus method will inform clinical decision-making related to the management of treatment-related GI AEs in patients with SMA who receive risdiplam.

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ABSTRACTS

Topic: Traumatic Brain Injury

EPNS25_314 - Adherence to Scandinavian pediatric traumatic brain injury guidelines and clinical features of head injury patients in Southwest Finland

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Objectives

To retrospectively evaluate the adherence to Scandinavian guidelines for the initial management of minor and moderate head trauma in children (SCN guidelines) and to report the clinical features and neuroimaging findings of the head injuries in the pediatric cohort from a tertiary care center.

Methods

Patients aged <16 years were identified by a diagnosis-based register search covering 2010-2016. All data were gathered from the medical records, and the indications for neuroimaging and traumatic brain injury (TBI) diagnosis were re-evaluated.

Results

653 patients who had their first hospital-treated head trauma and neuroimaging during the study period were included in the study. 58% were male (n=380). The mean age was 9.3 years (range 0.02-15), and 48% of the head injuries occurred in the age group of 11–15 years. The most common injury cause was incidental falls (44%). 63% (n=412) of the study population was evaluated according to the SCN guidelines. Overall, 93% of the patients fulfilled the criteria for neuroimaging. 80% of the head injuries were defined as mild TBIs. Head computed tomography (CT) was the primary neuroimaging modality (85%) in an acute setting. The number of head magnetic resonance imaging (MRI) as a first-line neuroimaging and hospital admissions increased during the study period. 26% (n=171) had traumatic intracranial findings on head CT or MRI. The most common neuroimaging findings were extra-axial hematomas and contusions. Neurosurgical interventions were performed on 5% (n=30) of the patients. Six patients (0,01%) needing neurosurgical intervention were initially missed but identified the next day after head injury.

Conclusions

The guideline adherence was high (93%) in the group with acute neuroimaging (n=412). Despite the good adherence, six patients needing neurosurgical intervention were initially missed. The number of patients with head MRI as a primary neuroimaging method was higher than expected. The patients requiring neurosurgical intervention were identified regardless of the neuroimaging method. The study population was comparable to previous epidemiological studies. The rate of severe injuries and neurosurgical interventions were similar to those in previous studies.

ABSTRACTS

Topic: Neurogenetics

EPNS25_315 - The impact of Vanishing White Matter on unaffected family members

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Objectives
Vanishing White matter (VWM) is one of the more prevalent leukodystrophies and is caused by biallelic pathogenic variants in any of the *EIF2B1–5* genes. It is characterized by chronic progressive neurological decline and additionally stress-provoked episodes of rapid worsening, leading to severe neurological impairment and early death. The impact of VWM on unaffected family members has not been investigated.
Methods
This international cross-sectional study enrolled parents, partners, and unaffected siblings. We used online administration of 1) health-related quality of life questionnaires (quantitative, comprising the EuroQol 5 Dimensions [EQ5-D]– 5 Levels questionnaire [EQ-5D-5L], EuroQol 5 Dimensions – Youth 3 Levels questionnaire [EQ-5D-Y], Pediatric Quality of Life Family Impact Module [PedsQL™ -FIM], PedsQL™ Child-Adult Self Report [PedsQL™ -SC]); 2) VWM-specific customized questionnaires (quantitative, comprising the impact of VWM inventory questionnaires for parents, partners and siblings); and 3) in-depth semi-structured interview (qualitative). Results were analyzed in comparison to the general population using a one-sample t-test (Wilcoxon or independent) or a Fisher's exact test.
Results
A total of 100 family members were included: 52 mothers, 29 fathers, 13 unaffected siblings and 6 partners. Mothers and partners scored significantly poorer on the EQ5D-5L than the general population. Fathers and mothers scored significantly poorer on the PedsQL™-FIM than the general population. Siblings scored similar to the general population on the EQ5D-5L/Y and all domains of the PedsQL™-SC, with the lowest score on the emotional domain. Qualitative interviews revealed three main drivers of the impact of VWM: 1) lack of knowledge and communication of healthcare professionals, 2) unpredictable disease course, and 3) caregiver responsibilities. Mothers reported significant impacts on their emotional well-being and dissatisfaction with their professional development. Fathers reported pressure to provide financially and heightened family responsibility. Partners mentioned emotional exhaustion and difficulty in managing family responsibilities. Siblings expressed internal struggles, finding it challenging to express their feelings.
Conclusions
Mothers and partners indicated a significant and consistent reduction in their quality of life on standardized questionnaires. Qualitative interviews revealed more in-depth details of the impact of VWM on all family members. Improved healthcare communication, symptom management resources, and support networks are essential for alleviating the impact of VWM on families. Including the entire family system of VWM patients provides a multi-faceted understanding of the disease's impact and emphasizes the need for tailored approaches that address full impact of a severe disease like VWM.

ABSTRACTS

Topic: Movement Disorders/ Cerebral Palsy

EPNS25_316 - Towards Automated Assessment of Movement Disorders from Gait Videos

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Objectives: This study introduces a Gait Feature Fusion (GFFusion) framework for automated gait analysis using 2D video recordings, aiming to aid the diagnostic workup for pediatric movement disorders, including early-onset ataxia (EOA) and developmental coordination disorder (DCD).

Methods: The study analyzed gait videos of 83 children classified into EOA, DCD, and Healthy Control (HC) groups. Using AlphaPose and PoseFlow algorithms, 17 skeleton keypoints were extracted from each video. Gait cycle and body movement features were derived from the skeleton data to convert qualitative clinical observations into quantitative metrics. SHapley Additive exPlanations (SHAP) analysis was used to identify clinically significant gait features. An XGBoost model was employed for classification, and statistical analysis focused on identifying key features distinguishing the groups.

Results: The XGBoost model achieved a mean F1 score of 0.73 in classifying EOA, DCD, and HC groups. Key features, such as double support phase duration and ankle distance, were identified as significant for differentiating EOA and DCD from HC. These metrics provided objective insights into gait phenotypes relevant to clinical diagnostics.

Conclusions: The proposed framework demonstrates the potential for objective and accessible assessment of pediatric gait abnormalities using 2D video data. It highlights clinically relevant biomarkers for diagnosis and monitoring, supporting integration into clinical workflows. Further validation with larger datasets is needed to confirm its utility for tracking disease progression and therapeutic outcomes.

ABSTRACTS

Topic: Neuromuscular Disorders

EPNS25_317 - Impact of satralizumab on bone strength and muscle function in Duchenne muscular dystrophy (DMD): design of the SHIELD-DMD study

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Objectives

DMD is characterised by progressive muscle atrophy, chronic inflammation and low bone mass causing bone fragility, which is exacerbated by long-term corticosteroids. In DMD, elevated interleukin (IL)-6 is associated with muscle atrophy, increased inflammatory response and increased bone resorption; IL-6 receptor (IL-6R) concentration is also negatively correlated with total body less head bone mineral density (BMD) Z-score. In rheumatoid arthritis, anti-IL-6R monoclonal antibody (mAb) therapy inhibits IL-6 signalling, leading to reduced inflammation and fibrosis, and balances bone remodelling in favour of formation. SHIELD-DMD (NCT06450639) is a prospective, open-label Phase 2 study evaluating the impact of satralizumab, a humanised, recycling anti-IL-6R mAb, on bone strength and muscle function in DMD.

Methods

SHIELD-DMD is enrolling boys with DMD who are receiving daily corticosteroids. Group 1 includes ambulatory and non-ambulatory boys aged ≥8 to <16 years with existing low-trauma fractures (n=16). Group 2 includes fracture-naïve ambulatory boys aged ≥8 to <12 years (n=34). Initially, non-ambulatory boys aged ≥12 years (n=8) will be enrolled into Group 1, with subsequent enrolment gated on interim safety and pharmacokinetics (PK). Fixed doses of subcutaneous satralizumab (determined by baseline weight) are administered at baseline, Week 2 and Week 4 and every 4 weeks thereafter for a total duration of 2 years. Endpoints include change from baseline to Week 52 in lumbar spine (LS) BMD Z-score with appropriate bone size adjustments in fracture-naïve patients (primary), change from baseline in LS BMD Z-score and serum bone turnover markers in all patients, the proportion of patients with new low-trauma long bone or vertebral fractures and the mean number of fractures per patient, and change from baseline in rise from the floor velocity. Safety, PK and immunogenicity will be assessed.

Conclusions

SHIELD-DMD is the first trial in DMD to evaluate IL-6R inhibition as a mechanism for improving bone strength and muscle function.

ABSTRACTS

Topic: Neuromuscular Disorders

EPNS25_318 - Patients' lived experience of thymidine kinase 2 deficiency (TK2d): results from the Assessment of TK2d Patient Perspectives (ATP) study

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Objectives

Thymidine kinase 2 deficiency (TK2d) is an ultra-rare, genetic, mitochondrial disease, associated with progressive, life-threatening myopathy that affects motor function, breathing, and feeding. The aim of this study was to capture patients' and caregivers' experiences of TK2d and its impact on patients' health-related quality of life (HRQoL). Patient findings are presented here.

Methods

Individuals with genetically confirmed TK2d (or proxy caregivers) were invited to complete an online survey co-created by a patient steering committee as part of a cross-sectional, mixed-methods study. The survey was shared via mitochondrial disease patient organizations from September 2023 to February 2024.

Results

Thirty patients or their proxy caregivers (median patient age [range]: 31 [2–54] years) and two bereaved caregivers from 12 countries participated. Most responses were about patients aged ≥16 years (n=26). Three 'age of TK2d symptom onset' phenotypes from the literature were equally represented: age of TK2d symptom onset ≤2 years (n=12), >2 to ≤12 years (n=10), and >12 years (n=10). Eight patients were receiving/had previously received pyrimidine nucleoside therapy via compassionate use.

The most frequent TK2d signs and symptoms were categorized as muscular/myopathy (n/N=32/32), neurological (29/32), and psychological (25/32). The most frequently reported impacts of TK2d were on walking/eating/toileting (26/32), breathing (25/32), development (delayed or loss of ability, 20/32), and feelings of isolation (17/32). Difficulties with lower body muscle weakness and/or walking, breathing, and fatigue most negatively affected patients' HRQoL. Among those who rated impact levels, 12 out of 22 reported an 'extreme' impact on their HRQoL due to walking difficulties, 7 out of 25 due to breathing difficulties, and 5 out of 19 due to eating/swallowing difficulties.

Most patients (78.1%, 25/32) needed home modifications and support to help with daily activities, and 12.5% (4/32) required full-time medical support.

Conclusions

The clinical manifestations experienced by patients with TK2d are associated with debilitating physical impacts and severe psychological strain. This reflects the high burden of TK2d and its impact on patients' HRQoL. Walking, breathing, and eating/swallowing difficulties were reported as having 'extreme' impact on HRQoL by some patients.

UCB funded this study.

ABSTRACTS

Topic: Neurodevelopmental Disorders / Developmental Neuroscience

EPNS25_320 - Efficacy and Safety of Trofinetide for the Treatment of Rett Syndrome: Results From the Pivotal Phase 3 LAVENDER Study

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Objectives : Rett syndrome (RTT) is a debilitating genetic neurodevelopmental disorder that primarily affects females. Trofinetide is a synthetic analog of glycine–proline–glutamate, a naturally occurring tripeptide cleaved from insulin-like growth factor 1. Phase 2 studies in RTT demonstrated a clinical benefit over placebo in clinician- and caregiver-assessed efficacy measures. Here, we present the efficacy and safety results of LAVENDER, a randomized, placebo-controlled, phase 3 study of trofinetide in girls and young women with RTT.

Methods Females with RTT, aged 5–20 years, were randomized 1:1 to twice-daily oral trofinetide or placebo for 12 weeks. Efficacy endpoints included the Rett Syndrome Behaviour Questionnaire (RSBQ), a caregiver assessment of core RTT symptoms (co-primary), the Clinical Global Impression–Improvement (CGI-I) scale (co-primary), and the Communication and Symbolic Behavior Scales Developmental Profile™ Infant-Toddler Checklist-Social (CSBS-DP-IT Social) composite score (key secondary). Safety measures included adverse events.

Results Overall, 187 participants were randomized to trofinetide (n=93) or placebo (n=94). After 12 weeks of treatment, trofinetide demonstrated a statistically significant improvement over placebo for co-primary and key secondary endpoints. Least squares (LS) mean change from baseline to week 12 in the RSBQ for trofinetide vs. placebo was -4.9 vs. -1.7 (p=0.0175; Cohen's d effect size = 0.37), LS mean CGI-I score at week 12 was 3.5 vs. 3.8 (p=0.0030; Cohens' d effect size = 0.47), and LS mean change from baseline to week 12 in the CSBS-DP-IT Social composite score was -0.1 vs. -1.1 (p=0.0064; Cohen's d effect size = 0.43). Serious adverse events were reported in 3.2% of participants in the trofinetide and placebo groups. The most common adverse event in the trofinetide and placebo groups was diarrhea (80.6% and 19.1%, respectively) with 97.3% of all cases experiencing mild-to-moderate severity.

Conclusions This study demonstrated that trofinetide is efficacious and has an acceptable safety profile in girls and women with RTT.

ABSTRACTS

Topic: Neurodevelopmental Disorders / Developmental Neuroscience

EPNS25_321 - Trofinetide for the Treatment of Rett Syndrome: Long-Term Safety and Efficacy Results From the Open-Label LILAC and LILAC-2 Studies

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Objectives : Trofinetide significantly improved core symptoms of Rett syndrome (RTT) with an acceptable safety profile in LAVENDER. Here, we report the safety and efficacy results of LILAC and LILAC-2, open-label extension studies of LAVENDER.

Methods Females with RTT, aged 5–21 years, received twice-daily, oral trofinetide in LILAC for 40 weeks. Participants who completed LAVENDER and LILAC continued trofinetide in LILAC-2, a 32-month extension study. Safety assessments included the incidence of adverse events (AEs). Efficacy endpoints included the Rett Syndrome Behaviour Questionnaire (RSBQ) and the Clinical Global Impression–Improvement (CGI-I) scale.

Results Overall, 154 patients were enrolled in LILAC. The most common AEs were diarrhea (74.7%) and vomiting (28.6%). The mean (standard error [SE]) change from the LAVENDER baseline to Week 40 in the LILAC study in RSBQ was −7.3 (1.62) and −7.0 (1.61) for participants treated with trofinetide and placebo in LAVENDER, respectively. Mean (SE) CGI-I scores compared with the LILAC baseline at Week 40 were 3.1 (0.11) and 3.2 (0.14) for patients treated with trofinetide and placebo in LAVENDER, respectively. Similar safety and efficacy trends were observed in LILAC-2.

Conclusions Trofinetide continued to improve symptoms of RTT in LILAC and LILAC-2 with a safety profile consistent with LAVENDER.

ABSTRACTS

Topic: Neuromuscular Disorders

EPNS25_322 - Using the Genomics England National Genomic Research Library (NGRL) and UK Biobank to investigate the genetic, phenotypic and clinical landscape of thymidine kinase 2 deficiency (TK2d)

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Objectives: Thymidine kinase 2 deficiency (TK2d) is an ultra-rare, often life-threatening autosomal recessive mitochondrial myopathy. Numerous pathogenic thymidine kinase 2 (*TK2*) variants cause heterogeneous phenotypes, with TK2d often misdiagnosed or undiagnosed. Improving the diagnostic yield is vital to inform appropriate disease management. To gain a better understanding of the genetic landscape of TK2d, this study used large sequencing data sets to investigate *TK2* variants and characterize their phenotype and penetrance.

Methods: Two Genomics England National Genomic Research Library (NGRL) de-identified participant cohorts were included: the 100,000 Genomes Project (Release 17) and the NHS Genomic Medicine Service (GMS; Release 3). Whole genome sequences were screened for small and structural *TK2* variants. A comprehensive annotation strategy prioritized variants based on allele frequencies, confirmed pathogenicity or predicted deleteriousness. Expert clinical review screened participants with prioritized variants for TK2d-related phenotypes. Variant–disease segregation filters were applied and penetrance assessed. To further explore their potential clinical relevance, prioritized alternate homozygous small variants were screened for in UK Biobank whole exome sequencing data.

Results: In total, 113 823 participants were included from the NGRL; 4 small variants, 4 structural variants and 3 copy number variants (CNV) of note were identified. Variant p.Thr108Met (previously identified in Genomics England's diagnostic pipeline) carried as alternate homozygous showed complete penetrance. Variant p.Arg32Trp carried as alternate homozygous or heterozygous showed reduced penetrance. Of 469 707 UK Biobank participants, 25 carried p.Arg32Trp as alternate homozygous with no TK2d-related phenotypes. Structural variant chr16:66543128_66546738_C_<DEL> was also carried as heterozygous by NGRL participants with TK2d-related phenotypes. Participants with the remaining small variants (c.156+6T>G, carried as alternate homozygous; p.Pro41His, carried as alternate homozygous or compound heterozygous), structural variants (carried as heterozygous) or CNVs either had no TK2d-related phenotypes or unlinked secondary data, thus phenotypic consistency with carrier status could not be interpreted.

Conclusions: This analysis shows how large sequencing data sets can be used to study ultra-rare diseases such as TK2d. Further assessment of variants carried as heterozygous is needed given the biallelic mode of inheritance of TK2d. The 11 *TK2* variants identified could be further explored by integrating multi-omics data and cross-referencing with TK2d-focused data sets. Findings could improve TK2d diagnostics.

Study funded by UCB. This research was made possible through access to data and findings in the NGRL via the Genomics England Research Environment.

ABSTRACTS

Topic: Neuromuscular Disorders

EPNS25_323 - Retrospective assessment of feeding and nutrition after 2 years of risdiplam treatment in children with Type 1 spinal muscular atrophy (SMA) using a novel scale

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Objectives

Children with Type 1 spinal muscular atrophy (SMA) have severe motor neuron degeneration including bulbar dysfunction which can lead to swallowing and feeding difficulties, poor respiratory health and faltering growth. Routine assessment of bulbar function is essential for children with SMA; however, it is not assessed consistently across studies. The 6-point graded Children's Eating and Drinking Activity Scale (CEDAS) was developed to improve the definition of feeding level scoring to reflect both sensory and motor needs, ensuring usability for all children with a paediatric feeding disorder.

The objective of these analyses is to provide context to feeding and swallowing data from the FIREFISH trial (NCT02913482), by independent retrospective rescoring of the data using the CEDAS.

Methods

Data were collected from 58 children in FIREFISH who had received the pivotal dose of risdiplam for two years. Two independent experts retrospectively rescored the FIREFISH data using the CEDAS.

Results

Retrospective scoring with the CEDAS confirmed feeding and swallowing findings in FIREFISH: 48 (83%) children were able to feed orally at Year 2 (feeding exclusively orally [n=41] and mixed oral and tube feeding [n=7]). The majority of children maintained (48%) or improved (16%) their CEDAS scores over two years of treatment.

An exploratory analysis of correlation between CEDAS scores and respiratory-related serious adverse events (SAEs), suggested that lower CEDAS scores (i.e. worse feeding/swallowing ability) were associated with the occurrence of respiratory-related SAEs, increased respiratory-related hospitalisations and longer hospital stays. CEDAS scores were not correlated with motor function, as assessed using the Children's Hospital of Philadelphia Infant Test of Neuromuscular Disorders (CHOP-INTEND), at any time point over two years in FIREFISH.

Conclusions

Feeding and swallowing outcomes reported in the FIREFISH study are consistent with outcomes when data is retrospectively assessed using the CEDAS. These data show a maintenance of swallowing function in patients with Type 1 SMA, which differs greatly from outcomes observed in untreated children in the same age range.

ABSTRACTS

Topic: Neuromuscular Disorders

EPNS25_325 - Acute Foot Drop in a Teenager: A rare case of Slimmer Paralysis

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Objectives

We aim to discuss the clinical presentation of peroneal neuropathy associated with rapid, uncontrolled weight loss in adolescents with the goal of enhancing awareness among healthcare providers.

Methods

Peroneal neuropathy (PN), characterized by foot drop and sensory impairment, commonly arises from external compression near the fibular head where the nerve is superficially located. Various factors, such as prolonged leg-crossing, immobilization, direct pressure, and systemic conditions such as diabetes and recreational use of nitric oxide, are often implicated.

Interestingly, rapid and significant weight loss, also known as Slimmer's paralysis, has emerged as a potential cause. The cause is presumed to be the depletion of protective subcutaneous fat, which exposes the nerve to mechanical injury. Moreover, rapid and uncontrolled weight loss can lead to severe metabolic deficiencies that impair the function of the PNS and disrupt lipoprotein metabolism, catecholamine levels, and hormonal activity.

Results

A 14-year-old girl presented to the A&E department with a one-week history of sudden-onset of left-sided foot drop and lower limb paraesthesia.

Her neurological examination revealed weakness in left foot dorsiflexion, with a power of 3/5. A detailed review of her history revealed a significant weight loss of 21.5 kg over the previous 6 months. Her family history was notable for a sister currently under the CAMHS Eating Disorder (ED) team for treatment.

Initial investigations, including MRI of the brain and spine, showed normal findings, with no evidence of neural or spinal cord compression or signal abnormalities. Blood tests revealed normal levels of folate, B12, ferritin, vitamin D, HbA1c, thyroid profile, lactate, and acylcarnitine. However, further evaluation with nerve conduction studies revealed reduced conduction velocity, consistent with moderate-to-severe left-sided common peroneal nerve palsy. An MRI knee scan ruled out compressive lesion.

The patient was counselled on the importance of adhering to a balanced diet rich in essential nutrients to support nerve health and overall recovery and was referred to the ED clinic.

Conclusions

This case highlights the rare but significant association between rapid, uncontrolled weight loss and peroneal neuropathy in adolescents, emphasizing the need for early recognition and dietary management in cases presenting with sudden foot drop.

ABSTRACTS

Topic: Neurogenetics

EPNS25_326 - Approaches in Genetic Diagnostics for Rare and Undiagnosed Diseases: Challenges, Re-analysis, and Future Directions

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Objectives: Rare and undiagnosed diseases (RUD), particularly those affecting the neurological system, pose significant challenges in understanding their mechanisms and developing effective treatments. Advances in next-generation sequencing (NGS), such as whole exome sequencing (WES), have enhanced the diagnostic process for neurogenetic disorders (NGDs) by identifying their genomic aetiologies. This study aims to evaluate the diagnostic yield of genetic tests and outline planned diagnostic strategies for cases assessed in interdisciplinary RUD Patient Advisory Boards, involving pediatric neurology and clinical/basic genetics departments. Additionally, the study investigates the role of this collaboration in the diagnostic pathway.

Methods: Between 2019 and 2024, WES results of 61 patients who remained undiagnosed with existing tests were retrospectively analyzed. The contribution of WES re-analyses to diagnostic outcomes was also assessed. Cases reviewed during RUD Board meetings were included under the RareBoost ERA Chair project.

Results: The study included 61 patients with a median age of five years (IQR: 8 years); 44 (72.1%) were male. The most common neurological conditions were cognitive delay (n=40, 65.5%) and epilepsy (n=36, 59.0%). A stable and slowly progressive course was observed in 37 patients (60.6%), while 22 (36.0%) had progressive disease. Initial clinical characterization suggested neurogenetic disorders in 30 cases (49.1%), neurodegenerative diseases in 16 cases (26.2%), and metabolic diseases in 6 cases (9.8%). In 7 cases, differentiation between metabolic and genetic aetiologies was not possible initially.Karyotype analysis in 43 patients yielded no diagnoses. Microarray analysis in 17 patients resulted in 2 diagnoses (11.7%). NGS gene panels were applied to 32 patients (54.2%), leading to 4 diagnoses (12.5%). WES analysis in 40 patients (67.8%) diagnosed 15 (25.4%). In RUD Board discussions, 22 patients were reviewed. Re-analysis was performed for 11 cases, identifying new variants in 4 (36.3%), advanced evaluations in 2 (18.1%), and WGS planned for 5 (45.4%). Re-analyses were instrumental in guiding the diagnostic process for more than half of the patients.

Conclusions: The diagnostic yield of WES in this study aligns with the literature, highlighting the importance of appropriate indications for its use. Re-analyses identified variants that directly informed diagnoses and guided further investigations. Regular reevaluation of undiagnosed patients with an interdisciplinary approach remains crucial. With advancing genomic technologies, genetic testing holds an increasingly significant role in diagnosing NGDs.

Key Words: Neurogenetic disorders, genetic testing, variant analysis, neurodevelopmental disorders, epilepsy

ABSTRACTS

Topic: Neuromuscular Disorders

EPNS25_328 - Juvenile myasthenia gravis: long-term follow-up of 92 patients

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Objectives: to analyze the course of juvenile myasthenia gravis (JMG) during long-term follow-up.

Methods: 92 patients with JMG were analyzed retrospectively: 75 (81.5%) female and 17 (18.5%) male. The average age of JMG onset was 14 [11; 16] years. Ocular JMG was diagnosed in 16 (17.4%) patients, generalized JMG in 76 (82.6%). The average duration of the disease was 20 [15; 28] years.

Results: The maximum MGFA class for the entire period of the disease was as follows: MGFA 1 had 15 (16.3%) patients, MGFA 2 - 19 (20.7%), MGFA 3 - 33 (35.9%), MGFA 4 - 15 (16 .3%) and MGFA 5 (myasthenic crisis) - 10 (10.9%). No deaths have been recorded. The time, during which the maximum severity was reached, was 1 [1; 2] year. All patients received pyridostigmine bromide as initial therapy: 19 (20.7%) of them had complete compensation of symptoms, 57 (62.0%) had incomplete compensation, and 16 (17.4%) had no effect. Patients with ocular JMG more often had complete compensation (p=0.043). Corticosteroids were used in 70 (76.1%) patients: 7 (43.8%) with ocular JMG and 63 (82.9%) with generalized JMG (p=0.002). 43 (46.7%) patients began steroid therapy in the first year from the JMG onset. Other immunosuppressants were used in 25 (27.2%) patients (azathioprine - 23 (25.0%), cyclosporine - 6 (6.5%), mycophenolate - 2 (2.2%), rituximab - 1 (1.1%)). Thymectomy was performed in 51 (55.4%) cases: in 24 (26.1%) until 18 years old, in 27 (29.3%) after 18 years old. 35 (46.7%) women had a pregnancy, during which 9 (25.7%) women experienced a worsening of myasthenic symptoms, while 26 (74.3%) were stable. Over the past year, myasthenic symptoms persisted in 62 (67.4%) people, while 30 (32.6%) had no symptoms. Patients with symptoms had the following severity: MGFA1 - 12 (13.0%), MGFA2 - 45 (48.9%) and MGFA3 - 5 (5.4%) people. Over the last year 39 (42.4%) patients do not receive immunosuppressive therapy, 51 (55.4%) continue to take it (data on 2 (2.2%) patients are unknown).

Conclusions: In JMG, the most severe symptoms developed already in the first years of the disease. Every tenth patient had a myasthenic crisis. At long-term follow-up, 32.6% of patients were free of myasthenic symptoms.

ABSTRACTS

Topic: Epilepsy: Diagnosis and Investigations

EPNS25_329 - Evaluation of kidney damage due to valproic acid and levetiracetam use in children with epilepsy

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Objectives Cystatin C is a protein from the cysteine protease inhibitor family that is produced by all nucleated cells in the body. The search for new serum biomarkers for earlier identification of kidney damage has led to the recognition of NGAL. Kidney injury molecule-1 (KIM-1) is a transmembrane glycoprotein. Valproic acid and levetiracetam, which are antiepileptic drugs used in epilepsy patients, In order to determine kidney damage due to regular use, it is aimed to evaluate the effects of antiepileptic drugs used on the kidney by looking at NGAL KIM-1 Cystatin C parameters, which are considered as indicators of kidney damage

Methods : Patients presented clinical symptoms and signs and were diagnosed with epilepsy in correlation with EEG. is the patient group that receives 100 patients diagnosed with epilepsy and 50 patients in the control group will be examined in our study.

Results : In our study, there are a total of 150 patients, 50 of whom are epilepsy patients using valproic acid, 50 of whom are epilepsy patients using levetiracetam, and 50 of whom are in the control group. Cystatin-c level, one of the markers of acute kidney injury, was found to be higher in both groups compared to the control group. However, no data could be obtained regarding NGAL and KIM-1 levels and acute kidney injury

Conclusions : As a result of our study, it was found that renal glomerular functions of patients using valproic acid and levetiracetam were affected while tubular functions were preserved.

ABSTRACTS

Topic: Epilepsy: Medical and Surgical treatment

EPNS25_331 - Safety and Tolerability of Bexicaserin in Adolescents and Adults with Developmental and Epileptic Encephalopathies: Interim Results of the Phase 1b/2a PACIFIC Study Open-Label Extension (OLE)

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Objectives

Developmental and epileptic encephalopathies (DEEs) are the most severe group of epilepsies characterized by drug-resistant seizures, epileptiform abnormalities, and developmental slowing or regression. DEE trials have historically focused on patients with specific epilepsy syndromes such as Dravet syndrome (DS), Tuberous Sclerosis Complex, and Lennox-Gastaut Syndrome (LGS), with the latter having etiological heterogeneity. Here, we present long-term safety follow-up of a novel phase 1b/2a study of bexicaserin, a potent and highly selective 5-HT_{2C} receptor superagonist, for the treatment of seizures in patients with a variety of DEEs.

Methods

The PACIFIC OLE study (LP352-202; NCT05626634) investigated the safety, tolerability, and efficacy of bexicaserin for seizure treatment in patients aged 12-65 years with DEEs (DS, LGS, and DEE Other). Patients who completed the PACIFIC study were given the option to enroll in the OLE. They underwent a 15-day flexible titration period (maximum dose of 12 mg TID, based on tolerability), followed by up to one year of maintenance treatment. Key inclusion/exclusion criteria were based on enrollment criteria from the PACIFIC Study.

Results

Forty-one patients (32 bexicaserin, 9 placebo) were enrolled (20 LGS, 3 DS, and 18 DEE Other) in the OLE and received bexicaserin across 34 sites. As of this 6 month interim analysis, 40 patients received bexicaserin and are evaluable in the full analysis set. Only 2 subjects discontinued (adverse event, withdrawal of consent). All patients initially randomized to the placebo group have entered the maintenance phase and have continued in the study. The most common adverse events are consistent with those seen in the initial PACIFIC study.

Conclusions

Bexicaserin continues to exhibit a favorable safety and tolerability profile in this ongoing OLE study. Because they are typically chronically administered, it is important to continue to evaluate the efficacy, safety and tolerability of antiseizure medications.

This study was funded by Longboard Pharmaceuticals (a wholly owned subsidiary of H. Lundbeck A/S.

ABSTRACTS

Topic: Neuropsychiatric Disorders / Functional Neurological Disorders

EPNS25_332 - "A comparative analysis of the qualitative characteristics of the sleep among school-aged children"

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Objectives

to analyze the most frequent reasons of sleep disturbance among school-aged children and to elicit factors which influence the growth of insomnia negatively.

Methods

A statistical analysis of regularity of the insomnia growth among schoolchildren of different age depending on their physical activity, mental workload and a concomitant neurological anamnesis, on the basis of an elaborated inquirer.

Results

The most frequent type of insomnia among children (especially among the school-aged ones) is behavioural insomnia. Common complaints of parents of the children with this type of insomnia are: a decline of overall duration of the sleep a day (taking into consideration day and night sleep), later time of going asleep in the evening, a prolonged period of falling asleep and frequent night awakenings.

In the research 313 inquiry forms of primary school children (53.7% of boys and 46.3% of girls) have been analyzed. More than a half of them are taught at a secondary school, about 30% of them are taught at a gymnasium or at a lyceum.

The most prevalent sleep disturbance in the population of children is insomnia. And the most frequent variant of it is behavioural insomnia.

Conclusions

In this research it has been found out that 79.2% of parents think that their children don’t have sleep disturbance. Meanwhile the majority of respondents have some deviation from the norm in the regime of sleep and vigil. Insufficient attention to the problems of insomnia can cause in the future other mental and neurological disorder, which can become apparent at different stages of socialization. Taking into consideration the above-mentioned information, we can see great significance in the research of these problems among children of an early school age as well as among senior school children with the purpose of early recognition and control of external factors that influence the state of a child. Children of an early school age are overloaded by educational programmes and at the same time they attend a lot of different sports clubs which give an additional negative effect on the regime of recovery of a child’s organism. Teaching parents to organize an efficient regime of a day and sleep hygiene of a child is a significant preventive measure of insomnia formation and neurological disorder.

ABSTRACTS

Topic: Neurological Emergencies

EPNS25_335 - Incidence, etiology and long-term sequelae of pediatric acquired brain injury: a population-based study

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Objectives
In 2017, our regional public hospital started a program for pediatric acquired brain injury (PABI), motivated by a patients' association and driven by pediatric neurologists and clinical psychologists. The multidisciplinary team includes medical rehabilitation specialists, speech, physical and occupational therapists, nurses and social workers. In the acute phase, the team is activated from intensive care (PICU) or hospitalization. Upon discharge, the team establish monthly follow-ups with multidisciplinary meetings. The program also involves active collaboration with palliative care team and school counselors. Our objective was to describe the clinical characteristics of a cohort with PABI, with focus on etiology and long-term sequelae. Since our hospital is the referral centre in the region, annual incidence of PABI may be calculated.
Methods
PABI was defined as damage to the brain, which occurs from 28 days to 15 years of life, and was not associated to congenital or degenerative disease. In our program, PABI was related to 8 types: trauma, tumor, infection, vascular, autoimmune, anoxia, toxicity and epilepsy surgery. We included 123 patients prospectively recruited (2017-2023). A retrospective cohort (before 2017) was included (71 patients). A cognitive tests battery was applied 6 to 12 months after discharge. To calculate the annual incidence of PABI in our population 0-14 years (n=123, 2017-2023), we excluded 7 patients that were residents in different regions and the epilepsy surgery group (7) as well.
Results
Incidence was 16.8/100,000 children 0-14 years per year (range: 12.9-19.27), with slight increase over 7 years period. In the whole cohort (n=194), mean age at admission was 5.8 years (SD 4.5), 54% males. The most frequent etiologies were tumor (21.6%) and trauma (19%). Other etiologies were infection, vascular and autoimmune (14.9% each), anoxia (7.7%) and toxicity (3%). During the acute phase, 153 patients (79%) were admitted to PICU, 70 (36%) required a neurosurgery intervention, and 7 (3.6%) died. At discharge, 16 patients (8.2%) were admitted in palliative care program. In 108 (56%), long-term sequalae were ascertained: motor involvement (28%), cognitive and/or behavior problems (28%), and epilepsy (18.6%).
Conclusions
In our PABI program, most of the cases that occurred in the region are admitted and followed in time, so data on incidence, etiology and long-term sequelae can be recorded. In almost 80% of them the program is activated in the PICU. Brain tumor remains the leading cause with slight increase of trauma over time. From discharge, 56% of them will require long-term multidisciplinary intervention.

ABSTRACTS

Topic: Epilepsy: Medical and Surgical treatment

EPNS25_336 - Safety, Tolerability, and Efficacy of Bexicaserin in a Cohort of Participants With Developmental and Epileptic Encephalopathies: Interim Results of a Phase 1b/2a PACIFIC Study Open-Label Extension

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Objectives

Developmental and epileptic encephalopathies (DEEs) are the most severe group of epilepsies and are characterized by drug-resistant seizures, electroencephalogram background abnormalities, and developmental plateauing or regression. Bexicaserin is a highly specific and selective 5-HT_{2C} receptor superagonist that demonstrated a favorable safety, tolerability, and efficacy profile in the double-blind Phase 1b/2a PACIFIC study in participants with Dravet syndrome (DS), Lennox-Gastaut syndrome (LGS), and other DEEs. The objective of this study was to assess the long-term safety, tolerability, and efficacy of bexicaserin in participants newly exposed to bexicaserin in the open-label extension (OLE) of the PACIFIC study in individuals with DEEs.

Methods

The OLE of the PACIFIC study further investigated the safety, tolerability, and efficacy of bexicaserin for the treatment of seizures in participants aged ≥12 and ≤65 years with DS, LGS, and DEE Other. After completing PACIFIC, participants were given the option to enroll in the OLE. They underwent a 15-day flexible titration period (maximum dose of 12 mg TID, based on tolerability), followed by up to one year of maintenance treatment.

Results

Forty-one participants (32 bexicaserin, 9 placebo) enrolled (3 DS, 20 LGS,18 DEE Other) in the OLE and received bexicaserin. All 9 placebo participants who then received bexicaserin in the OLE successfully titrated to their maximum tolerated dose and entered the OLE maintenance phase. In this interim analysis of the placebo-to-bexicaserin cohort, at approximately 6 months, no new serious adverse events were reported. Furthermore, a 57.3% reduction in countable motor seizures and a 61.2% reduction in total seizures were observed. Moreover, 55.6% of participants demonstrated a ≥50% reduction in countable motor seizure frequency.

Conclusions

All participants successfully transitioned from placebo to bexicaserin in the OLE with no discontinuations, reinforcing the tolerability of bexicaserin in an inclusive DEE population. The comparable seizure reductions in the double-blind PACIFIC study and the placebo-to-bexicaserin cohort in the OLE reinforce the consistency of bexicaserin across heterogeneous DEE subgroups and are supportive of Phase 3 development.

This study was funded by Longboard Pharmaceuticals (a wholly owned subsidiary of H. Lundbeck A/S.

ABSTRACTS

Topic: Neuromuscular Disorders

EPNS25_337 - SUNFISH Parts 1 and 2: 5-year efficacy and safety data of risdiplam in Types 2 and 3 spinal muscular atrophy (SMA)

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Objectives: Risdiplam (EVRYSDI®) is a centrally and peripherally distributed, oral survival of motor neuron 2 (*SMN2*) pre-mRNA splicing modifier, approved to treat spinal muscular atrophy (SMA) in more than 100 countries worldwide. The objectives of this study are to investigate the efficacy and safety of risdiplam in patients with Types 2 and 3 SMA.

Methods: SUNFISH (NCT02908685) is a multicentre, two-part, randomised, placebo-controlled, double-blind study in patients with Types 2 and 3 SMA, aged 2–25 years at enrolment. Part 1 (N=51) assessed the safety, tolerability and pharmacokinetics/pharmacodynamics of risdiplam in patients with Types 2 and 3 SMA (ambulant and non-ambulant). Part 2 (N=180) assessed the efficacy and safety of the Part 1-selected dose in Type 2 and non-ambulant Type 3 SMA. Part 2 participants were treated with risdiplam or placebo for 12 months; then risdiplam in a blinded manner until Month 24, when patients could enter the open-label extension phase. The SUNFISH study is now complete.

Results: The primary endpoint (Part 2) of change from baseline in the 32-item Motor Function Measure (MFM32) total score in patients treated with risdiplam (n=120) versus placebo (n=60) was met at Month 12. Previously reported results showed that increases in motor function were sustained over 4 years of risdiplam treatment, as measured by MFM32, Hammersmith Functional Motor Scale – Expanded, and Revised Upper Limb Module. After 4 years of risdiplam treatment, there were no treatment-related safety findings leading to withdrawal from SUNFISH Part 1 or 2.

Here we present the final efficacy and safety results from the SUNFISH study after 5 years of risdiplam treatment (data cut-off 2 October 2023).

Conclusions: SUNFISH provides long-term efficacy and safety data of risdiplam in a broad population of children, teenagers and adults with Types 2 and 3 SMA.

ABSTRACTS

Topic: Neuromuscular Disorders

EPNS25_338 - RAINBOWFISH: 2-year efficacy and safety data in risdiplam-treated infants with presymptomatic spinal muscular atrophy (SMA)

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Objectives: In patients with spinal muscular atrophy (SMA), motor neuron degeneration begins before the onset of symptoms. Risdiplam (EVRYSDI®) is a centrally and peripherally distributed, oral survival of motor neuron 2 (*SMN2*) pre-mRNA splicing modifier that increases and sustains levels of functional SMN protein. The objectives of this study are to investigate the efficacy, safety, pharmacokinetics and pharmacodynamics of risdiplam in infants with presymptomatic SMA.

Methods: RAINBOWFISH (NCT03779334) is a global, open-label, single-arm, multicentre, Phase 2 study of risdiplam in infants from birth–6 weeks old at first dose, regardless of *SMN2* copy number. Enrolled infants had genetically diagnosed SMA but were not showing any clinical signs and symptoms of SMA.

Results: The study enrolled 26 infants with two (n=8), three (n=13) and ≥4 (n=5) *SMN2* copies. The median age at first risdiplam dose was 25 (range 16−41) days. At Month 12, the primary endpoint was met, with 4/5 (80%) infants with two *SMN2* copies and baseline ulnar compound muscle action potential amplitude ≥1.5 mV, sitting without support for ≥5 seconds (assessed by the Bayley Scales of Infant and Toddler Development, third edition [BSID-III]).

Twenty-three infants completed 2 years of treatment with risdiplam (data cut-off: 27 March 2024). After 2 years, the majority of infants were able to sit and walk without support (assessed by the BSID-III and Hammersmith Infant Neurological Examination, Module 2), and most achieved age- appropriate motor milestones within the World Health Organization windows of typical development.

For infants who completed 2 years of treatment, mean scaled scores from the BSID-III cognitive scale were consistent with skills typical of normal child development. All infants maintained feeding and swallowing abilities, and none required respiratory or nutritional support. Most infants (92%) did not require hospitalisation over 2 years of risdiplam treatment.

No treatment-related adverse events led to withdrawal or treatment discontinuation.

Conclusions: RAINBOWFISH is ongoing globally to provide additional safety and efficacy data of risdiplam in infants with presymptomatic SMA.

ABSTRACTS

Topic: Neurodevelopmental Disorders / Developmental Neuroscience

EPNS25_339 - The Effectiveness of Vojta Reflex Therapy in the Psychomotor Development of Children

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Objective: The aim of the study was to evaluate the impact of Vojta Reflex Therapy (VRT) on the psychomotor development of children with developmental delay from both qualitative and quantitative perspectives.

Methods: The research was conducted as a prospective observational study in 42 kids (23 boys and 19 girls) with developmental delay diagnosed according to R62 (ICD- 10), aged from 6 weeks to 8 months at the time of the initial examination. All children underwent a comprehensive kinesiological examination, including the assessment of spontaneous motor activity, Vojta's positional reactions, examination of the presence of primitive reflexes, and determination of the achieved developmental age according to Vojta's locomotion stages. This scale monitors and evaluates the level of gross motor skills in relation to the level of mental development. Based on the determination of developmental age, the retardation quotient (RQ) was calculated as the ratio between the developmental age according to the locomotion stage and the chronological age. The retardation quotient (RQ), the number of negative positional tests, and the number of negative reflexes were compared. To determine statistical significance, paired T-test and Pearson's correlation coefficient were used. The difference in values before and after the therapy was considered. VRT was performed twice a week, for 40 minutes over a period of two months, during which exercises and exercise positions were monitored, and new positions were taught if necessary. The exercises were then performed at home by the mother four times a day.

Results: The average value of the retardation quotient improved from the initial 0.66 (± 0.09) to 0.82 (± 0.14), representing an improvement of 0.17 points, $p < 0.001$. The average number of negatively assessed primitive reflexes improved by almost 19%. Only 7 children in the entire sample showed no improvement in the assessment of any reflexes. The results confirmed that with increasing age of the child at the start of therapy, the increase in RQ after the end of therapy decreases ($r = -0.326$). No significant relationship was found between gender and therapy success, $p > 0.05$. This means that gender does not affect the success of the therapy.

Conclusion: The processed data show significant improvement in all areas after the application of therapy, indicating a positive impact of VRT on the psychomotor development of children with developmental delay.

ABSTRACTS

Topic: Neuromuscular Disorders

EPNS25_341 - Clinical outcomes amongst risdiplam-treated patients with spinal muscular atrophy (SMA) in the Cure SMA clinical data registry

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Objectives

The objective of this analysis was to describe demographics, clinical characteristics and motor function outcomes of individuals treated with risdiplam (EVRYSDI®) in the Cure SMA clinical data registry (CDR). The CDR comprises data from >1,100 patients with SMA across 24 care sites in the USA, sourced from electronic medical records and clinician-entered electronic case report forms (eCRFs).

Methods

This retrospective study included data captured in the CDR on or before June 2023. Included patients had a completed eCRF, were treated with risdiplam, and had both pre- and post- treatment functional assessments. Individuals were categorised by treatment sequence: risdiplam only, risdiplam following onasemnogene abeparvovec (post-OA), or risdiplam after switching from nusinersen. Data such as age at symptom onset and risdiplam start, sex, race/ethnicity, survival of motor neuron 2 (*SMN2*) copy number, census region, and baseline functional status (pre-risdiplam) were described. Mean change in motor function, as measured by the Children's Hospital of Philadelphia Infant Test of Neuromuscular Disorders (CHOP-INTEND), Hammersmith Functional Motor Scale – Expanded (HFMSE) and Revised Upper Limb Module (RULM), was evaluated in patients who had both a baseline motor function assessment within 12 months prior to the index date (risdiplam start date) and a post-risdiplam assessment. Analyses were completed using descriptive statistics.

Results

Forty-nine patients met the inclusion criteria (risdiplam only: n=13; post-OA: n=10; switch from nusinersen: n=26). Median ages at symptom onset and risdiplam start were 9.0 months and 10.5 years, respectively. The post-OA subgroup presented symptoms of SMA earlier (median age: 4.0 months) and began risdiplam at a younger age (median age: 1.8 years) compared with the other subgroups. Most patients (80%) in the post-OA subgroup had two *SMN2* copies, whereas patients in the other subgroups had a mixed distribution. Fourteen patients (29%) were ambulant at baseline. The median (interquartile range) time on risdiplam treatment was 23.6 (17.9, 29.4) months. The mean (standard deviation) change in score from baseline to post-risdiplam assessment was 9.3 (11.2), 1.0 (5.6) and –0.5 (1.7) for the CHOP-INTEND, HFMSE and RULM, respectively.

Conclusions

Overall, this analysis showed that individuals with SMA who received risdiplam improved or maintained motor function in real-world settings, regardless of risdiplam treatment sequence.

ABSTRACTS

Topic: Epilepsy: Medical and Surgical treatment

EPNS25_343 - Brivaracetam Adjunctive Therapy in Paediatric and Adult Patients With Focal-Onset Seizures in Mid-European Countries: 12-Month, Real-World Outcomes from the BRIVA-REG Study

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Objectives

Evaluate utilisation/effectiveness of adjunctive brivaracetam (BRV) in paediatric and adult patients in the clinical standard-of-care setting.

Methods

Final analysis from prospective, non-interventional, post-marketing study BRIVA-REG/EP0099. BRIVA-REG included patients aged ≥4 years with focal-onset seizures (FOS) with/without focal to bilateral tonic-clonic seizures in Bulgaria, Czech Republic, Greece, Hungary, Poland, Romania. Selection criteria: no prior BRV treatment, ≥1 antiseizure medication (ASM) at BRV initiation. Data for Safety Set are presented; some paediatric data were analysed post hoc.

Results

798 patients received ≥1 BRV dose (Safety Set), including 56 (7.0%) aged <18 years. Baseline characteristics in overall population and paediatric patients, respectively, were median age: 40.0, 13.0 years; median time since diagnosis: 14.41, 7.23 years; median number of lifetime ASMs (prior ASMs/concomitant ASMs at BRV initiation): 3.0 (n=796), 3.0 (n=56). At 12 months, BRV retention-rate (overall population, paediatric patients): 83.8% (n=798), 83.9% (n=56); ≥50% responder-rate: 82.4% (n=612), 87.5% (n=40). Clinical Global Impression of Change at 12 months versus baseline in overall population (n=667): 75.6% of physicians reported any improvement (minimally/much/very much) in their patients, 20.4% no change, 4.0% any worsening (minimally/much/very much). Patient Weighted Quality of Life in Epilepsy Inventory-Form 31 total score reported by patients aged ≥18 years: median 60.11 at baseline (n=131) and 60.88 at 12 months (n=59) (median change from baseline: 0.99 [n=46]). Pediatric Quality of Life Inventory total score reported by patients aged ≥8–<18 years: median 66.33 at baseline (n=8), 80.47 at 6 months (n=4) (median change from baseline: 5.47 [n=3]). Drug-related treatment-emergent adverse events were reported in 7.9% of overall population.

Conclusions

BRV retention- and responder-rates at 12 months suggest adjunctive BRV was effective in paediatric patients with FOS in routine clinical practice; results were similar in overall population. In overall population, >75% of physicians reported improved condition in their patients at 12 months versus baseline; BRV was well-tolerated.

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ABSTRACTS

Topic: Neurogenetics

EPNS25_344 - Serial Analysis of Brain Connectivity in a patient with SHANK3 mutation

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Objectives

Shank proteins are multidomain scaffold proteins of the postsynaptic density and also play a role in synapse formation and dendritic spine maturation. Mutation or disruption of the SH3 and ankyrin repeat domains 3 (SHANK3) gene is a cause of neurodevelopmental symptoms in Phelan–McDermid syndrome. Patients with a SHANK3 gene mutation often exhibit global developmental delay, lack of speech or severe language delay, severe sleep disturbances, and characteristic features of autism spectrum disorder such as social impairments and stereotypies. As it is a disorder of connectivity, we tried to identify the characteristics of functional connectivity in this patient. We investigated serial EEG connectivity in this patient.

Methods

This thirteen-year old boy showed SHANK3 c.4683C>G p.Tyr1561Ter heterozygous mutation. He presented autistic features and could not speak a word. He also presented seizures after 7 years. We collected three serial EEGs from this patient at age 6, 7 and 9. EEGs were recorded according to the international 10-20 system. Resting-state sleep EEG data were collected and artifacts were removed. We evaluated the default mode network (DMN) of 28 regions and small-world networks. Small-world networks were calculated by clustering coefficient (Cp)/path length (Lp).

Results

At age 6, EEG showed slow and disorganized background. As time goes by, sharp waves from both frontal areas were aggravated. Overall, high DMN network strengths were observed in the alpha bands. There were definite high DMN network strengths in higher frequency bands: beta and gamma at age 6. There were definite high DMN network strengths in lower frequency bands: delta at age 9. Small-world networks were increased in the alpha and beta band at age 7 and 9.

Conclusions

Functional hyperconnectivity in alpha frequency was observed in the patient with SHANK3 mutation. It suggests that Phelan–McDermid syndrome has characteristic abnormal neuronal connectivity features.

ABSTRACTS

Topic: Miscellaneous

EPNS25_346 - Consensus recommendations in the implementation of advanced therapies and experimental neurotherapeutics in paediatric neurological disorders

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Objectives: The unmet need, urgency, and complexity of neurological disorders prompt interest and requests to access research, including clinical trials, new therapies and technologies. The purpose of this study is to inform and facilitate decision making for stakeholders in the application of advanced and/or experimental neurotherapeutics within a public health system.

Methods: The study used a modified two round Delphi methodology to form and grade recommendations. A panel of 18 experts was purposively recruited with expertise in paediatric medicine, clinical and research ethics, clinical research, governance, clinical trials, development of experimental therapeutics and patient advocacy. A scoping review was presented to panel members through an online workshop, facilitating iterative discussion on the scope, population, settings and clinical priorities to be considered in the study. The workshop generated 106 statements which were embedded in an electronic questionnaire (Q1). Using a 5-point Likert scale, the steering group defined the rating of each statement and provided qualitative data through open text. Consensus was defined a priori as an agreement by at least 75% of the participants. Qualitative content analysis and descriptive data analysis of Q1 was used to construct the second questionnaire (Q2) which also included feasibility rating.

Results: Four key domains were identified (i) access and responsibilities for trials and treatments, (ii) communication and engagement with families (iii) trial and treatment eligibility and patient selection and (iv) evaluating the effects of trials or treatment. Following Q1, 11/106 (10.4%) statements did not reach consensus. Q2 included 9 amended and 3 new recommendations. Following Q2 a total of 97 statements were agreed by consensus.

Recommendations relating to communcation and engagement with families were most feasible. Examples include:

Start and stop criteria should be discussed, established and documented, ideally early in communications, and before treatment initiation to set realistic expectations. (100% agree, 100% very feasible/feasible)

As soon as families express interest in advanced therapies, or experimental neurotherapeutics health professionals should:

- *establish expectations of the mode and frequency of communication back and forth.* (100% agree, 92.3% very feasible/feasible)
- *describe the process of accessing therapies including the wait for due diligence processes.* (100% agree, 100% very feasible/feasible)

Respondents noted challenges to feasibility in recommendations regarding sustainability, scalability, equitable access and staffing.

Conclusions: These are current, clinician-led consensus recommendations addressing the safe, informed and effective implementation of rapidly developing neurotherapeutics and research in paediatric neurology within a public hospital system.

ABSTRACTS

Topic: Neurometabolic Disorders

EPNS25_347 - Seizures and movement disorders in patients with CLN2 disease treated with cerliponase alfa in the real-world setting

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Objectives: To evaluate the incidence and progression of seizures and movement disorders in patients with neuronal ceroid lipofuscinosis type 2 (CLN2 disease) treated with cerliponase alfa (recombinant hTPP1) in a real-world setting.

Methods: This retrospective, observational analysis was based on data collected in the DEM-CHILD International NCL Database (NCT04613089) and included 24 patients with CLN2 disease enrolled in the registry who received cerliponase alfa and were followed for ≥6 months from the date of first cerliponase alfa infusion (index) to the earliest of death, disenrolment or data cut-off (31 December 2022). Seizure types, frequency and complications were assessed based on information collected on the CLN2 Disease Seizure Inventory. Dystonia and myoclonus data were from the CLN2 Disease Movement Disorder Inventory; time to onset or worsening of movement disorders was assessed using Kaplan–Meier methods.

Results: Overall, 24 patients were included in this analysis (58% female), with a mean (standard deviation [SD]) follow-up time of 43.8 (19.0) months. Mean age (SD) at diagnosis was 53.1 (25.6) months and mean age (SD) at enzyme replacement therapy (ERT) initiation was 61.4 (27.3) months. At baseline, 20 patients (83.3%) had history of seizures, 18 (75.0%) had ataxia, 3 (12.5%) had myoclonus, and 5 (20.8%) had dystonia. The proportion of patients experiencing primary generalised seizures increased from 37.5% at baseline to 56.5% between months 10 and 12, then declined over the following 18 months, before increasing again to ~35% between months 31 and 48. Occurrence of atonic seizures remained relatively stable over follow-up (~30–50%). Among patients without the symptom at baseline, 33.3% developed myoclonus and 78.9% developed dystonia (median time to onset: 71.4 and 19.4 months, respectively; mean age at onset: 87.6 and 79.6 months, respectively).

Conclusions: This analysis provides the first comprehensive description of the time course of seizures and movement disorders in a cohort of patients with CLN2 disease receiving treatment with cerliponase alfa in the real-world setting.

ABSTRACTS

Topic: Headache / Migraine

EPNS25_348 - Lifting the burden of headaches from Georgian schools

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Introduction: Headache attributed to Q O L in adolescents between 12–17 years of age is unknown in Georgia.

Objectives: The aim of our study was to investigate the prevalence of primary headaches and headache-related burden in adolescents in Georgia.

Methods: The study is a cohort combined study with population number 1379 (marginal error 5%). Data was collected from schools in the large cities such as Tbilisi, Kutaisi and nine townships all over the Republic of Georgia. Data are collected according to socio-demographic headache features and headache-related Quality of Life (QOL). In total, there were 1818 students; 438 were absent. The data is analyzed using SPSS. Inferential statistical analysis is used (Pearson-Chi-square test, Linear by linear regression).The pain is classified into mild, moderate and severe headache.

Results: 94.9% of adolescents have headaches, 43.90% have migraine, 39.8% have tension-type headache and 0.1% have a combination of both. 1.245% have headaches for more than 15 days per month, 7% report severe overuse of anti-headache medications. The QOL is significantly lower in adolescents with headaches compared to those without. Both chronic headache and migraine are associated with a significant reduction in QOL. The results of the study show that the higher the frequency of headaches, the lower the quality of life. Also, the longer the headache is, the worse the quality of life. Bursting headache was positively associated with quality of life. The study reveals that chronic headaches are present at a fairly high frequency.

Conclusions: This is the first countrywide school-based study on the prevalence of primary headaches and headache-attributed burden in adolescents in the Republic of Georgia. It reveals a significant headache-related burden. These findings are in line with previous studies, which demonstrated a high prevalence of chronic headache in adults. These studies call for the need for a country-wide headache service according to the guidelines of the European Headache Federation.

References:

1. RB. Lipton, A. Manack: "Prevalence and burden of chronic migraine in adolescents "doi:10.1111/J1526-14610.2011.01885x

2. Andreas Staube, Florian Heinen "Headache in school children" doi:10.3238/ars.hebl.2013.0811

3. Marcus Antio, Daniel Algiero" chronic migraine inadolescents".doi:10.57.72/.90936

4. Ying Yang, Yu Cao "Rising trends in the burden of migraine and TTH" doi: 10.1186/s10194-023-01634-w

5. Agnese Onofri, U Pensato: "Primary headache of epidemiology in children and adolescents''doi:101186/510194-024-019 29-6

ABSTRACTS

Topic: Neurogenetics

EPNS25_349 - A Wide Clinical Spectrum of SPTAN1 Related Diseases: case series from Türkiye

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Objectives

The non-erythrocyte alpha 2 spectrin 1 gene (SPTAN1) encodes a structural alpha 2 spectrin protein that forms heterotetramers with beta spectrin in the cell membrane. This protein is responsible for the regulation of receptor binding and the formation of the cellular skeleton. It also has important role in ensuring the integrity of myelinated axons, axonal and dendritic development, and synaptogenesis. In addition, it plays a role in presynaptic vesicle release by interacting with syntaxin. SPTAN1 related diseases were first described in 2008 by Tohmaya et al. in patients with severe epileptic encephalopathy and white matter hypomyelination. As the number of cases described increases, the spectrum has expanded from benign epilepsy, developmental epileptic encephalopathy (DEE) with hypomyelination, hereditary spastic paraplegia (HSP), migraine, epilepsy and subependymal heterotopias to motor neuropathy. Although monoallelic forms are generally associated with the disease, biallelic forms have also been reported to be associated with complex HSP. Due to their rarity, a case series of SPTAN1-related diseases with different clinical phenotypes have been presented.

Methods

Herein, we report a case series of SPTAN1 related diseases with different clinical presentation.

Results

Five different SPTAN1 cases who were followed up in our clinic are presented. Three of them were girls. All cases have monoallelic pathogenic or likely pathogenic variants and three of them have inherited form. The first case was followed up with a diagnosis of complex HSP, the second case with DEE, the third case with pure HSP, the fourth case with benign epilepsy, and the last case with neurodevelopmental delay and epilepsy. Interestingly the first case has lactate peak and T2 hyperintensity in basal ganglia. Since both WES and mitochondrial genome analysis were normal for mitochondrial diseases, this finding was thought to be related to SPTAN1 mutation.

Conclusions

Although HSP has been rarely reported in cases with SPTAN1 mutation, both pure and complex HSP cases were described in our series. We have also seen cases of benign epilepsy and epilepsy with mild intellectual disability with SPTAN1 mutation, which are also rare. Since we described for the first time the lactate peak and T2 hyperintensity in the basal ganglia, we extend the SPTAN1-related radiological involvement. As genes, the proteins they encode, and their molecular mechanisms of action become better understood, the disease phenotypes associated with these gene mutations are expanding.

ABSTRACTS

Topic: Fetal and Neonatal Neurology

EPNS25_351 - Outpatient assessment of patients on anti-seizure medications in the neonatal intensive care unit

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Objectives: The administration of anti-seizure medication for seizures in neonatal intensive care units is a prevalent occurrence. The brain exhibits a greater vulnerability to seizures during the neonatal period. The majority of these seizures are symptomatic. Recent studies and guidelines recommend the prompt cessation of initiated anti-seizure medication. This study aims to evaluate the approach to patients discharged from the neonatal intensive care unit who utilized anti-seizure medication, examining practical applications in relation to existing literature through retrospective and cross-sectional analysis.

Methods: The research comprised patients admitted to the pediatric neurology outpatient clinic from July 2022 to April 2023. The files of patients with a history of hospitalization in the neonatal intensive care unit and those using anti-seizure medications were retrospectively reviewed. Patient records were reviewed for information such as the diagnosis for hospitalization, the patient's age at admission, the antiseizure drugs, and the findings of electroencephalograms (EEGs). A statistical evaluation was performed using SPSS for Windows, version 23.0 software. (IBM SPSS Inc., Chicago, IL).

Results: The study comprised 28 patients. 67.9% of the patients were male (n=19). 42.9% of the patients (n=12) were admitted at an age of 1 month or younger. The oldest age for admittance was 6 months. Fifty percent of the patients (n=14) received phenobarbital; three patients received both levetiracetam and phenobarbital, and eleven patients were treated with levetiracetam. Electroencephalograms (EEGs) from 25 patients were acquired, 19 of which were assessed as age-appropriate normal. Focal epileptic disorder was identified in two patients, paroxysmal disorder in two patients, burst suppression in one patient, and cerebral malfunction in one patient. Antiseizure medication was terminated in 18 individuals (64.3%). 67.9% of patients were admitted to the neonatal critical care unit with a diagnosis of hypoxic ischemic encephalopathy. Three patients were diagnosed with metabolic disease. The mean duration from application to cessation of medication was 34.7 days.

Conclusions: The most recent guidelines for neonatal seizures advise the prompt discontinuation of antiseizure medications, preferably prior to discharge. Our study has not yet captured new literature data on antiseizure medication discontinuation; however, an increase in medication discontinuation has been observed compared to previous years.

ABSTRACTS

Topic: Neurodevelopmental Disorders / Developmental Neuroscience

EPNS25_352 - Neurological Diagnoses in Children Phenotypically Fulfilling the Criteria for Developmental Coordination Disorder

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Objectives

In children who phenotypically fulfill the diagnostic criteria for Developmental Coordination Disorder (DCD), we aimed to investigate: 1) whether initial neurological phenotypical assessment by pediatric neurologists at our tertiary centrum can predict the diagnostic outcome; 2) potentially distinguishing clinical and/or diagnostic features between children with the diagnosis of DCD and children with underlying neurological diagnoses.

Methods

We retrospectively investigated the medical records of 50 children initially fulfilling the criteria for DCD, referred to the Pediatric Neurology Outpatient Clinic of the UMCG between the years 2016-2022. Based on the reported diagnosis after diagnostic evaluation, the included children were retrospectively grouped into the DCD or the alternative diagnosis (i.e., other underlying neurological diagnoses) groups. We calculated predictive values based on the initially suspected- and finally reported diagnosis. We statistically compared clinical and diagnostic parameters (n=51) between the DCD and alternative diagnosis groups.

Results

Of the included patients, 62% received the diagnosis DCD (n=31/50) and 38% received an alternative diagnosis (n=19/50). An underlying genetic etiology was identified in 58% of patients with alternative diagnoses (n=11/19). The positive predictive value for DCD was 52%, and for alternative diagnoses 21%. There were no statistically distinguishing clinical or diagnostic features between both groups.

Conclusions

In children phenotypically fulfilling the DCD criteria, initial neurological phenotypical assessment is insufficiently predictive of the diagnostic outcome. In perspective of lacking distinctive features between DCD and alternative diagnoses and the high prevalence of underlying genetic mutations, additional neurogenetic assessment is recommended.

ABSTRACTS

Topic: Epilepsy: Diagnosis and Investigations

EPNS25_353 - Structural abnormalities in pediatric epilepsy with genetic mutation

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Objectives

To understand the differences in brain volumetry of the total and each brain region in genetic pediatric epilepsy compared to those in non-genetic focal epilepsy and healthy controls.

Methods

We analyzed the mean surface areas, brain volume, and cortical thickness of patients with genetic-related pediatric epilepsy (n=25) using FreeSurfer. We compared these measurements with those of children with non-genetic focal epilepsy (n=25) and healthy controls (n= 23). In patients who underwent follow-up brain magnetic resonance imaging (MRI; n=11), we investigated age-related serial changes in brain volume or cortical thickness.

Results

Total brain, total grey matter (GM), cortical and subcortical GM, white matter (WM), cerebellar and cerebellar GM volumes were considerably smaller in children with genetic epilepsy than in children in the other groups. In the genetic group, a marked reduction was observed in the surface area measurements across brain regions associated with higher brain function. The mean cortical thickness was not significantly different among the three groups. Longitudinal MRI studies revealed age-related brain volume changes; both genetic and non-genetic groups showed increases in total brain, subcortical GM, and WM volume. Interestingly, the non-genetic group showed an increase in cortical GM volume (R=0.77, p=0.009), whereas the genetic group showed a decrease (R=-0.42, p=0.13).

Conclusions

Quantitative brain MRI volumetry serves as an essential screening instrument for genetic evaluation in children with epilepsy, even when qualitative MRI does not indicate any structural abnormalities. Reduced brain volumes in specific areas of cerebral cortex, responsible for higher brain functions, suggest a genetic etiology.

ABSTRACTS

Topic: Movement Disorders/ Cerebral Palsy

EPNS25_354 - Relationship between positional plagiocephaly and motor development in infants in medical care

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Objectives

Infants are prone to positional skull deformity owing to the softness of their skulls. These are not only cosmetic, but there are also concerns about their motor developmental effects. Infants undergoing medical care are particularly susceptible to positional plagiocephaly because of the length of time they spend in bed. However, few studies have been conducted. This study investigated the incidence of positional plagiocephaly in infants receiving medical care. We also investigated the relationship between the severity of positional plagiocephaly and motor development.

Methods

This single-center, prospective, cross-sectional study assessed the medical care of infants enrolled in a Japanese home care nursing station. Infants diagnosed with craniosynostosis or intracranial trauma were excluded, as were infants undergoing or who had previously undergone craniofacial corrective helmet therapy. The participants were evaluated for positional plagiocephaly and motor development. Positional plagiocephaly was assessed using the Argenta classification, which rates cranial deformities from Category 1 (mild) to Category 5 (severe). In the present study, positional plagiocephaly of less than 1 was defined as 0. The infants were divided into two groups based on the results of the Argenta classification: a non-positional plagiocephaly (non-PP) group (classifications 0 and 1) and a positional plagiocephaly (PP) group (classifications 2–5). Motor development was assessed using the Alberta Infant Motor Scale (AIMS) and scores were calculated for the supine, prone, sitting, and standing positions. We compared the AIMS scores between the two groups using an unpaired t-test.

Results

The analysis included 51 infants undergoing medical care (mean age 1.5±1.1 years). The participants included infants with brain-induced diseases, chromosomal abnormalities, and genetic disorders. The non-PP and PP groups comprised 33 and 18 participants, respectively. The PP group scored significantly lower than the non-PP group on the AIMS scores in the supine (5.4±5.7 vs. 9.0±7.7), sitting (2.9±3.2 vs. 5.3±5.1), and standing (1.6±1.5 vs. 4.2±5.2) positions. No significant differences were observed in the prone position.

Conclusions

More than 30% of the infants receiving medical care exhibited positional plagiocephaly of Argenta classification 2 or higher. Because positional head deformity is caused by asymmetric external forces on either side of the skull, head deformity occurs in children who spend time lying on their backs and have few antigravity postures.

ABSTRACTS

Topic: Neurodevelopmental Disorders / Developmental Neuroscience

EPNS25_356 - Development and Validation of a Mobile Application for Evaluating Development Through Video Analysis in Infants and Toddlers

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Objectives

Evaluating children's developmental status is crucial not only for monitoring typical growth but also for ensuring timely detection and intervention for developmental disorders and delays. Infants and toddlers with neurological risks often encounter delays, yet conventional assessments typically require substantial resources, specialized expertise, and considerable time, creating barriers to early diagnosis. To address these constraints and improve accessibility, a mobile, AI-driven assessment application was developed to enable caregivers to record and securely upload brief videos of their children completing structured tasks for automated analysis. These video-based assessments generate developmental scores in conjunction with newly constructed parent-report questionnaires, which are validated against established measures.

Methods

Since early identification of developmental disorders and delays by 1-3 years of age is critical for timely intervention and treatment efficacy, questionnaires and corresponding behavioral tasks for video analysis targeting children aged 14-36 months were designed. These measures cover gross/fine motor skills, cognition, expressive/receptive language, and social functioning, in line with established developmental milestones for specific ages and genders. To validate the questionnaire, 137 participants aged 14-36 months completed both the questionnaire and the K-Bayley-III assessment, serving as a normative reference for the new measure. A novel algorithm was also developed to analyze the video component of the application.

Results

When comparing mobile assessment scores with the K-Bayley-III scores for each age interval, preliminary data revealed correlations coefficients ranging from .56 to .84 for gross motor skills, .10 to .84 for fine motor skills, .07 to .91 for expressive/receptive language, and .04 to .81 for cognition domain. Individual items correlating above .60 were selected for inclusion in the final version of the mobile questionnaire.

Conclusions

By integrating video observations, parent-reported questionnaire data, and AI-driven analytics, this mobile application aims to provide a reliable and accessible tool for detecting developmental disorders and delays at a critical age. Furthermore, data gathered through this application will form a large-scale, reliable database, supporting clinical benchmarking and algorithm refinement.

ABSTRACTS

Topic: Epilepsy: Medical and Surgical treatment

EPNS25_357 - Monoaminergic modulation of limbic and thalamocortical neural networks using vagus nerve stimulation in patients with drug-resistant epilepsy (DRE)

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Objectives

Vagus nerve stimulation (VNS) is an add-on therapy approved in the EU for refractory epilepsy. Its aim is to reduce the frequency of seizures in patients with partial (with or without secondary generalization) or generalized seizures.

VNS is also indicated for the treatment of chronic or recurrent depression in patients undergoing a treatment-resistant major depressive episode.

Stimulation of the vagus nerve and the so-called vagal afferent network, triggers a cascade of neurochemical and electrophysiological events that have an anticonvulsant and antidepressant effect.

Methods

Based on the extensive published literature, a 3-step model was developed summarizing the main hypotheses on the therapeutic effects of VNS in DRE and DTD, taking into account the complexity of brain anatomy and physiology.

Results

First, activation of the brainstem leads to an increase in monoamines in certain brain regions. Furthermore, changes in excitability and neuronal activity in the amygdala and hippocampus, as well as increased metabolism in the thalamus, may control synaptic plasticity with a neuroprotective role. In addition, it is possible that a combination of electrophysiological and neurochemical changes in the cortex (e.g. normalization of GABAA receptor expression) may at least partially explain the efficacy of VNS. As shown with diffusion tensor imaging (DTI), VNS also alters functional connectivity, which is known to be abnormally high in the epileptogenic zone and can be significantly reduced in VNS responders.

Conclusions

Mapping and understanding the mechanism of action of VNS helps clinicians and researchers to differentiate between different neuromodulation therapies.

ABSTRACTS

Topic: Epilepsy: Diagnosis and Investigations

EPNS25_358 - The incidence and etiology of drug-resistant epilepsy in children in Estonia

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Objectives Epilepsy is one of the most common neurological disorders worldwide. Drug-resistant epilepsy (DRE), affecting about one-third of persons with epilepsy, is defined by the International League Against Epilepsy as ongoing epileptic seizures despite two tolerated, appropriately chosen and used antiepileptic drug regimens. The aim of the study was to investigate the incidence and etiology of DRE in children in Estonia.

Methods A retrospective population-based epidemiological study of childhood DRE was conducted from January 1, 2013, to December 31, 2017, in Estonia at Children's Clinic of Tartu University Hospital and Tallinn Children's Hospital. In Estonia, epilepsy in children is diagnosed only in two tertiary health care centers by pediatric neurologists according to the consensus document. Therefore, our study gathered all children in Estonia with DRE whose epilepsy was diagnosed for the first time in the study period by reviewing digital medical documents.

Results 1,085 children with first time epilepsy diagnosis were identified in both centers from 2013 to 2017. The overall incidence rate of childhood epilepsy was 84.1/100,000 in Estonia. DRE was identified in 10% of patients (n=110). The overall incidence rate of DRE in children was 8.5/100,000. The highest incidence rate of DRE was among patients whose epilepsy was diagnosed from one month to four years of age. Magnetic resonance imaging (MRI) of brain had been performed in 98% of the patients with DRE and etiologically relevant MRI changes were found in 43% of them. The most common structural pathology was congenital brain malformation (19%). 84% of patients with DRE had one or multiple genetic analyses performed, including chromosomal microarray analysis, next-generation sequencing techniques such as single gene sequencing, gene panels, whole exome and/or genome sequencing, and in some cases karyotyping. Some genetic changes, most commonly single gene variants, were found in 53% of tested children with DRE. However, many of them had variants with unknown significance or novel disease gene candidates. The etiology was found in 61% of patients with DRE. The most frequent etiology was structural (29%), followed by genetic (19%). Combined etiology was also considered an important factor of DRE accounting for 13% of patients.

Conclusions Our research is the first epidemiologic study of DRE in Estonia and Baltic countries in children. Describing the epidemiology of DRE in childhood will improve the management of epilepsy.

ABSTRACTS

Topic: Infectious and Inflammatory Diseases/ Neuroimmunology

EPNS25_362 - The Use of Therapeutic Plasma Exchange in Pediatric Neurology Patients: A Single Tertiary Center Experience

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Objectives This study analyzed our local experience with TPE, focusing on indications, timing of plasma exchange and safety in pediatric patients with neurological disorders

Methods This retrospective cohort study covers hospital records from from January 2023 to January 2025 identifying pediatric patients who underwent TPE (for neurological disorders)

Results The study included six patients, with an equal gender distribution. The median hospital stay was 56 days, with an average of 13 days in the pediatric intensive care unit (PICU). Presenting symptoms were varied and included fever (n=2), seizures (n=4), limb weakness (n=1), facial muscle weakness (n=1), and acute psychosis ((n=1). Notably, 4 out of 6 cases (66%) experienced seizures. Indications for TPE included relapsed ADEM (n=1), myasthenia gravis (n=1), FIRES (n=2), autoimmune encephalitis (n=1), and NORSE due to POLG mitochondrial disorder (n=1). All six patients were admitted to the PICU, and mechanical ventilation was required for 83% for a mean duration of 10.75 days. Magnetic resonance imaging was performed in 5 out of 6 patients (83%), with one patient also undergoing a CT scan of the thorax. Forty percent (2 out of 5) of the patients had abnormal MRI findings, and follow-up MRIs were conducted. The median cycles of TPE was 5 , with 4 out of 6 patients receiving 5 cycles of TPE, and 5 out of 6 patients undergoing plasma exchange within the first week of presentation. All patients completed a 5-day course of high-dose intravenous methylprednisolone before plasma exchange. The diverse patient cohort also trialed other treatment modalities such as IVIG (n=5), rituximab (n=1), mycophenolate mofetil (n=2), anakinra (n=1), and ganciclovir (n=1). There were no fatalities among the 6 patients, all of whom achieved recovery. Complications observed during and after plasma exchange included acute kidney injury (n=1), behavioral changes (n=4), sudden desaturation episodes (n=1), hallucinations (n=1), while 1 patient experienced no complications.

Conclusions Our study highlights the effectiveness of early TPE in treating autoimmune-driven neurological disorders, with manageable complications. There is a need for more clinical data to establish streamlined guidelines for TPE.

ABSTRACTS

Topic: Neurometabolic Disorders

EPNS25_363 - Multimodal MRI as a potential diagnostic biomarker for X-linked adrenoleukodystrophy

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Objectives

X-linked adrenoleukodystrophy (ALD) is an X-linked-recessive disease caused by defects in the ABCD1 gene, leading to the accumulation of very long chain fatty acids in the nervous system, adrenal glands, blood, and other tissues. Male ALD patients may present neurologically as either cerebral ALD (CALD), characterized by severe inflammatory demyelination in the white matter and rapid neurological deterioration, or as adrenomyeloneuropathy (AMN), featuring spinal cord disease. We aimed to identify pathological changes in the brain tissue of asymptomatic ALD (AALD) patients prior to the onset of CALD or AMN by exploratory analysis of multimodal magnetic resonance imaging (MRI) data.

Methods

Multimodal MRI data - including structural images, diffusion tensor imaging (DTI), myelin transfer imaging (MTI), and MR-spectroscopy (MRS) - was obtained from AALD patients with regular follow-up MRI. We analyzed longitudinal MRI data from 12 AALD patients aged 10 to 18 years who did not receive a CALD diagnosis during our surveillance and 12 healthy age-matched male controls. We performed volumetric analysis of brain structures on structural MRI data and conducted region-of-interest measurements on DTI-, MTI-, and MRS data. Statistical analysis was performed using linear mixed models.

Results

Volumetric analysis indicated white matter hypertrophy in patients with AALD. DTI analysis suggested a global increase of radial and mean diffusivity values in deep white matter tracts. MRS showed increased inositol levels in the frontal white matter. Additionally, MTsat values derived from MTI were increased in the cortical and subcortical gray matter but not in the white matter.

Conclusions

Our findings from DTI and MRS in AALD patients suggest early pathological alterations in the cerebral white matter, similar to those observed in adult AMN patients. In addition, we identified white matter hypertrophy and increased gray matter MTsat as novel MRI phenotypes associated with juvenile AALD. Our results suggest that in adolescent AALD patients, both gray and white matter are pathologically altered even before AMN or CALD become apparent. Furthermore, multimodal MRI data may be valuable biomarkers for the early diagnosis of CALD or AMN.

ABSTRACTS

Topic: Movement Disorders/ Cerebral Palsy

EPNS25_364 - Plasma Neurofilament Light Chain in pediatric hereditary spastic paraplegia

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Objectives

Plasma neurofilament light chain (NfL) is increasingly used as a biomarker of axonal damage in several neurological disorders, including hereditary spastic paraplegias (HSPs). However, studies focused on pediatric population are lacking. We aimed to explore the utility of NfL in a pediatric HSP cohort and its possible correlation with disease-specific and non-specific features.

Methods

Plasma NfL levels were measured during routine blood examinations in 38 pediatric subjects (under age 18 years) affected by genetically solved or unsolved HSPs. Longitudinal NfL data were available for 24 subjects.

Results

The median age of participants at enrollment was 12 years, with a median disease duration of 9.5 years and a median NfL level of 7.5 pg/mL. At baseline, no significant differences in NfL levels were observed between subjects with SPG or “non-SPG genes” HSPs, among GMFCS levels, between pure vs complex forms (with a non-statistically significant increase in the latter) and between congenital- and childhood-onset forms. A significant inverse correlation was found between baseline NfL levels and disease duration. Plasma NfL levels exhibited an age-related trend similar to that seen in the healthy pediatric population, but at higher reference centiles. No differences were observed in longitudinal evaluation after a median follow-up period of 9 months.

Conclusions

NfL appears to be a potential peripheral biomarker of axonal damage in pediatric-onset HSPs, with levels often at the higher centiles of the norm, more elevated in complex forms, in younger subjects, and in those with shorter disease duration. However, due to limitations of our work, larger and longer studies are needed to further establish NfL's diagnostic and prognostic relevance in these conditions.

ABSTRACTS

Topic: Neuromuscular Disorders

EPNS25_365 - Survival Analyses in Patients With Thymidine Kinase 2 Deficiency (TK2d) Aged ≤12 Years at Symptom Onset Who Received Pyrimidine Nucleos(t)ide Therapy

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Objectives: To assess survival outcomes and safety of pyrimidine nucleos(t)ides in patients with thymidine kinase 2 deficiency (TK2d) with an age of TK2d symptom onset ≤12 years. TK2d is an ultra-rare, autosomal recessive, progressive mitochondrial disease. Understanding survival outcomes and safety in this subgroup of patients is important given that young age of symptom onset is associated with rapid disease progression and premature death, often from respiratory failure. No treatments are approved; however, pyrimidine nucleoside therapy with doxecitine and doxribtimine is in development.

Methods: Patients treated with pyrimidine nucleos(t)ides were pooled from retrospective (NCT03701568, NCT05017818) and prospective (NCT03845712) sources and a company-supported expanded access program (EAP); untreated patients were pooled from literature reviews of case series and reports (2019; updated 2021) and a retrospective chart review (NCT05017818). Survival in 50th-percentile matched-pairs of treated and untreated patients was assessed using proportional hazard and marginal Cox models and restricted mean survival time (RMST) analyses.

Results: Survival analyses included 82 treated patients (median [quartile (Q)1, Q3] treatment duration: 54.8 [15.2, 78.4] months) and 93 untreated patients, all with an age of TK2d symptom onset ≤12 years. Three treated patients (3.7%) and 53 untreated patients (57.0%) died. Treatment reduced risk of death by 92–94% (hazard ratio=0.06–0.08; p<0.0001) and 87–95% (hazard ratio=0.05–0.13; p<0.0001) in the time from symptom onset and treatment initiation, respectively. RMST (95% confidence interval) for treated and untreated patients, respectively, was 29.2 (28.2–30.3) years and 14.4 (11.1–17.6) years over 30 years after symptom onset, and 5.8 (5.5–6.0) years and 2.8 (2.2–3.5) years over 6 years after treatment initiation. In the safety population (n=50; EAP not included), two patients (4.0%) experienced treatment-emergent adverse events (TEAEs) leading to treatment discontinuation; among those with available data, diarrhea was the most common TEAE (33/39 [84.6%]).

Conclusions: In patients with an age of TK2d symptom onset ≤12 years, pyrimidine nucleos(t)ide therapy significantly decreased mortality, increased survival time, and was well tolerated.

UCB funded this study.

ABSTRACTS

Topic: Miscellaneous

EPNS25_366 - Pain prevalence and characteristics in neurofibromatosis type 1

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Objectives: Pain is a global health problem. The global prevalence of chronic pain (lasting at least 3 months prior the survey) in adult population is around 20% with 10% of newly diagnosed with chronic pain annually. Regarding the global prevalence of pain in the past 30 days prior the survey, it ranged between 9.9 – 50.3% and was higher in females and in lower income group. The global prevalence of chronic pain in children was 20.8% and it was higher in girls. Regarding the localisation, the headache and the musculoskeletal pain were the most common and the general pain/multisite pain was the third most represented. The pain is common in the neurofibromatosis type 1 (NF1) with prevalence ranging from 29% up to 70% but it is often overlooked. Approximately 70% of children and adults with NF1 use prescription pain medications. The aim of this pilot study is to estimate the prevalence and characteristics of the pain in adolescents and adults with NF1.

Methods: The study included 29 patients with NF1. The mean age was 22.6±11.2 years (range 13 – 65 years; 72% female subjects). The short telephone survey addressed: the presence of the pain at the moment of the survey and in the past three months, severity (from 1 to 10), localisation, description of the pain, usage of pain medications and influence on the quality of life (none, a little, moderate, profound).

Results: At the moment of survey 13.8% of subjects reported pain (pain severity mean 7, pain severity range 4 – 10; 75% reported trunk localisation). 31% of subjects reported chronic pain (pain severity mean 7.2, pain severity range 4 – 10; pain localisation: 55.6% head, 44.4% extremities and 33.3% trunk). 88.9% of subjects reporting chronic pain used over-the-counter pain drugs. Regarding pain negative impact on the quality of life: 55.6% of subjects reported a little, 11.1% reported moderated and 22.2% of subjects reported profound impact.

Conclusions: The prevalence of chronic pain in NF1 is more common than general population with majority of subjects using pain medication and reporting negative influence on the quality of life. The pain should be addressed as the common clinical characteristic in the future studies of subjects with NF1.

ABSTRACTS

Topic: Neurometabolic Disorders

EPNS25_367 - Incidence of Peroxisomal Diseases in Southern Spain. Newborn Screening for X-linked adrenoleukodystrophy: exceptional pilot study using home-made LC-MS/MS method

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Objectives

X-linked adrenoleukodystrophy (XALD) is the most common leukodystrophy and peroxisomal disease, with an estimated prevalence 1:10,000 live births. In 2013, New York became the first state to introduce newborn screening (NBS) for X-ALD. Our laboratory has started, for the first time in Europe, a universal prospective NBS pilot study for XALD from July 2022 using LC-MS/MS as a first and second tier.

Methods

From July 2022 to January 2025, C24:0-LPC and C26:0-LPC levels were measured in DBS by an inhouse LC-MS/MS in both the first and second tier in 75,500 dot blood spots (DBS) samples. Also, biochemical and genetic analysis were carried out.

Results

A total of 15 newborns were positive, being 9 males and 6 females. The first one ([1] patient), expressed variants in the HSD17B gene c.1369 A>T (p.Asn457Tyr) pathogenic heterozygous and c.1681G>C (p.Ala561Pro) likely pathogenic. The [2] patient, also for HSD17B4 gene, c.742C>T (p.Arg248Cys) homozygous including other mutation in the ACADM gene c.985A>G (p.Lys329Glu) causing comorbidity MCAD deficiency. The [3] patient, homozygous for the PEX6 gene c.2111 C>T (p.Ala704Val), VUS variant. These three patients died before six months of life. The rest of newborns were asymptomatic. Seven of them showed ABCD1 mutations. [4] patient c.761 C>T (p.Thr254Met) heterozygous pathogenic; [5] patient c.1900 G>A (p.A634T) hemizygous likely pathogenic; [6] patient c.1747 G>A (p.V583M) hemizygous likely pathogenic; [7] patient c.1415_1416delAG (p.Gln427fs) heterozygous pathogenic; [8] patient c.2111 C>T (p.Ala704Val) hemizygous VUS; [9] patien t c.893G>A p.Gly298Asp heterozygous likely pathogenic; [10] patient c.872A>G p.(Glu291Gly) heterozygous pathogenic. The other five newborns are still under study.

Conclusions

Neonatal screening for XALD is an effective tool for early detection of the disorder. Our study is the first universal neonatal screening performed in Europe. The prevalence of peroxisomal disorders could be higher than estimated in our population (rate of NBS positive result detection 1/5,033). NBS for XALD allows identification of other peroxisomal diseases characterized by the increase of C26:0-LPC.

ABSTRACTS

Topic: Neuromuscular Disorders

EPNS25_368 - Functional Outcomes in Patients With Thymidine Kinase 2 Deficiency (TK2d) Aged ≤12 Years at Symptom Onset Who Received Pyrimidine Nucleos(t)ide Therapy

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Objectives: To assess functional outcomes and safety of pyrimidine nucleos(t)ides in patients with thymidine kinase 2 deficiency (TK2d) with an age of TK2d symptom onset ≤12 years. TK2d is an ultra-rare, autosomal recessive, mitochondrial disease associated with progressive, life-threatening proximal myopathy. Understanding motor function and use of supportive care in the subgroup of patients with a young age of symptom onset is important given that they tend to experience rapid disease progression. No treatments are approved; however, pyrimidine nucleoside therapy with doxecitine and doxribtimine is in development.

Methods: Patients treated with pyrimidine nucleos(t)ides were pooled from retrospective (NCT03701568, NCT05017818) and prospective (NCT03845712) sources and a company-supported expanded access program (EAP; function outcomes not collected). Developmental motor milestone profiles and use of ventilatory and feeding support were compared pre- and post-treatment.

Results: Overall, 82 patients with an age of TK2d symptom onset ≤12 years were treated with pyrimidine nucleos(t)ides (median [quartile (Q)1, Q3] treatment duration: 54.8 [15.2, 78.4] months). Pre-treatment, 83.7% of patients (41/49) lost ≥1 motor milestone and 40.8% (20/49) lost ≥4 (missing/not-at-risk=33); 4.9% of patients (2/41) regained ≥1 previously lost motor milestone (missing/not-at-risk=41). Post-treatment, 21.7% of patients (10/46) lost ≥1 motor milestone and 2.2% (1/46) lost ≥4 (missing/not-at-risk=36); 75.0% (30/40) regained ≥1 previously lost motor milestone, and 22.5% (9/40) regained ≥4 (missing/not-at-risk=42). Of 31 patients (37.8%) using ventilatory support at treatment initiation (missing=29), 16.1% (5/31) reduced hours of use and 16.1% (5/31) discontinued support post-treatment. Of 19 patients (23.2%) using feeding support at treatment initiation (missing=30), few (2/19 [10.5%]) discontinued support post-treatment. In the safety population (n=50; EAP not included), two patients (4.0%) experienced treatment-emergent adverse events (TEAEs) leading to treatment discontinuation; among those with available data, diarrhea was the most common TEAE (33/39 [84.6%]).

Conclusions: In patients with an age of TK2d symptom onset ≤12 years, pyrimidine nucleos(t)ide therapy is well tolerated and may improve functional outcomes, including retaining or regaining motor milestones and stabilizing ventilatory and feeding support use.

UCB funded this study.

ABSTRACTS

Topic: Infectious and Inflammatory Diseases/ Neuroimmunology

EPNS25_369 - Differentiating Pediatric acquired demyelinating syndromes based on HLA typing, clinical, radiological, and immunological features- an ambispective observational study

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Objectives
The prototype Pediatric acquired demyelinating disorders (ADS) are acute disseminated encephalomyelitis (ADEM), clinically isolated syndrome (CIS), myelin oligodendrocyte glycoprotein associated demyelination (MOGAD), neuromyelitis optica spectrum disorders (NMOSD), and multiple sclerosis (MS). Human leukocyte antigen (HLA) DRB1:15 and DQB1:06 alleles are predictive of Pediatric MS in Caucasians. The objectives of the current study are to describe clinical, immunological, and radiological features and compare HLA alleles for various subtypes of Pediatric ADS in an ambispective Indian (non-Caucasian) cohort.

Methods
Patients aged 6 months-18 years, with ADS, presenting during 2021-2023 (on follow-up or newly diagnosed) at a north Indian tertiary teaching hospital were enrolled for the study. Acute presentations were treated with pulse methylprednisolone followed by tapering oral steroids. Azathioprine was started in all recurrent/progressive cases. Rituximab was given in refractory acute cases and chronic cases who relapsed on Azathioprine. Plasma exchange and/or IVIG was instituted in sero-positive acute cases refractory to first-line therapy. HLA alleles were studied by Luminex technology.

Results
Ninety consecutive cases were enrolled (56.7% males, median age at onset: 120 months, IQR:72-144). Commonest diagnosis was MOGAD (33/90, 36.7%), followed by monophasic CIS (24/90, 26.7%), MS (18/90, 20%), NMOSD (10/90, 11.1%) and ADEM (5/90, 5.6%).
At latest follow-up, 84.4% (76/90) had a Pediatric cerebral performance category scale score of 1-2 (no significant difference between subtypes). A non-ON (optic neuritis)-non-TM (transverse myelitis) CIS in the first episode was significantly associated with a diagnosis of MS (p=0.001) in follow-up. Amongst MOGAD, 42.4% (14/33) cases recurred. The presence of ON in the first episode significantly predicted recurrence (p=0.03).
HLADRB1:03 (p=0.02) and HLADQA1:05 (p=0.005) alleles were significantly associated with a diagnosis of MS. HLDRB1:15 allele distribution was comparable between MS and the rest.

Conclusions
Overall, Pediatric ADS is associated with good functional outcome irrespective of subtype. HLA allelic distribution may show ethnic variation in Pediatric MS. Clinical, radiological, and immunogenetic features should be evaluated in larger samples to develop predictive models for Pediatric MS to aid in timely institution of long-term immunomodulation.

ABSTRACTS

Topic: Infectious and Inflammatory Diseases/ Neuroimmunology

EPNS25_370 - Anxiety and Depression in Paediatric Multiple Sclerosis

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Objectives: Paediatric multiple sclerosis (PedMS) is a rare, immune-mediated, chronic and neurodegenerative diseases of the brain and spinal cord. Basic pathophysiological mechanisms include inflammation, demyelination and axonal degeneration. PedMS is characterized with a variety of clinical manifestations. Neuro-ophthalmological, sensory, cognitive and motor deficits in PedMS are commonly accompanied by anxiety and depression. Anxiety and depression can significantly affect school achievement and social interactions. Some studies have shown that PedMS patients have a higher prevalence of depression and anxiety than healthy subjects. The lifetime prevalence of depression ranges from 19% to 54% in the adult population, while the prevalence in PedMS patients is about 27%. The aim of this study is to examine the presence of anxiety and depressive symptoms in PedMS.

Methods: The study included 44 patients with PedMS who were diagnosed and treated at the Clinic of Neurology and Psychiatry for Children and Youth in cross-sectional observational study. Neurological disability was assessed via the Extended Neurological Disability Scale (EDSS). The assessment of anxiety and depressive symptoms was performed using the SMFQ and SCARED questionnaires, in which an elevated score indicates the presence of anxiety or depressive symptoms. PedMS patients with high scores were referred to a child psychiatrist for further evaluation and clinical assessment.

Results: 16 (36.4%) boys and 28 (63.6%) girls were included in the study. The mean age of patients at onset was 14.7 ± 1.5 years (range: 10-17.5 years). All 44 (100%) patients have relapsing-remitting PedMS at the onset of the disease. The median EDSS is 1.5 (0-3.5). The average SMFQ was 2.98 (0-19), while the average SCARED was 13.43 (0-54). Clinically relevant anxiety and depressive symptoms were present in 7 (15.9%) patients. The diagnosis of depression was confirmed in 5 (11.4%).

Conclusions: The most common form is relapsing-remitting PedMS. The presence of anxiety and depressive in our cohort is more frequent than reported for general populations, but less common than reported in adult MS patients.

ABSTRACTS

Topic: Epilepsy: Diagnosis and Investigations

EPNS25_371 - Genetic Insights and Management Strategies in Pediatric Refractory Epilepsy

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Objectives: To describe the characteristics of patients with refractory epilepsy and investigate the correlation between clinical and genetic profiles, highlighting the impact of genetic variants on disease presentation and management.

Methods: A single-center prospective study included pharmacoresistant epilepsy patients across three age groups: neonatal, infancy, and childhood. Data were collected from medical records, including demographics, disease features, comorbidities, electroencephalogram (EEG) findings, and magnetic resonance imaging (MRI) results. Genetic analyses involved Whole Exome Sequencing and Whole Genome Sequencing.

Results: Nineteen patients with a median diagnostic age of 11.8 months (range: 0–48) were studied, with genetic evaluations completed after 44.9 ± 43.5 months. Diagnoses included Infantile epileptic spasms syndrome, Severe myoclonic epilepsy of infancy, Genetic epilepsy with febrile seizures plus, Continuous spike and waves during sleep, Developmental and epileptic encephalopathies (DEE). Seizure types encompassed febrile, generalized tonic-clonic, absence with eyelid myoclonus, focal seizures with impaired consciousness, and epileptic spasms. EEG findings revealed focal/generalized epileptiform discharges, hypsarrhythmia, and burst suppression, aligning with clinical and genetic profiles. Brain MRI showed structural abnormalities such as delayed myelination, cystic encephalomalacia, and hypoplasia of corpus callosum.

Genetic testing identified variants in epilepsy-related genes (e.g., *SCN1A, SCN1B, KCNQ2, CDKL5*). Variants of uncertain significance (VUS) were noted in genes such as *FLNA, NSF* and *NGLY1.* Two patients had no identifiable genetic cause. Autosomal recessive mutations were significant, with parents often carrying pathogenic variants (*CRELD1, NGLY1*). De novo mutations were predominant in autosomal dominant conditions. Some families reported additional neurological symptoms - migraine or febrile seizures in siblings, suggesting modifying effects of secondary variants.

Genetic findings informed treatments for 8 patients, including ganaxolone for CDKL5 deficiency disorder, fosdenopterin for *MOCS1*-related Molybdenum cofactor deficiency, vigabatrin and everolimus for Tuberous sclerosis complex disorder, stiripentol for SMEI, topiramate, perampanel, benzodiazepines, and sodium-channel blockers for DEE, and molybdenum and galactose in Congenital Disorder of Glycosylation Type II.

Conclusions: This study emphasizes the critical role of genetic testing in diagnosing and managing refractory epilepsy syndromes. Identifying pathogenic variants informs treatment strategies and provides valuable insights into inheritance patterns and familial risk. Further research into VUS and emerging genetic syndromes is essential for advancing personalized medicine in pediatric epilepsy.

ABSTRACTS

Topic: Neurogenetics

EPNS25_372 - 20 Years International Network for Therapy of rare Epilepsies (NETRE)

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Background: In 2005, case-based discussions among pediatric epileptologists and neuro-pediatricians led to the formation of an informal network to discuss and share treatment recommendations for patients with rare epilepsies, which subsequently formed the basis of NETRE (Network for Therapy in Rare Epilepsies). In addition to facilitating the exchange of treatment experiences, NETRE enables clinicians to collect data on genetics, clinical presentation, and comorbidities of patients with rare genetic epilepsies. Here we describe the structure of the rapidly growing NETRE and summarize some of the findings of the last 20 years

Method/Structure of NETRE: NETRE is organized in subgroups according to patient-related genetic findings for which medical coordinator(s) are appointed. Data are exchanged and/or collected by contacting the subgroup coordinator who sends an e-mail request to all registered NETRE members, using a data collection form. Treatment options and information on individual treatment trials are collected. In addition to information on treatment options such as anti-seizure medication (ASM), ketogenic diet or epilepsy surgery, the focus is on clinical and scientific aspects of the disorders, which are covered in numerous collaborations with international research groups and self-help organizations, leading to numerous scientific publications in various medical journals. NETRE is neither funded nor sponsored. NETRE members are informed about new members, new groups and projects through a quarterly newsletter. In 2023, team channels were opened as an additional interaction channel for the individual groups as part of the restructuring and renewal due to the enormous growth in membership.

Results: As of December 2024, there are 1037 NETRE members from 52 countries with more than 609 NETRE groups, according to single gene mutations, numerical or structural chromosomal alterations, metabolic disorders or genetic/epilepsy syndromes.

In the past NETRE was able to describe e. g. the pathognomonic chewing- induced seizures in *SYNGAP1*, the MRI phenotype of *FOXG1*, collect data on treatment in rare epilepsies on medications (RATE) such as Perampanel and ketogenic diet (ongoing study with 240 patients), contribute to genotype-phenotype correlations (actual big cohorts on *IQSEC, COL4A1/2* and *FOXG1*), conduct pilot projects with self-help organizations such as Patient Reported Outcome Measures (PROMs) in rare genetic epilepsies (e.g. *SYNGAP1*).

Prospects: NETRE enables clinicians to quickly and easily share clinical and therapeutic experiences in rare diseases with colleagues around the world, helping to improve care of these special patients. At the same time, this easy exchange provides a basis for further research projects

ABSTRACTS

Topic: Infectious and Inflammatory Diseases/ Neuroimmunology

EPNS25_373 - A single-center retrospective cohort study of paediatric and adult subjects: Comparison of Maintenance Therapy in Multiphasic MOGAD

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Objectives

The study aims to enhance understanding of optimal maintenance treatment for multiphasic myelin oligodendrocyte glycoprotein antibody-associated disease (MOGAD).

Methods

A retrospective review was conducted on patients treated for MOGAD at Ghent University Hospital between 2010 and 2024. Diagnosis was made according to the criteria established by Banwell et al., 2023.

Results

The cohort (n=36) included 19 paediatric patients (acute disseminated encephalomyelitis (ADEM) n=11, neuritis optica (ON) n=6, transverse myelitis (TM) n=2) and 17 adult patients (ADEM n=2, ON n=8, TM n=2, neuromyelitis optica spectrum disorder (NMOSD) n=4). The male-to-female ratio was 3:1. The median follow-up was 26 months [3.5-147 months].

Following the initial episode, five patients started with maintenance therapy (mycophenolate mofetil (MMF) n=2, rituximab (RTX) n=3). Overall, 9 out of 36 patients experienced a first relapse, including one patient on RTX. Relapses were characterized as ON (n=6), ADEM (n=2) and NMOSD (n=1). Of these, seven patients achieved relapse-free status with MMF of whom one was switched to alternated day therapy with corticosteroids due to poor tolerance. One patient remained relapse-free after a single relapse without any therapy.

Three patients experienced multiple relapses: two began maintenance therapy only after the second relapse, while one started after the fifth relapse. One patient had eight relapses and became relapse-free on alternate-day therapy with corticosteroids. In total, five relapses occurred during RTX treatment, compared to two with MMF.

Conclusions

In this cohort, RTX appeared less effective in relapse prevention compared to MMF. Given the retrospective nature of the study and the limited sample size, findings should be interpreted cautiously. Alternate-day corticosteroids may be a viable option for refractory MOGAD cases.

ABSTRACTS

Topic: Epilepsy: Medical and Surgical treatment

EPNS25_374 - Sleep Quality in Children with Confirmed Genetic Epilepsy undergoing Vagus Nerve Stimulation

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Objectives

Many drug-resistant genetic epilepsy syndromes are associated with sleep problems in children leading to additional stress for the patients themselves and caregivers. The effects of vagus nerve stimulation (VNS Therapy) on sleep quality are not fully understood: some studies report improved sleep quality in patients with drug-resistant epilepsy (DRE) undergoing VNS, others report reduced sleep quality, and some show no difference at all. This analysis aims to assess sleep quality in children with confirmed genetic epilepsy (CGE) undergoing VNS Therapy in the prospective, mulitcenter, multinational observational study, CORE-VNS.

Methods

Participants with CGE who received VNS Therapy were selected. Changes in the global score and subdomains of the Children's Sleep Habits Questionnaire (CSHQ) were analysed for children aged 2-17. The CSHQ is a 33-item parent-report questionnaire designed to assess the following sleep problems in children (night waking, daytime sleepiness, behavior during sleep, and bedtime behavior). CSHQ response options are on a 5-point scale from "Always" (occurs every night) to "Never" (occurs less than once a week) based on frequency during the past week (or most recent typical week). CSHQ has been validated for screening for sleep disorders in children presenting an internal consistency of 0.68 for the global score in a population-based sample and ranging from 0.36 - 0.70 for the subscales.

Results

Full CSHQ data was available from 48 patients with CGE at baseline and from 29 patients at 24 months. At baseline the mean global CSHQ score was 54.21 (5.1) which is distinctly above the abnormality cut-off points of 41. CSHQ scores were lower at all follow-up visits after initiation of VNS Therapy, and this reached statistical significance at three months (p=0.005) and at six months (p=0.028) of VNS Therapy. However, this improvement was no longer significant at subsequent visits. At three months (p=0.041) and 12 months (p=0.019), the domain of morning waking and daytime sleepiness was improved compared to baseline. However, this improvement was no longer significant at 24 months. The only domain that showed significant change at 24 months of VNS Therapy compared to baseline was "waking during the night": scores improved from 3.87 (1.4) at baseline to 3.33 (1.4) at 24 months (p=0.002).

Conclusions

Global sleep habits did not show significant change in the course of 24 months of VNS Therapy. However, VNS Therapy for DRE may be associated with an improvement of certain sleep behaviors, like waking during the night in children with CGE.

ABSTRACTS

Topic: Neuromuscular Disorders

EPNS25_375 - In search of longitudinal objective outcome measures in X-ALD: postural sway and gait analyses over time

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Objectives

The predominant clinical presentation of X-ALD is a slowly progressive myeloneuropathy, characterized by a spastic paraparesis which leads to impairment in postural control and gait disturbances. The clinical heterogeneity is wide, ranging from mildly affected patients with minor walking problems to severe spastic paraparesis resulting in wheelchair dependency. There is a lack of objective outcome measures to quantify disease progression. Currently used scoring methods include the Expanded Disability Severity Scale (EDSS) which has a high intra-rater variability and is prone to subjective interpretation [1]. Our research group previously showed in a cross-sectional report the clinical relationship between spinal cord disease and gait and balance disturbances, using wearables [2]. The aim of this study is to analyze the longitudinal changes in sway and gait parameters and to assess whether the changes are correlated to clinical change over time.

Methods

Data will be collected from prospective cohorts followed in two centers. Postural sway and gait parameters will be analyzed using wearable devices in four different paradigms: feet apart eyes open (FAEO), feet apart eyes closed (FAEC), feet together eyes open (FTEO) and feet together eyes closed (FTEC). Disease severity for spinal cord disease and bladder and bowel dysfunction is measured by the EDSS. Information on quality of life (QoL) is collected for all patients. The relationship between changes in disease in severity and changes in gait speed, toe-off angle and sway parameters during follow-up will be evaluated.

Results

Fifty six male patients from the Amsterdam UMC cohort are included. We analyzed fifty six baseline and 22 follow-up assessments in the two year follow-up period. There were statistically significant decreases in toe-off angle (1.5 degrees) and gait speed (0.12 m/s) during follow-up. Changes in sway parameters were seen in all four paradigms, but there was only a significant change in the FTEO and FTEC paradigms during follow-up. The Timed up and Go test also showed statistically significant changes during two-year follow-up.

Conclusions

We have shown in our preliminary results statistically significant changes in sway and gait parameters during follow-up. These results are very promising to propose sway and gait parameters as objective outcome measures to assess disease severity in X-ALD. Data from the Kennedy Krieger Institute are yet to be added to our analyses. Further analyses on sway and gait progress rates between mildly and severely affected patients will be conducted.

ABSTRACTS

Topic: Epilepsy: Diagnosis and Investigations

EPNS25_376 - Anxiety, depressed mood, and fear of siblings of pediatric patients diagnosed with epilepsy: a cross-sectional study

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Objectives: The study primarily aims to assess the impact of psychosocial symptoms—namely anxiety, depressed mood, and fear—on the siblings of individuals with epilepsy. Its specific objectives are twofold: first, to identify the range of psychosocial symptoms, including anxiety, depressed mood, and fear, experienced by siblings of patients with epilepsy; and second, to explore the relationship between these psychosocial symptoms and factors such as age, gender, educational attainment, birth order, and family size.

Methods: Participants were siblings of a pediatric patient diagnosed with epilepsy (aged 0 months to 18 years) who attended follow-up consultations with a pediatric neurology physician at a tertiary hospital. The questionnaire used was adapted from Sibling voices survey where the psychosocial impact of growing up with a sibling with epilepsy can be explored according to specific age groups. The survey focused on a range of psychosocial symptoms, including symptoms of anxious or depressed mood, and fear and were measured using visual analog scale scores. The questionnaire was accessed through Google Forms where assent or consent was obtained after reading the description of the study.

Results: A total of 108 respondents were gathered in the study. The majority of respondents were aged 18 and above with 24.1% being female and 23.1% being male. 46.3% came from larger families, and 42.6% were first or second-born children. Additionally, 32.4% of females were in primary or secondary school, reflecting the diverse age range of siblings participating in the study. Fear (p-value .025) and depressed mood (p-value .005) were statistically significant among siblings aged 18 years old and above. Fear was also common in first and second-born children (p-value .047), as well as in tertiary school-aged students and those already working (p-value .016).

Conclusions: The study highlights that older siblings are significantly impacted by the emotional strain of living with a sibling with epilepsy. The study also underscores the importance of recognizing the emotional toll on first and second-born children, who often take on caregiving roles, and tertiary school-aged students and working individuals, who experience compounded stress from academic or professional pressures alongside emotional caregiving. Proposed emphasis on the need for targeted interventions and support systems to address the unique psychosocial needs of siblings.

ABSTRACTS

Topic: Neurometabolic Disorders

EPNS25_377 - Treatment of device colonisations under ICV-ERT in CLN2 patients: Development and long-term assessment of an antibiotic lock therapy

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Objectives

Biweekly intracerebroventricular enzyme replacement therapy (ICV-ERT) with Cerliponase alfa is the only approved treatment for CLN2 disease. We have treated a total of over 70 patients with more than 8000 ICV-ERTs at our centre. Both, long infusion time of 4 hours as well as recurrent administration of the enzyme significantly increase the risk for device related adverse events such as device infection and device colonisation. Device colonisations are defined as cases where two consecutive CSF culture results are tested positive for Cutibacterium acnes (C. acnes), in the absence of any accompanying clinical symptoms as well as without any signs of CSF pleocytosis. Any other positive bacterial CSF culture result is diagnosed as device infection and treated accordingly with device explantation and intravenous antibiotic regimen.

The objective of this study was (i) to analyse the occurence of device colonization, (ii) to develop an antibiotic lock therapy (ALT) to prevent recurrent device replacement and (iii) to perform a long-term assessment of the newly developed treatment.

Methods

This is a single center retrospective observational study. Per institutional standard of practice, CSF was obtained prior to each ICV-ERT and tested for pleocytosis and presence of microorganisms by long-term culture.

Results

Device colonisations with C. acnes were detected in a total of 16 devices in 12 patients between October 2013 and August 2024. As no clinical signs nor pleocytosis were present in all events, we stopped explanting the devices and instead performed an ALT using 10 mg of Vancomycin dissolved in 2 ml of 0.9% NaCl administered into the device at the end of each subsequent ICV-ERT.

Long-term follow-up of 12 patients treated with ALT after each ICV-ERT for up to 4 years showed no clinical signs of device infection, no clinical impact on ICV-ERT or the device. Since start of ALT, CSF samples prior to each ICV-ERT were assessed for any re-occurrence of C. acnes including an antibiotic resistogram. No resistance to vancomycin was detected in the treated patients.

Conclusions

ALT of device colonisations with C. acnes using Vancomycin has been successful in preventing subsequent C. acnes derived device infections and avoiding necessity for device replacement. Therefore, distinction between device infection and colonisation is important in order to provide optimal treatment for these patients.

ABSTRACTS

Topic: Cerebrovascular Disorders

EPNS25_378 - The Natural History of Paediatric Sturge-Weber Syndrome: A MultinationalCross-Sectional Study

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Objectives

The Sturge-Weber Syndrome (SWS) is a rare neurocutaneous disease, characterized by a capillary venous malformation of the skin, the brain and the eye. It results in a facial portwine birthmark, often therapy resistant epilepsy, and glaucoma. Contemporary comprehensive data on epidemiology, clinical symptoms, diagnostic procedures and therapy are scarce.

Methods

We conducted a cross-sectional, multinational observational study using a well-established neuropaediatric network ("ESNEK" at University Medicine Göttingen) including Germany, Switzerland and Austria. All types of SWS including Roach types I-III were eligible. For the study, participating parents/ caregivers and child neurologists filled in questionnaires on patient history, diagnostic procedures, current symptoms, and therapy. Data analysis was exploratory.

Results

Our neuropaediatric network recorded 111 notifications, corresponding to an estimated SWS prevalence of 7.37/million in Germany, 4.60/million in Switzerland, 2.61/ million in Austria. 47 patients (43%) agreed to participate in our study. Age at inclusion ranged from 115 days to17 years (median 4.2 years). 83 % of the cohort were diagnosed with SWS within the first year of life. MRI detected leptomeningeal capillary malformation in all cases, and cerebral atrophy in 35/47 (75 %). Paresis was frequent (60 %). Forty-three patients (91 %) were diagnosed with epilepsy, 53 % required antiseizure medication (ASM) combination therapy for seizure control. 8.5 % received epilepsy surgery, resulting in seizure freedom in 50 % of operated patients. 45% of the cohort were treated with aspirin. No significant differences were observed between patients with and without aspirin regarding seizure frequency, number of current ASM, overall SWS neuroscores. Both stroke-like episodes and cases with severe/significant paresis were numerically lower in the aspirin group (3 vs 5 stroke-like episodes, and 7 vs. 10 significant/severe paresis). Neuroscores showed low, positive correlations with age at inclusion (rho 0.369, 95 % CI 0.092; 0.593).

Conclusions

We present detailed clinical profiles of a contemporary multinational paediatric cohort diagnosed with Sturge-Weber Syndrome, as well as disease prevalence estimates for Germany, Switzerland and Austria. Our data show that many patients require ASM combination therapy for seizure control, and that both administration of aspirin and epilepsy surgery are promising therapy options.

ABSTRACTS

Topic: Neuromuscular Disorders

EPNS25_380 - Exploring higher doses of nusinersen in spinal muscular atrophy (SMA): final results from Parts B and C of the 3-part DEVOTE study

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Objectives

DEVOTE (NCT04089566), a 3-part, prospective, Phase 2/3 trial, was designed to evaluate an investigational higher-dose regimen of nusinersen (two 50 mg loading doses 14 days apart, then 28 mg maintenance doses every 4 months) in participants with spinal muscular atrophy (SMA).

Methods

DEVOTE enrolled 145 participants aged 15 days to 65 years across SMA types. The pivotal Part B cohort enrolled treatment-naive infantile-onset participants (n = 75) randomized (2:1) to receive the 50/28 mg regimen or the currently approved 12/12 mg regimen. A prespecified matched sham control group from ENDEAR (NCT02193074) (n = 20) served as the primary comparator for the 50/28 mg regimen (n = 50). Part C (supportive; open-label) enrolled children and adults with infantile-onset or later-onset SMA who transitioned from the 12/12 mg regimen to the 50/28 mg regimen (n = 40).

Results

The 50/28 mg regimen was generally well tolerated, with adverse events broadly consistent with the 12/12 mg regimen of nusinersen. In Part B, the 50/28 mg regimen (baseline mean Children's Hospital of Philadelphia Infant Test of Neuromuscular Disorders [CHOP-INTEND] score of 20.9) showed a statistically significant improvement over the matched sham comparator on the primary endpoint of change in CHOP-INTEND from baseline to Day 183 (least-squares mean +15.1 versus −11.1; difference [95% confidence interval]: 26.19 [20.7, 31.7]; $p < 0.0001$). Results favored the 50/28 mg regimen relative to sham across secondary endpoints (Hammersmith Infant Neurological Exam section 2, plasma neurofilament light chain, event-free/overall survival). Results also trended in favor of the 50/28 mg regimen over the 12/12 mg regimen on key biomarker and efficacy measures. Supportive data from Part B also demonstrated the benefit of the 50/28 mg regimen in treatment-naive later-onset participants.

In Part C, participants experienced improvements in motor function after transitioning to the 50/28 mg regimen, with mean (standard deviation) increases from baseline at Day 302 of 1.8 (3.99) points on the Hammersmith Functional Motor Scale Expanded and 1.2 (2.14) points on the Revised Upper Limb Module.

Conclusions

Collectively, these data demonstrate the safety and efficacy of the 50/28 mg regimen of nusinersen.

ABSTRACTS

Topic: Miscellaneous

EPNS25_381 - Pediatric Brain Death and Organ Donation: A Single Center Experience

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Objectives: Brain Death (BD) is a clinical diagnosis compatible with an irreversible loss of all brain functions, including the brain stem. We aimed to reveal the causes of BD and the organ donation rates in our center.

Methods: Data of 25 patients diagnosed with BD between Augst 1, 2019, and December 31, 2024 at Ondokuz Mayıs University, Pediatric Intensive Care Unit (PICU) were reviewed retrospectively.

Results: During the period, 3085 patients were hospitalized at the PICU, with an overall mortality of 10% (n = 309). BD was identified in 25 patients (8.09%). Their median age was 78.6 months (1-178months ± 57.41), and the male-to-female ratio was 5.25:1. The most frequent cause of BD was traumatic brain injury in (n=9) 36%, followed by hypoxic-ischemic injury due to cardiac arrest (n=6) 24%. The mean time to diagnosis after BD suspicion was 23.6±18 hours. Computed tomography angiography was the most performed ancillary method at 100%. Of the cases, hemodynamic instability developed in 14 (56%), multiple organ failure in six (24%) and diabetes insipidus in five (20%). We used the Pediatric Cerebral Performance Category (PCPC) as a metric of preillness developmental status. Most patients (n=19, 76%), did not have preexisting neurological dysfunction. Sixteen of 25 patients were suitable for organ donation. Out of the 16 cases, eight (50%) families accepted organ donation. Five patients (20%) became organ donors.
Conclusions: Pediatric BD is a highly complex and sensitive in pediatric practice issue. Organ transplantation is a life-saving intervention for pediatric patients with end-stage organ failure. We aimed to draw attention to the importance and awareness of the diagnosis of BD regarding organ donation.

ABSTRACTS

Topic: Neurogenetics

EPNS25_383 - Biallelic MED29 variants cause pontocerebellar hypoplasia with cataracts

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Objectives

Pontocerebellar hypoplasia (PCH) represents a group of disorders characterized by cerebellum and pons hypoplasia, variable cerebral involvement, microcephaly, severe global developmental delay (GDD) and seizures. We sought the genetic cause of PCH in two siblings.

Methods

Genetic workup was performed by whole-exome sequencing followed by Sanger validation. Morpholino-knockdown zebrafish embryos with human wild-type gene rescue were used to assess cerebellar development and motor function. Transfected mouse hippocampal cultures and electroporated mouse embryos were employed to assess functional effects on neuronal morphology and development.

Results

Both patients presented with profound GDD, severe microcephaly, cataracts and variably seizures. Their MRIs demonstrated marked cerebellar and pontine hypoplasia. Both were homozygous for a c.416T>C, p.(Leu139Pro) *MED29* variant which was predicted to be pathogenic. Locomotion and cerebellar GABAergic neurons development were both impaired in *MED29* Morpholino-knockdown zebrafish and rescued by human wild-type gene expression. ShRNA-knockdown of *MED29* in mouse hippocampal neurons decreased neurite length and arborization *in-vitro*, and caused defective embryonic neuronal migration *in-vivo*. Overexpression of MED29 p.(Leu139Pro) was consistent with a loss-of-function.

Conclusions

The Mediator complex regulates transcription processes, and defects in particular subunits are associated with distinct neurodevelopmental phenotypes involving PCH. We conclude that *MED29* is a novel risk gene for PCH.

ABSTRACTS

Topic: Epilepsy: Diagnosis and Investigations

EPNS25_384 - Expanding the spectrum of DNM1L epilepsy: an emerging cause of atypical FIRES

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Objectives: Pathogenic variants in the *DNM1L* gene have been associated with a range of neurological phenotypes including optic atrophy, movement disorders and epilepsy. We sought to further delineate the epilepsy phenotypic spectrum associated with this gene and advance understanding of the disease mechanism.

Methods: Individuals with epilepsy and variants in *DNM1L* were identified through an international collaboration with review of phenotypic data. We performed *in silico* mutagenesis of the DNM1L protein and used a *Drosophila* fly model expressing c.1207C>T variant in a Drp1-sensitized background in muscle and neuronal tissues.

Results: We identified 13 patients; 11 presented aged 4-13 years with a clinical picture resembling febrile infection-related epilepsy syndrome (FIRES). 3/11 had bi-phasic refractory status epilepticus and 7/11 had prior mild developmental delay. Non-specific T2 hyperintensities were noted with no consistent MRS findings or metabolic abnormalities. One patient deteriorated on ketogenic diet. All atypical FIRES patients had poor outcomes: 2 died, 5 in a vegetative state and 5 have severe intellectual disability. Early-infantile developmental epileptic encephalopathy and Leigh disease-like picture were identified in individuals; both died. 9 patients had a recurrent heterozygous c.1207C>T variant, 8 were *de novo* and 1 inherited with parental mosaicism; 4 had compound heterozygote variants. Structural analyses suggest dominant-negative and recessive mechanisms; certain variants integrate into oligomeric assemblies and block extension, while others alter protein conformation or disrupt phosphorylation sites. Functional analysis in *Drosophila* larvae exhibited widened and fragmented mitochondria in brain and muscle in contrast to controls, and peroxisomes were tubular

ABSTRACTS

and elongated with a deficit in organelle turnover. These abnormalities led to impaired energy production, increased oxidative stress and disrupted metabolic balance.

Conclusions: We demonstrate that variants in *DNM1L* are associated with an atypical FIRES presentation in children. Patients are more likely to have prior developmental delay, multi-phasic status epilepticus and poorer outcomes than typical FIRES. Our structural and functional studies suggest a dominant-negative mechanism with both mitochondrial and peroxisomal dysfunction. Future studies are needed to advance understanding of disease mechanisms and identify potential novel treatments for this devastating disease.

ABSTRACTS

Topic: Movement Disorders/ Cerebral Palsy

EPNS25_385 - Movement disorders spectrum in KCNQ2-related developmental epileptic encephalopathy

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Objectives: The primary objective was to characterize the movement disorders(MD) spectrum in *KCNQ2* developmental epileptic encephalopathy(*KCNQ2*-DEE). Additionally, we aimed to assess the severity, and extension of MD, considering the potential impact on long-term outcome and treatment strategies.

Methods: Single center retrospective, descriptive, and observational study of pediatric individuals with *KCNQ2*-DEE. Participants were assessed with Burke-Fahn-Marsden Dystonia Rating Scale(BFMDRS), Abnormal Involuntary Movement Scale(AIMS), Gross Motor Function Classification System(GMFCS) and Manual Ability Classification System(MACS). Descriptive analysis performed.

Results: 22 individuals with KCNQ2-DEE are followed in our center; 11, with *KCNQ2*-DEE and MD. Up to this moment, 8 were included in the study (4 females, mean age of 7.1 years (±SE0.16, range: 2.5 - 17). Seizure onset occurred within the first days of life in 7 individuals. At the last follow-up, all individuals were seizure-free, with 1 patient off antiseizure medication and the others receiving one sodium channel blocker. One individual, diagnosed with epilepsy at 2 months of age, remained pharmacoresistant at the last follow-up. A wide variety of MD were identified, with dystonia in all cases. Dystonia was generalized, being limbs and speech/swallowing the most affected regions, followed by the neck and mouth. None of the patients had eye or trunk involvement. Other MD observed included exaggerated startle reaction (7), stereotypies (5), dyskinesia (2), and paroxysmal tonic upward gaze deviation (1). Hypotonia was present in 7 individuals. Seven individuals exhibited a striatal finger, and hyperreflexia was seen in 7. Spasticity was noted in 5, clonus in 4, and joint retractions in 3. Asymmetries in muscle tone were observed in 3. Additionally, 5 had convergent strabismus. The mean BFMDRS-Motor score was 61.87 (±SE2.52, range: 39.5–86.8), and the BFMDRS-Disability score was 25.25 (± SE 4.03, range: 18–30). The mean AIMS score was 3.38 (±SE0.25, range:0–6). The GMFCS distribution was as follows: II(2), III(2), IV(2), and V(3). The MACS distribution was: II(1), III(3), IV(1), and V(3). All individuals presented *de novo* heterozygous *KCNQ2* variants (all loss of function). Brain MRI was normal.

Conclusions MD, particularly generalized dystonia, are a prominent and persistent feature of *KCNQ2*-DEE, often coexisting with epilepsy. Despite effective seizure control, MD persist throughout life, with consequent impact in quality of life. We highlight the need for comprehensive evaluation of MD in KCNQ2-DEE. The pleiotropy of the *KCNQ2* gene expands the clinical phenotype of *KCNQ2*-DEE, emphasizing the importance of early assessment and tailored interventions addressing seizures and MD.

ABSTRACTS

Topic: Epilepsy: Diagnosis and Investigations

EPNS25_386 - OVERCOMING CHALLENGES IN EPILEPSY CLINICAL TRIALS: THE ROLE OF EUROPEAN CONSORTIUM FOR EPILEPSY TRIALS

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Objectives

The European Consortium for Epilepsy Trials (ECET) was established by the regional Executive Committee of the International League Against Epilepsy (ILAE-Europe) and endorsed by the European Reference Network for Rare and Complex Epilepsies, ERN EpiCARE, in 2021. As a legal entity, ECET Ltd. aims to elevate the standard of epilepsy trials - on medical therapies, devices, epilepsy surgery and natural history studies – in the European region, focusing on both adult and pediatric populations. This mission is driven by fostering collaboration among experts, patient advocates, academia, and industry.

Methods

New-onset epilepsy affects annually 130,000 children and adolescents, 96,000 adults (20–64 years), and 85,000 elderly individuals in Europe, with over 30% developing a rare or complex form, often drug-resistant. ECET, under the guidance of a Scientific Advisory Committee, unites 93 experts from reference centers in 32 countries in Europe, offering expertise to optimize trial design and implementation.

Results

Since its creation, ECET has supported the development of high-quality trials through targeted surveys, scientific review of trial designs and site selection. It has contributed to two natural history studies and organized educational activities to enhance the skills of researchers and clinicians involved in clinical trials. ECET has identified key shortcomings in epilepsy trials, including inadequate adaptation of methodologies to specific epilepsy types, neglect of comorbidities, and insufficient patient advocacy involvement. ECET addresses these gaps by offering expert advice, standardizing adjudication processes, and fostering international collaboration.

Conclusions

ECET represents a pivotal initiative in transforming epilepsy clinical trials in Europe, addressing the complexities of epilepsy research and fostering collaboration across stakeholders. ECET aims to improve treatment outcomes, enhance patients' quality of life, and reduce the societal impact of epilepsy. ECET emphasizes the necessity for robust, representative trials to drive innovation in epilepsy care.

ABSTRACTS

Topic: Epilepsy: Diagnosis and Investigations

EPNS25_387 - Shaping the future of epilepsy research in europe: the ern epicare priorities

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Objectives

The European Reference Network for Rare and Complex Epilepsies (ERN EpiCARE), with its Research Council and members of the network, has identified six key priorities to address critical gaps in epilepsy research.

Methods

ERN EpiCARE unites more than 60 expert centers, accredited by their respective health authorities and the European Commission, specializing in the diagnosis and management of rare and complex epilepsies. Since its creation in 2017, the network has accumulated substantial expertise, enabling to identify research priorities through a consensus process involving internal discussions, analysis of patient needs, and collaboration with the 23 other ERNs. A collaborative effort is underway to draft comprehensive articles for each priority.

Results

The six research priorities identified include:

1. **Prevention of epileptogenesis**: Identify early interventions to prevent epilepsy development and reduce comorbidities.
2. **Genetics and targeted therapies**: Enhance understanding of genetic causes and advance genetic testing and precision medicine.
3. **Improved surgical decision-making**: Optimize surgical practices and enhance patient outcomes for epilepsy surgery.
4. **Innovative trial designs** focusing on adaptive approaches and patient-centered outcome measures.
5. **Artificial intelligence (AI)** to improve diagnosis, seizure prediction, and patient care.
6. **Understanding and preventing comorbidities and mortality** by addressing mental health, cognitive disturbances, premature/sudden mortality and cardiovascular risks, and premature death.

Conclusions

EpiCARE's six research priorities serve as a roadmap to drive innovation and collaboration across the epilepsy research community. These efforts aim to align with the WHO global action plan on "Epilepsy and other Neurological Disorders" and support ongoing initiatives such as HORIZON Europe and inter-ERN collaborations. By focusing on causes rather than symptoms, EpiCARE aims to transform epilepsy care and improve quality of life for patients with rare and complex epilepsy. We will present a comprehensive outline of the strategies and actionable steps for addressing in Europe, within the next decade, each of the six priorities.

ABSTRACTS

Topic: Neurogenetics

EPNS25_388 - Polygenic modifiers in epilepsy: understanding incomplete penetrance in people carrying pathogenic variants

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Polygenic modifiers in epilepsy: understanding incomplete penetrance in people carrying pathogenic variants

Objectives

Over the last decades, the identification of various epilepsy genes has been instrumental in establishing diagnosis and prognosis of people with a monogenic epilepsy. However, there are also healthy people carrying pathogenic variants in these epilepsy genes. It is unknown whether this incomplete genetic penetrance is due to environmental factors or due to other genetic factors that determine epilepsy risk. Here we tested whether differences in polygenic burden of common epilepsy risk variants could explain why some people remain healthy despite carrying a pathogenic epilepsy variant.

Methods

We use phenotypic and genotypic data from the Genomics England 100.000 Genomes Project (n~43.000). Within this cohort, we assessed who had epilepsy and who carried a pathogenic missense variant (as defined in ClinVar) in a developmental epileptic encephalopathy (DEE) gene with autosomal dominant inheritance. We used polygenic risk score (PRS) analyses to assess differences in polygenic burden of common epilepsy risk variants between people carrying predicted pathogenic epilepsy variants with and without epilepsy.

Results

Only 14 out of 49 people (28%) carrying a pathogenic epilepsy variant in a DEE gene had epilepsy. Among people carrying a pathogenic DEE variant, people with epilepsy had a higher PRS and people without epilepsy had a lower PRS than controls who did not carry a DEE variant. Only one out of 35 people without epilepsy despite carrying a pathogenic DEE variant had intellectual disability.

Conclusions

Our results suggest that carrying a pathogenic missense variant in an epilepsy gene is not always sufficient to get epilepsy. Polygenic burden of common epilepsy risk variants might aid in determining who will get epilepsy and who is resilient despite carrying a pathogenic variant. Our findings are limited by a small sample size and incomplete certainty of variant pathogenicity.

ABSTRACTS

Topic: Neurorehabiltation

EPNS25_389 - Brachial Plexus Injuries: Incidence, Risk Factors, and Treatment Approaches in Pediatric Patients

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Objectives
Brachial plexus injuries (BPI) are birth-related complications that can lead to significant functional impairments. Understanding the demographic characteristics, clinical severity, associated conditions, and management outcomes is crucial for optimizing care and improving long-term outcomes. This study aims to analyze these factors in a cohort of 195 pediatric BPI cases.

Methods

This retrospective study included 195 pediatric patients diagnosed with BPI. The cohort consisted of 52.8% females and 47.2% males, with an average age of 15.7 months (range: 10 days–168 months). Data were collected on delivery methods, gestational diabetes, injury localization, clinical severity, associated conditions, and treatment approaches. Imaging findings, including MRI and EMG, were also reviewed. Treatment modalities, including conservative management and surgical interventions, were analyzed.

Results

Right-sided injuries were observed in 55.9% of cases, and Erb's palsy was the most common type (77.4%). Clinical severity was categorized as mild in 24.1%, moderate in 40.5%, and severe in 35.4%. Difficult labor was reported in 33.8% of cases, and most deliveries (95.4%) were vaginal. Associated conditions included torticollis (23.1%), shoulder subluxation (15.4%), and Horner's syndrome (17.4%). Conservative treatment, primarily physical therapy, was recommended in 76.4% of cases, while 9.2% underwent surgical intervention. Imaging revealed MRI usage in 38.5% and EMG in 47.7%. Orthopedic complications were rare (4.6%), and 91.3% of patients had no comorbid medical conditions.

Discussion

This study underscores the predominance of right-sided injuries and Erb's palsy among BPI cases, reflecting similar findings in the existing literature. The high prevalence of vaginal deliveries and difficult labor highlights the need for improved obstetric practices to reduce risk. Conservative management proved effective for the majority of patients, aligning with current recommendations for mild to moderate cases. However, surgical intervention was necessary in severe cases, emphasizing the importance of timely referrals and individualized treatment planning. Associated conditions such as torticollis and shoulder subluxation require early identification to prevent secondary complications. Imaging modalities like MRI and EMG were critical in assessing injury severity and guiding treatment decisions. Overall, this study supports a multidisciplinary approach to optimize recovery and minimize long-term disability in children with BPI.

ABSTRACTS

Topic: Cerebrovascular Disorders

EPNS25_390 - Post-COVID Surge in Pediatric Varicella Zoster Virus-Associated Stroke in Denmark

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Objectives: We investigated the incidence of pediatric Varicella Zoster Virus (VZV)-associated Acute Ischemic Stroke (AIS) in Denmark from 2013–2023, where we aimed to investigate the possible impact of the COVID-19 pandemic. Additionally, we assessed associated clinical features, risk factors, and outcomes in a cohort of VZV-associated AIS cases observed in 2022 after the lifting of COVID 19 restrictions in a geographically confined area in Copenhagen, Denmark.

Methods: We analyzed national surveillance data on cerebrospinal fluid samples and VZV and AIS diagnoses from Danish patient registries to estimate the incidence of VZV-associated AIS across the pre-, during, and post-COVID-19 years. To evaluate clinical characteristics and outcomes in the post-COVID period, we conducted a retrospective case series of four pediatric patients diagnosed with VZV-associated AIS from Greater Copenhagen, Denmark.

Results: Our analysis identified a notable clustering of VZV-associated AIS cases in 2022, suggesting an increased incidence post-COVID-19 restriction. Clinical presentations of the cases were consistent with pre-COVID patterns and did not indicate a more virulent VZV subtype. The observed rise in incidence is likely attributed to diminished herd immunity due to reduced VZV exposure during the pandemic.

Conclusions: The post-COVID-19 increase in pediatric VZV-associated AIS highlights the potential impact of disrupted herd immunity on infectious disease patterns. While the clinical presentations remained consistent with previous reports at large, our findings underscore the importance of heightened awareness and early recognition in managing VZV-associated AIS in pediatric populations. Our results also suggests that pandemic-related restrictions may have broader and more profound effects on pediatric health and well-being than previously assumed, warranting further studies on the topic to improve public health strategies in the future.

ABSTRACTS

Topic: Neuromuscular Disorders

EPNS25_392 - 3-Year Functional Outcomes of Patients With Duchenne Muscular Dystrophy: Pooled Delandistrogene Moxeparvovec Clinical Trial Data vs External Controls

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Objectives

Delandistrogene moxeparvovec is an rAAVrh74 vector-based gene therapy for Duchenne muscular dystrophy encoding an engineered, functional form of dystrophin shown to stabilize or slow disease progression. It is approved in the US and in other select countries. Here we compare 3-year functional outcomes of ambulatory patients age 4.0-8.9 y treated with delandistrogene moxeparvovec (treatment group) with those of external controls (EC), well matched using propensity-score weighting of key baseline prognostic factors.

Methods

Delandistrogene moxeparvovec data (n=50) were pooled from studies 101 (NCT03375164, n=4), 102 (NCT03769116, n=26), and ENDEAVOR Cohort 1 (NCT04626674, n=20) and compared with an EC group (n=73) using a propensity-score–weighted median regression model and a mixed-effects model for repeated measures (MMRM). Changes from baseline (CFBLs) to year 3 in the North Star Ambulatory Assessment (NSAA) total score and timed function tests (TFTs) of time to rise (TTR) from floor and 10-meter walk/run (10MWR) were assessed.

Results

At baseline, treatment and EC groups had similar median ages (6.3 y vs 6.5 y), NSAA total scores (22.0 vs 21.0), TTRs (3.9 s vs 4.3 s), and 10MWR times (4.9 s vs 5.1 s). Median regression analyses showed clinically meaningful stabilization of disease over 3 years in the treatment group vs the EC group. Three-year CFBLs (SE) in the treatment group vs the ECs were as follows: NSAA total score, −2.55 (0.76) vs −5.55 (0.77) (between-group difference [SE]: 3.00 [0.80], P=0.0003); TTR, 2.8 (0.3) s vs 4.6 (0.3) s (between-group difference: −1.8 [0.3] s, P<0.0001); 10MWR, 1.4 (0.2) s vs 1.8 (0.2) s (between-group difference: −0.4 [0.2] s, P=0.059). MMRM analyses yielded similar results and will also be presented.

Conclusions

Our findings show that treatment with delandistrogene moxeparvovec results in long-term stabilization or slowing of disease progression compared with a rigorously matched EC group, with an increase in between-group divergence over time.

ABSTRACTS

Topic: Neuro-Oncology

EPNS25_394 - Granulocytic sarcoma of pediatric head and neck: MR Imaging Findings

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Objectives To assess the frequency, clinical presentation and MRI findings of Granulocytic Sarcoma (GS) in the head and neck of children with acute myelogenous leukemia (AML) or a leukemic presentation, with the aim of facilitating prompt diagnosis and appropriate patient management.

Methods Granulocytic Sarcoma (GS), also known as chloroma or extramedullary myeloblastoma, is a rare tumor composed of immature granulocytic white blood cells, including myeloblasts, promyelocytes and myelocytes. It is seen in patients with (AML), chronic myelogenous leukemia (CML), and other myeloproliferative disorders, such as myelofibrosis, hypereosinophilic syndrome or polycythemia vera.

GS can develop during leukemia progression or as an initial sign of the disease. It may appear months or years before leukemia, making it difficult to distinguish from lymphoma. Patients with GS linked to CML often have a poor prognosis, as the tumor typically emerges during acute transformation. GS is highly responsive to focal radiation or chemotherapy , usually resolving within three months.

The presentation examines the anatomical localization and MRI findings of GS in seven pediatric patients, ages seven months to seven years, confirmed through histopathological findings over the past five years.

Results Seven available MRI studies of the patients were retrospectively, reviewed. Masses were evident in paranasal sinuses (three), in the floor of the orbit (one), nasal cavity (two), and maxillary gingiva (one). All masses showed enhancement. Comparison was made between pre- and during therapy.

One patient died three months later because of relapse of AML and sepsis. The present cases indicate the importance of a correct initial diagnosis for adequate therapy.

Conclusions MRI enables precise tumor localization and can help identify lesions that require biopsy. Key to detecting GS is awareness of the condition and close collaboration between radiologists, clinicians, and pathologists.

ABSTRACTS

Topic: Movement Disorders/ Cerebral Palsy

EPNS25_395 - Decreased dopamine transporter as a potential neuroimaging biomarker in drug-naïve children with tic disorders

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Objectives

Tics are involuntary movements often preceded by premonitory urges or uncomfortable sensations. Tic disorders include provisional tic disorder, chronic tic disorder, and Tourette syndrome (TS). Structure and functional neuroimaging studies in TS have produced inconclusive and often contradictory results. This study aimed to investigate the relationship between symptoms and Tc-99m-TRODAT-1 SPECT imaging results, with the goal of identifying possible neuroimaging predictors for symptoms in pediatric patients with tic disorders.

Methods

Sixty-two drug-naïve children with tic disorders (provisional tic, chronic tic and TS) were enrolled. Clinical data, including Yale Global Tic Severity Scale (YGTSS) scores, and Tc-99m-TRODAT-1 SPECT results were recorded and analyzed using correlation and linear regression.

Results

The chronic tic and TS groups were significantly older than the provisional tic group. Dopamine transporter (DAT) uptake ratios in the left striatum and bilateral caudate nuclei were lower in the chronic tic and TS groups compared to the provisional tic group. Reduced DAT uptake in the right striatum and putamen was associated with higher motor tic scores. Additionally, older age, female gender, and a diagnosis of TS were potential predictors of higher YGTSS scores.

Conclusions

This study in pediatric patients with tic disorders demonstrated that certain neuroimaging parameters correlated with tic severity. Utilizing these neuroimaging parameters could enhance the classification of tic disorders and improve the prediction of treatment response and outcomes in affected patients.

ABSTRACTS

Topic: Infectious and Inflammatory Diseases/ Neuroimmunology

EPNS25_396 - Treatment Persistence in Pediatric-onset Multiple Sclerosis – A Swedish Nationwide Registry study

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Objectives

Pediatric-onset multiple sclerosis (PoMS) is more inflammatory than adult-onset Multiple Sclerosis (MS), underscoring the importance of early and effective treatment intervention. Nevertheless, traditional first-line disease-modifying therapies (DMTs) are still frequently prescribed in PoMS. This is likely because children are rarely included in trials, meaning newer, more effective DMTs lack approvals in this population. Thus, more robust comparative data on PoMS treatment outcomes are needed. Treatment persistence reflects real-world effectiveness and safety, as patients are unlikely to continue if they experience disease worsening or severe side effects. This study aimed to compare treatment persistence of common DMTs for PoMS in Sweden.

Methods

We conducted a nationwide cohort study using prospectively collected data from the Swedish MS registry (2000-2024). All MS patients who had their disease onset before age 18 and began therapy before age 20 were included. Treatment persistence was analyzed using survival analysis, which modeled the time from treatment initiation to either treatment discontinuation or the last known follow-up within the study period. We used a Kaplan-Meier model to estimate median persistence times and a Cox regression model to compare hazard rates of treatment discontinuation across DMTs.

Results

We included 331 PoMS patients, yielding 907 treatment episodes. Treatment persistence for rituximab never decreased to the median nor reached the 75th percentile. Among other DMTs, natalizumab showed the longest median persistence (35 months), followed by dimethyl fumarate (26 months), fingolimod (21 months), and lastly, injectables (20 months). Using injectables as the reference, the hazard ratio (HR) of treatment discontinuation was significantly lower with rituximab (HR 0.05; 95% confidence interval (CI) 0.03-0.08), natalizumab (HR 0.42; 95% CI 0.33-0.53), dimethyl fumarate (HR 0.60; 95% CI 0.43-0.84), and fingolimod (HR 0.63; 95% CI 0.46-0.86).

Conclusions

Treatment persistence was significantly higher with newer intravenous and oral DMTs than with traditional first-line DMTs. Rituximab, an antiCD20 monoclonal antibody used off-label for MS, demonstrated the highest persistence. This indicates that these therapies may be more appropriate as first-line options in this sensitive patient population. Further studies are needed to shed light on comparative benefit-risk profiles over longer treatment exposures.

ABSTRACTS

Topic: Neuropsychiatric Disorders / Functional Neurological Disorders

EPNS25_399 - Good outcome of patients with FND managed in outpatient setting in a third level hospital

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Objectives

To report the clinical features and outcome of patients diagnosed with functional neurologic disorder (FND) in a paediatric neurology clinic of a regional hospital after initial assessment and explanation of the disorder to the family.

Methods

Children diagnosed with FND since 2022 were retrospectively reviewed. The demographic and clinical data as well as the outcomes were extracted from electronic clinical records and a descriptive analysis was performed on them.

Results

We reviewed a total of 7 patients, 5 of them were female and 2 were male. The mean age at presentation was 8.3 years. 2/7 patients presented with visual symptoms, 2/7 patients presented with headaches, 2/7 with sensory disturbances and one with episodes of dizzyness.
All patients fulfilled DSM-5 diagnostic criteria and 6/7 of them presented from the first clinic positive signs of FND. In 6 of the 7 patients a potential trigger for the FND was identified. In 3 patients no further diagnostic tests were performed to support the diagnosis. After validating patient´s symptoms, explaining the diagnosis and providing the families with knowledge and strategies to manage the symptoms, there was an improvement in all of the patients. 3 patients have been discharged with almost complete resolution of the symptoms, 3 are now under psychiatrics due to comorbidities and 1 continues follow up within paediatric neurology.

Conclusions

FND remains a challenge for paediatric neurologist. Despite the current knowledge, for some professionals it remains as a diagnosis of exclussion what leads to inappropiate investigations with further negative impact on patient´s health. In our experience, based on possitive signs it can be diagnosed earlier providing the patient and the family with adecuate strategies to manage the symptos and therefore to improve the prognosis.

ABSTRACTS

Topic: Neurometabolic Disorders

EPNS25_400 - The challenge in making the diagnosis of neuronal ceroid lipofuscinosis – the improvement during the last decade at a tertiary center in a cohort of 32 children

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Objectives

To investigate diagnostic pathways and whether diagnosis in children with neuronal ceroid lipofuscinosis (NCL) were improved during the last decade.

Methods

The retrospective study included children with NCL treated in Institute during the investigation time which was divided in two periods (groups): before 2014 (first group), and from 2015- 2024 (second group). In all patients, clinical, neurophysiological, ophthalmological, neuroradiological, psychological, and laboratory evaluation were done, initially and during the follow up. Multiple standard video EEG recordings were done including low frequency intermittent photic stimulation. For definitive diagnosis, electron microscopy (EM) and targeted gene analyses were used before 2011, while later, symptom-based gene panels (since 2011) and the clinical and whole exome sequencing (WES) were used since 2015. Evaluated parameters are: etiology, diagnostic pathways and diagnosis delay, epilepsy phenotype, frequency of status epilepticus (SE) and treatment. Statistical analysis included tests: Chi-Square, Mann-Whitney and ANOVA, using SPSS version 25.

Results

The study included 32 patients, 17 in the first (CLN2-12pts, CLN5-2, CLN3-1, vLINCL-2), and 15 (CLN2-11, CLN8-2, CLN1-1, CLN7-1) in the second group including two atypical cases, one CLN1 case with juvenile onset, and one CLN2 case with fulminant regression without seizures. Definitive diagnosis was confirmed by genetic analyses in 29 pts (14/17 pts from first group and all 15 cases from second group) and in three by enzyme/EM. Electronic microscopy was performed in 12 cases. The average duration from initial symptoms to diagnosis was 3.9±3 years (first group) vs. 2.1±0.9 years (second). Initial manifestations were neurological, language and cognitive deterioration in all cases fallowed by behavior problems and different types of seizures in 28/32 pts (87.5%). Four cases (CLN3-1, CLN5-2, atypical CLN2) had no seizure. SE frequency rate (23.5% vs. 13.3%) were higher in the first group showing tendency towards, but not statistically significant difference. Symptomatic treatment was given in all cases. Five CLN2 cases had intraventricular enzyme replacement treatment with positive impact on slowing disease progression and seizure control**.**

Conclusions

The diagnosis and managing children with NCL were improved during the last decade. The most frequent NCL type is CLN2. The increasing knowledge of early clinical characteristics, and diagnostic algorithms of NCL are of the crucial importance in the early detection of NCL patients. The early diagnosis has become more important in “a new era” due to increasing possibilities for the treatment of NCL diseases.

ABSTRACTS

Topic: Neurogenetics

EPNS25_401 - Rare Genetic causes in Neurodevelopmental disorders (NDDs) in Children : A burden still to Explore in a Country with Limited Resources

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Objectives Neurodevelopmental disorders (NDDs) are a significant global health burden, with genetic factors playing a key role in their etiology. The present study aimed to investigate the genetic patterns of NDDs among pediatric patients in Bangladesh. In Bangladesh, genetic testing for NDDs is still not widely available. A lack of awareness, limited access to advanced diagnostics, and financial constraints contribute to underdiagnosis or misdiagnosis of genetic disorders. In this context, understanding the epidemiological pattern of genetic diagnosis among children with NDDs in Bangladesh may guide the physicians to provide more precised interventions. Hence, the objective of the present study was to determine the genetic pattern of neurodevelopmental disorders among pediatric patients referred to a tertiary care hospital of Bangladesh.

Methods In the present cross-sectional study, we included children under 18 years with suspected NDDs referred for genetic testing at the National Institute of Neurosciences and Hospital (NINS) in Dhaka, Bangladesh from January 2017 to December 2024. Peripheral blood samples preserved in were analyzed using clinical exome sequencing, whole exome sequencing, chromosomal microarray analysis, and karyotyping and MLPA.

Results Among 676 patients, 63% were male, with a mean age of 4.5 years (SD 2.5). Pathogenic or likely pathogenic variants were detected in 46.6% of cases. Duchenne/Becker muscular dystrophy was most common (19%), followed by spinal muscular atrophy (15%) and developmental and epileptic encephalopathy (7%). Autosomal recessive inheritance was prevalent in 50% of cases, and heterozygous variants were most frequent (38%). Chromosomal abnormalities were identified in 10 patients, with Down syndrome comprising 70% of these cases. Other less common conditions included Rett syndrome, mitochondrial disorders, and various forms of congenital muscular dystrophies. Rare syndromic diagnoses, such as neurodegeneration with brain iron accumulation, were also observed

Conclusions Our study provided a comprehensive overview of the genetic patterns in pediatric NDDs in Bangladesh, identifying both common and rare genetic mutations. These findings indicates the importance of genetic testing in the accurate diagnosis of neurodevelopmental conditions, which could guide precised treatment and genetic counseling. Expanding access to genetic testing might improve early diagnosis and management these diseases.

ABSTRACTS

Topic: Neuromuscular Disorders

EPNS25_402 - Life-threatening uncommon events in Duchenne muscular dystrophy

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Objectives

Duchenne muscular dystrophy (DMD) is a progressive muscle-wasting disease caused by mutations in the gene encoding for dystrophin. Despite advances in the standards of care, life expectancy is unlikely to surpass the forth decade of life, with cardiac and respiratory failure as the main causes of death. Non-cardiopulmonary complications account for approximately 20% of overall mortality in DMD. The aim of this study was to investigate uncommon events with a significant impact on life expectancy and burden of disease.

Methods

We performed a retrospective nationwide study of male patients with DMD, born and deceased during the time period 1970-2019. Information regarding causes of death was retrieved from the Cause of Death Registry and cross-checked with the medical records along with diagnostics and comorbidities.

Results

129 patients were included with a median lifespan of 24.3 years. Severe gastrointestinal and hepatobiliary complications occurred in 23% with a direct effect on mortality in 5%. Vascular complications including venous thromboembolism and cerebrovascular events affected 11%, five of them occurring before the age of 20. Post-fracture pulmonary embolism was the primary cause of death in four patients. Fracture recurrence in general was as high as 15% and was mainly seen among adolescents. Acute kidney injury within three months before death was present in five patients, on the basis of severe heart failure in three of them.

Conclusions

We highlight less common, life-threatening complications in DMD occurring throughout adolescence and early adulthood with an impact on life expectancy. These data provide additional evidence of the disease complexity and the importance of multi-organ monitoring, to early detect their occurrence and to ensure timely intervention.

ABSTRACTS

Topic: Neuromuscular Disorders

EPNS25_405 - Neuropathy and myositis in an adolescent oncological patient treated with Brentuximab

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Objectives: Antibody (Ab)-mediated therapy (anti-CD30) with Brentuximab Vedotin (BV) is approved as consolidation treatment of relapses after autologous stem cell transplantation (ASCT) for Hodgkin lymphoma (HL) patients. Hereby, two-third of patients develop a reversible peripheral neuropathy (PN) as an adverse event (AE). Myositis as a possible AE has not been reported until now.

Methods: Clinical assessment, MR-imaging, microscopic-based myopathological evaluation in addition to proteomic analyses performed on muscle biopsy (MB) in a patient with HL diagnosis and under BV therapy.

Results: At the age of 16 years, an ASCT was performed in a female patient due to MH recurrence, followed by BV therapy. During this therapy, she experienced a progressive worsening of muscle weakness and pain in the lower extremities, alongside existing clinical signs of peripheral neuropathy (tremor and weakness in foot dorsiflexion), ultimately leading to wheelchair dependency. A severe side effect was suspected and therapy was discontinued before completing the cycle. Muscle MRI showed signs of myositis in both gastrocnemius muscles, laboratory tests revealed an increase in CK level (985 U/l) with negative myositis-Ab-panel. MB revealed neurogenic (numerous atrophic, partially angular shaped and grouped fibers) and myogenic-inflammatory changes supporting a diagnosis of myositis in addition to neuropathy. Proteomic analyses showed clear evidence of complement activation (most pronounced increased protein was HPRT1) in combination with dysregulation of mitochondrial proteins. She showed a decrease in CK levels and an improvement in muscle strength after switching from intravenous (i.v.) pulsed methylprednisolone (without effect) to i.v. immunoglobulins. Five months after initiation of immunoglobulin therapy, the patient was able to walk few steps without support and pain. Consistent with this, a six months follow-up MRI scan showed a regression in myositis signs.

Conclusions: Apart from PN, BV-therapy may cause myositis. Complement activation and mitochondrial dysfunction may represent pathophysiologic relevant pathways. This case illustrates that new targeted oncological treatment concepts require an age-independent assessment of immune-related neurological AEs.

ABSTRACTS

Topic: Infectious and Inflammatory Diseases/ Neuroimmunology

EPNS25_406 - Exploring Cladribine Treatment in Pediatric-Onset Multiple Sclerosis: Clinical Insights and Outcomes

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Objectives

Pediatric-onset multiple sclerosis (POMS) presents challenges related to high inflammatory activity and treatment adherence. While cladribine tablets have shown efficacy in adults, evidence for their use in children remains limited. This study aimed to evaluate the efficacy and safety of cladribine in POMS patients.

Methods

A retrospective cohort study was conducted involving 47 POMS patients, 31 treated with cladribine and 16 with standard disease-modifying therapies (DMTs). Inclusion criteria required at least two years of continuous DMT use with annual MRI monitoring. Patients with prior use of natalizumab or ofatumumab were excluded. Data were collected from two tertiary centers. Statistical analysis included Fisher’s exact test, t-tests, and mixed-effects logistic regression for longitudinal outcomes.

Results

The mean age at MS onset was 15.1 ± 2.5 years in the cladribine group and 13.8 ± 2.2 years in controls ($p = 0.08$). Disease duration was longer in the cladribine group (3.8 ± 3.4 years vs. 2.3 ± 1.8 years, $p = 0.04$). Baseline rates of no evidence of disease activity (NEDA) were comparable (29% vs. 25%, $p = 1.00$). During follow-up, relapse rates were higher in the cladribine group at Year 2 (odds ratio [OR] = 11.29, $p = 0.009$). Imaging outcomes showed no significant differences between groups. However, the cladribine group demonstrated better adherence, with a lower withdrawal rate (16% vs. 44%, $p = 0.04$), and no severe adverse events were reported.

Conclusions

Cladribine tablets are safe and well-tolerated in POMS patients, with strong adherence rates offering an important advantage over standard DMTs. Further studies are needed to explore factors influencing relapse prevention and optimize its role in pediatric MS management. Despite its limitations, cladribine is a promising treatment option that warrants consideration in this population

ABSTRACTS

Topic: Epilepsy: Diagnosis and Investigations

EPNS25_407 - Evaluation of serum nitric oxide and orexin-a levels in patients diagnosed with rolandic epilepsy

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EVALUATION OF SERUM NITRIC OXIDE AND OREXIN-A LEVELS IN PATIENTS DIAGNOSED WITH ROLANDIC EPILEPSY

Objectives

It is known that there are mechanisms in the pathogenesis of epilepsy that have not yet been fully elucidated. Orexin-A and nitric oxide play a role in sleep control, but their relationship with epilepsy in children is complex. This study aimed to investigate serum orexin-A and nitric oxide levels in benign rolandic epilepsy and evaluate their effects on seizure control.

Methods

42 patients newly diagnosed with benign rolandic epilepsy and 45 healthy individuals were included in this study. Serum samples were taken twice from the patients, before diagnosis and after treatment, and once from the control group. Serum orexin-A and nitric oxide levels were measured by enzyme-linked immunosorbent test.

Results

A statistically significant difference was found between orexin-A levels between the pre-treatment and post-treatment groups ($p<0.001$). Additionally, a statistically significant difference was found between orexin-A levels between the pre-treatment and healthy control group ($p<0.001$). Furthermore, a statistically significant difference was found between orexin-A levels between the post-treatment and healthy control group ($p<0.003$).

Conclusions

Serum orexin-A and nitric oxide levels were found to be high in patients with benign rolandic epilepsy. These results suggest that serum orexin and nitric oxide monitoring can be used as a possible marker in the diagnosis of patients.

ABSTRACTS

Topic: Neuromuscular Disorders

EPNS25_408 - The pattern of upper limb function in later-onset SMA: Long-Term outcomes of Nusinersen treatment

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Objectives

Disease-modifying therapies for spinal muscular atrophy (SMA) have been shown to improve gross motor functions, including upper limb function. However, the response to treatment varies depending on the patient's age and disease severity. This study evaluates changes in upper limb function patterns among patients with later-onset SMA receiving Nusinersen treatment.

Methods

The study assessed overall motor and upper limb functions using the Hammersmith Functional Motor Scale–Expanded (HFMSE) and the Revised Upper Limb Module (RULM) scores at multiple time points. Changes in specific tasks that patients could perform over time were analyzed in relation to disease severity and the age at which treatment was initiated.

Results

Six patients were included in the study: five with SMA type 2 and one with SMA type 3. The median age at treatment initiation was 6.3 years (range: 1.9–22.5 years), with a median follow-up period of 4.85 years (range: 1.5–5.4 years). All patients, except one with a treatment interruption of 20 months, showed improvements in RULM and HFMSE scores. Long-term follow-up demonstrated not only enhancements in RULM scores but also sustained functional stability, even in chronic patients. The most significant RULM improvement after 18 months of treatment was observed in a patient with SMA Type 2 who started treatment earliest, at 23 months of age. Adolescents with a longer disease duration showed improvements primarily at the table level, whereas younger patients with a shorter disease duration progressed from mid-level to shoulder-level improvements over time. Improvements in distal upper limb functions, such as tracing paths and tearing paper, were noted and correlated with the patients' treatment response and motor development.

Conclusions

These findings suggest that Nusinersen treatment contributes to continuous improvements in upper limb function in patients with later-onset SMA. Furthermore, the pattern of functional changes differs based on the age at treatment initiation and the duration of the disease, underscoring the importance of early intervention and individualized care.

ABSTRACTS

Topic: Neuromuscular Disorders

EPNS25_411 - A Cross-Sectional Survey on the Management of Bulbar Function in SpinalMuscular Atrophy SL45498

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Objectives

Spinal muscular atrophy (SMA) patients often experience bulbar dysfunction, which includes difficulties in communication and swallowing due to weakness in the oropharyngeal musculature. However, the assessment of bulbar function in routine practice remains limited, with no standardized or comprehensive approach widely adopted. This study aims to describe the current management and follow-up practices for bulbar function impairment in SMA patients in Spain.

Methods

The survey was designed collaboratively by a multidisciplinary team including a neuropediatrician, two phoniatrics and speech-language experts from reference neuromuscular centers, along with representatives from Roche Medical department and methodological experts. The team reviewed existing literature and incorporated their professional experience and understanding of SMA care in Spain. The survey is intended for healthcare professionals involved in SMA management and consists of questions addressing demographics, clinical practices, and challenges in bulbar function management. Questions were designed to be user-friendly and aligned with the study objectives, utilizing multiple-choice formats, hypothetical case scenarios, and visual analog scales.

Results

This is a cross-sectional, non-interventional study conducted via an electronic survey targeting 50 healthcare professionals managing SMA patients across Spain including: pediatric neurologists, neurologists, physiatrists, physiotherapists, speech therapists, gastroenterologists, neumologists, Otorhinolaryngologists and phoniatrics. The recruitment of participants will focus on specialists involved in the national patient registry, “CuidAME.”The primary objective is to describe the management and follow-up of bulbar function impairment in SMA patients in Spain. Secondary objectives include characterizing healthcare professionals, assessing their knowledge and challenges in managing bulbar impairment, exploring improvements in care, evaluating procrastination, regret, empathy, burnout, risk aversion, and analyzing attitudes toward evidence-based practices. Data will be analyzed using descriptive and inferential statistics to address study objectives.

Conclusions

This study will provide knowledge of current practices and challenges in managing bulbar dysfunction in SMA patients in Spain. By exposing gaps in assessment and care, it aims to support the development of standardized tools, enhance interdisciplinary care, and promote evidence-based improvements in clinical practice.

ABSTRACTS

Topic: Miscellaneous

EPNS25_412 - Sleep problems in children with refractory epilepsy

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Objectives

Sleep and sleep-related problems are one of the most common comorbidities in epilepsy. The preliminary results of a comprehensive multidisciplinary assessment of sleep problems and comorbidities in patients with refractory epilepsy admitted to the pediatric video-EEG monitoring unit are presented.

Methods

Patients admitted to our pediatric video-EEG monitoring unit between 2018 and 2023 and diagnosed with refractory epilepsy were included in the study. The demographic and clinical data of the patients were reviewed from medical records. The Children's Sleep Habits Questionnaire (CSHQ) and the Sleep Disturbance Scale for Children (SDSC) were administered at follow-up.

Results

The median age of patients evaluated to date (n=85, F/M=42/43) was 166.4 (48.3-218) months. The etiology of the epilepsy was genetic in 19 (22.4%), structural in 43 (50.6%), immune in 3 (3.5%), and unknown in 18 (21.2%) patients. Two patients had a genetic and structural etiology. On average, half of the patients (n=43, 50.6%) had comorbid conditions. Psychiatric/behavioral problems (functional seizures, depression, anxiety, autism spectrum disorder, and attention deficit hyperactivity disorder) constituted the most common comorbidity seen in 23 (27%) patients, followed by various medical comorbidities: 14 (16.5%) patients with endocrinologic, 10 (11.8%) with musculoskeletal, and 8 (9.4%) with gastrointestinal problems. The patients had previously received a median of 6.5 anti-seizure medications (ASMs). At the time of evaluation, the patients were on a median of 3.5 (1-5) ASMs, with clobazam, lamotrigine, stiripentol, and valproic acid being the most frequently used. The total CSHQ scores of 68 (80%) patients were higher than the cut-off value, indicating the presence of sleep problems. Only 34.1% (n=29) of patients were able to fall asleep within the first 15 minutes. According to the SDSC subgroups' scores, 12 (14.1%) patients had initiating and maintaining sleep disorders, 5 (5.8%) patients had sleep breathing disorders, 13 (15.3%) patients had disorders of arousal/nightmares, 8 (9.4%) patients had sleep-wake transition disorders, 18 (21.2%) had disorders of excessive somnolence, and 3 (3.5%) had sleep hyperhidrosis. Fourteen (16.5%) patients had symptoms of sleep disturbance, and 44 (62%) had sleep disturbance risk in the remaining patients.

Conclusions

Our study assessed sleep problems in children with refractory epilepsy, which is the first step to address this comorbidity. Our results reveal therapeutic implications, which may potentially improve seizure control and/or the quality of life of children with refractory epilepsy.

ABSTRACTS

Topic: Movement Disorders/ Cerebral Palsy

EPNS25_413 - Morbidity rate of children's cerebral palsy in Baku city

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Objectives To study the morbidity rate of children's cerebral palsy (CP) in X in children born in 2006-2016.

Methods During 2006-2016, 35 891, 37 130, 37 459, 40 050, 34 726, 34 192, 33 258, 30 373, 29 722, 29 654 and 29 564 children were born in X. CP was diagnosed in 1162 of these children. Newborns and children with CP were divided into 3 groups by body mass (<1500; 1500- 2500; 2500 and more) and into 4 groups by the gestational age (<28, 28-32; 32-36, 36 and more weeks). The morbidity rates were detected in these groups. The statistical significance of morbidity rates was assessed by χ2criteria.

Results The morbidity rate of CP changed within the interval 0.27% (95% CI 0.22-0.33%) in 2006 to 0.37% (95% CI 0.30-0.44%) in 2016. The difference between the minimum and maximum morbidity rates was not statistically significant (p>0.05). The morbidity rate of CP in newborns with body mass <1500 grams was 10.35% (95% CI 0-21.65%) and was 6.1 times higher than in the group of newborns weighing 1500-2500 grams at birth (1.72%; 95% CI 0.20-3.25%) and 30.4 times higher than in the group of newborns with body mass ≥2500 grams (0.34%; 95% CI 0.27-0.41%). The difference between morbidity rates of CP in groups depending on birth body mass was significant (p<0.0001).

Conclusions The incidence rate of CP in a cohort of newborns during the first 60 months after birth in 2006-2016 fluctuated in the range of 0.27-0.37% and had a weak growth trend. The morbidity rate of children's CP is significantly higher in children with body mass at birth <1500 (10.34%) and 1500-2500 grams (1.72%) than in children with body mass at birth 2500 and more grams (0.34%). The gestational age of newborns affects the morbidity rate of CP, which is 5.48; 1.78 and 0.34% at gestational age <32, 32-36 and ≥36 weeks. The structure of subtypes of this pathology is close to that in other populations against the background of the comparative morbidity rate of CP in Baku, the proportion of spastic unilateral, spastic bilateral, dyskinetic and atonic CP is 35.2; 58.0; 3.9 and 1.4%, respectively.

ABSTRACTS

Topic: Epilepsy: Diagnosis and Investigations

EPNS25_415 - Evaluation of Telomere Length in Children with Epilepsy

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Objectives
Telomere length (TL) is a biological marker for stress and cellular aging and is essential for maintaining genetic material stability. We aimed to to evaluate an association between telomere length in children with epilepsy.
Methods
This is a single-center, cross-sectional study done with 100 participants (50 epilepsy patients and 50 healthy controls). The median age of children in the epilepsy group was 144 months. Nine (18%) children were drug-resistant epilepsy (DRE) patients.
Results
The results of the study did not demonstrate a correlation between TL in children with epilepsy. Although statistically insignificant, the total telomere length (TTL) and the end of chromosome telomere length (CTL) in the epilepsy group was shorter than the control group. The difference in TL between children with DRE was not statistically significant. The TTL and CTL values of the females were longer ($p<0.05$). The TTL and the CTL values of children with a family history of epilepsy were longer ($p<0.05$).

Conclusions
The results of this study report that the TL in the epilepsy group is shorter than the control group, although the results are statistically insignificant. As mentioned, the study of telomere length in children with epilepsy is rare, and in the literature search, there are only two human studies regarding the correlation between telomere length and epilepsy. Accumulation of evidences about role of telomere in epilepsy might help to clear its pathogenesis.

ABSTRACTS

Topic: Neurodevelopmental Disorders / Developmental Neuroscience

EPNS25_416 - Rhombencephalosynapsis – consider associated anomalies: clinical data from three new cases of Gomez-Lopez-Hernandez syndrome.

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Objectives

Rhombencephalosynapsis (RES) is a rare cerebellar malformation characterized by the absence or deficiency of the vermis and the fusion of the hemispheres. The majority of patients exhibit associated anomalies, the most prevalent of which is alopecia as possible indication of Gomez-Lopez-Hernandez syndrome. This syndrome is characterized by three main features: RES, uni- or bilateral parietooccipital alopecia and trigeminal anesthesia or anatomically abnormal trigeminal nerve. The etiology of this rare neurocutaneous syndrome is presumed to have a genetic basis, though no consistent genetic causes have been identified so far. Here, we report clinical and radiological findings in three young patients between one year and 6 years of age.

Methods

We retrospectively analyzed data from 3 patients with RES and alopecia.

Results

Complete or partial RES was diagnosed in all patients by MRI and prenatal MRI. Additional findings included hypoplastic corpus callosum, focal dysgyria and hypoplastic trigeminal nerve. Due to the age of the patients, the assessment of trigeminal anaesthesia was not possible. All patients presented with an abnormal head shape, either plagiocephalic or turricephalic, without any indication of craniosynostosis. In addition to facial dysmorphism, such as high palate, hypertelorism, retrognathia and deep-set ears, all patients developed unilateral or bilateral alopecia areata. Two patients exhibited both speech and motor delay, necessitating intensive physiotherapy, occupational, and speech therapies. One patient exhibited severe behavioral abnormalities, characterized by aggressive behavior, restlessness, insomnia and motor stereotypies. Genetic testing including trio exome analysis as well as standard cytogenetic analysis did not reveal any (likely) pathogenic disease-causing variant. Whole genome sequencing is currently carried out.

Conclusions

We clinically diagnosed three new cases of Gomez-Lopez-Hernandez syndrome due to rhombencephalosynapsis and alopecia areata. Consistent to the literature the extent of neurodevelopmental outcome shows a broad spectrum. As the underlying genetic cause could not be determined by exome analysis, the results of ongoing whole genome testing are curiously expected.

ABSTRACTS

Topic: Neurological Emergencies

EPNS25_417 - Underpinning for pediatric neurology consultations at a tertiary center pediatric emergency department

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Objective: Neurological presentations show a broad variability in the pediatric emergency department (PED).
Methods: This retrospective study included 1,060 pediatric neurology consultations from 862 patients in PED between June 2021-June 2023. Admissions were classified as Group 1 and 2, depending on the presence or absence of a previous neurological disorder. Demographic data, complaints, examination findings, diagnostic work-up, comorbidities, categories, and relation between PED stay and hospitalization were documented.
Results: Of 1,060 admissions, 569 (53.7%) were female. The mean age was 7.74 ± 5.64 years. Six patients (0.6%) were newborns, 197 (18.6%) were infants, 176 were (16.6%) in preschool and 350 (33%) were in school-age period, 331 were (31.2%) adolescents, 1624 patients (58.9%) were classified as Group 1. Majority of the consultations (n= 1,004, 94.9%) were in acute setting. In 86.3% (n= 915) of the admissions, the root cause of consultation was neurological. The most common presenting neurological symptom was seizures (n= 588, 55.5%), followed by focal neurological signs (n= 83, 7.8%), headache (n= 81, 7.6%), and seizure mimics(n= 69, 6.5%). Top two non-neurological symptoms were gastrointestinal complaints (n=64, 6.4%) and fever (n=59, 5%). Recurrent admissions were either due to seizures (n= 431, 40.7%) or fever (n= 125, 28.7%) and gastrointestinal symptoms (n= 119, 27.3%). Neurological examination findings varied according to age, clinical presentation or final diagnosis. The most common final diagnosis were seizures (n= 642, 60.6%), [afebrile, n= 538 (84%); febrile, n= 85 (13%); status epilepticus, n= 16 (2.5%); epilepsy mimics, n= 67 (6.3%); febrile status, n= 3 (0.5%)], and headache (n= 73, 6.9%). A total of 313 brain MRIs (29.5%), 282 EEGs (26.6%), and 166 cranial CTs (15.7%) were obtained. Lumbar puncture was performed in 62 cases (5.8%), 29 with abnormal results. Tracheostomy was present in 2.4% (n= 25), gastrostomy in 3% (n=32) with 3% (n=32) requiring ventilatory support. Hospitalization was recommended for 126 (12.5%) of the consultations, mostly for PED stays over 73 hours. Antiseizure medications were most frequently prescribed. Ophthalmology (n=108, 10.2%), neurosurgery (n= 93, 8.8%), and cardiology (n= 86, 8.1%) were among other consultations. There was a change in treatment plan in 36.6% (n= 389) following neurology consultation.
Conclusion: A close collaboration between pediatric emergency and neurology specialists is crucial in PED. This retrospective study highlights the importance of awareness, education and implementation of pathways for appropriate approach to neurological emergencies with emphasis on seizures and epilepsy.

ABSTRACTS

Topic: Headache / Migraine

EPNS25_419 - Pain among Young Children during the COVID-19 Pandemic

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Objectives

This study aimed to understand the relationships among children's pain, physical activity levels (PA), age, and screen time (ST) before the COVID-19 pandemic, during the COVID-19-related curfew, and after the curfews were lifted. Additionally, it sought to identify factors that may contribute to pain in young children so that researchers and policymakers can address these issues in the future.

Methods

A cross-sectional online survey conducted during the summer of 2022, amid a partial curfew, gathered responses from 329 caregivers of children (median age = 8 years, 54% female, 47% male). The survey, distributed via social media platforms, collected data on pain, PA, and screen time across three periods: before the pandemic, during the curfew, and after. It included demographic details, pain frequency assessed with a five-point Likert scale, and questions about changes in pain. PA and ST measured using established tools for frequency, intensity, and duration. Ethics approval was obtained, and informed consent was filled by participants. Spearman's rank correlation coefficient analyzed the associations between variables.

Results

Pain before the COVID-19 pandemic had a weak inverse association with PA intensity ($r = -0.11$, $p = 0.04$) and a weak positive association with ST after the curfew ($r = +0.12$, $p = 0.04$). ST showed strong positive correlations across all periods ($r = +0.82, +0.62, +0.58$; $p = 0.00$). During the curfew, weak inverse correlations were noted with PA frequency, intensity, and duration ($r = -0.12$ to -0.25; $p = 0.00$-0.03). After the curfew, these inverse correlations continued ($r = -0.23, -0.25$; $p = 0.00$). Age had a weak positive correlation with ST across periods ($r = 0.18$ to $+0.17$; $p = 0.00$-0.01), but no significant associations with PA.

Conclusions

Our research revealed that pain in children, which started before the COVID-19 pandemic, worsened with longer ST. In contrast, those who increased PA after the curfew saw a reduction in pain levels. During and after the curfew, there was an inverse relationship between PA and ST, a trend not seen pre-pandemic. Children doubled their screen time during COVID-19, and there was a positive correlation between age and screen time across all periods.

ABSTRACTS

Topic: Epilepsy: Medical and Surgical treatment

EPNS25_421 - Non-seizure benefits of long-term fenfluramine treatment in pediatric patients with Dravet syndrome

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Objectives: Evaluate the impact of long-term fenfluramine treatment on cognition, adaptive behavior, quality of life (QoL), and caregiver burden in pediatric patients with Dravet syndrome.

Methods: Pediatric patients with Dravet syndrome, initiating fenfluramine treatment between February 2017 and October 2023, were assessed by a neuropsychologist. Fenfluramine-related benefits on cognition (via The Bayley Scales of Infant and Toddlers Development (Bayley-IV), or The Wechsler Intelligence Scale adapted to age), adaptive behavior (Vineland Adaptive Behavior Scales (VABS-III)), sleep (using Sleep Disturbance Scale for Children (SDSC)), QoL (using QoL in children with Epilepsy (QOLCE-55)), and other behavioral aspects (Behaviour Rating Inventory of Executive Function (BRIEF), Aberrant Behavior Checklist (ABC), Social Responsiveness Scale (SRS-2), Strength and Difficulties Questionnaire (SDQ)) were measured. Caregiver burden was estimated by standardized surveys (Depression, Anxiety and Stress Scale (DASS-21), Parental Stress Scale (PSS), International Trauma Questionnaire (ITQ) score for post-traumatic stress, and Perceived Control-VAS (PC-VAS)). Seizure outcomes were retrieved from medical records.

Results: All patients (n=20, 10 girls) had a verified pathogenic *SCN1A* variant, with a mean age to date of 12 years (range 4-23). Fenfluramine treatment lasted a mean of 59 months (range 25-93), with a mean maintenance dose of 0.57 mg/kg/day (range 0.24-0.7). A mean 75% reduction (range 30-100%) in generalized tonic-clonic seizures was observed at the last follow-up. Preliminary cognitive data from 9 children (mean age: 10.8 years, SD: 5.9, range 4-18; mild/moderate/severe: n=4/4/1) were markedly lower compared to the normal population but appear improved relative to a Swedish fenfluramine-naïve cohort, especially in social functioning (mean (SD) scores: Adaptive behavior composite: 57.9 (11.5); Communication ability: 53.0 (16.3); Daily functioning skills: 52.6 (17.7), Social ability: 60.0 (12.3), Motor ability 65.9 (9.5)). Cognitive assessments and caregiver burden evaluations are ongoing.

Conclusions: Once confirmed in the full cohort, findings will provide valuable insights into fenfluramine seizure efficacy in pediatric patients with Dravet syndrome and its impact on daily life function and caregiver burden.

ABSTRACTS

Topic: Neuromuscular Disorders

EPNS25_422 - Retrospective evaluation of 10 years of data for patients with Duchenne Muscular Dystrophy receiving rehabilitation in to Knee-Ankle-Foot Orthoses

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Objectives

This study aimed to evaluate the Knee-ankle-foot orthosis (KAFO) rehabilitation service for Duchenne Muscular Dystrophy (DMD) patients in our centre to assess efficacy, and inform future practice and service provision. KAFOs are orthoses that lock at the knee, control the foot and ankle, and provide ischial weight-bearing for standing/walking as an intervention for patients with (DMD) to prolong ambulation after loss of functional walking. Our service provides a 1-2 week block of inpatient rehabilitation at KAFO initiation. Some patients require Achilles tendon tenotomies to use KAFOs.

Methods

Patient records for all patients receiving KAFOs (2014-2024) were searched manually. Data collected: age, tenotomy or serial casting required, and duration of KAFO use after initiation.

Results

20 DMD patients started using KAFOs since 2014. The mean age of admission for KAFO rehab was 11.75 years (141 months). The range was 8-14 years. There was no significant correlation between age at provision, and duration of use. 9 patients required surgery prior to using KAFOs, 2 required serial casting, and 9 required no additional intervention. 81% of patients were still able to use KAFOs 1 year post provision, 63% at 18 months, 47% at 2 years, and 25% at 3 years. 11 patients had stopped using KAFOs at the time data were collected; the mean length of time used for was 18 months. The shortest time used was 1 month, however this patient was atypical as they received KAFOs immediately following a femur fracture and could not be fully assessed prior. The longest time a patient used KAFOs was 54 months (4.5 years).

Conclusions

The data show the majority of patients were still using KAFOs after 1 year, and half at 2 years. This is a significant length of time accessing walking, or standing, that would not otherwise have been possible. At the 2 year mark, 71% of patients who had surgery prior to rehab were still using KAFOs, compared to 25% of patients not requiring surgery. This may be due to therapists being more selective for appropriate candidates, due to the risks of surgery. These patients may have maintained range of movement longer due to surgical correction and post-surgical protocol. Other factors to consider are increased engagement from the surgical cohort, and this cohort receiving more rehab.

ABSTRACTS

Topic: Epilepsy: Medical and Surgical treatment

EPNS25_423 - Prospective evaluation of non-seizure benefits of treatment with fenfluramine in pediatric and adult patients with Dravet syndrome

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Objectives: Assess whether fenfluramine treatment affects cognition and adaptive behavior in pediatric and adult patients with Dravet syndrome, and if the outcome impacts caregiver burden.

Methods: We aim to prospectively include 15 patients with Dravet syndrome (verified by pathogenic *SCN1A* variants) starting fenfluramine treatment between August 2023 – August 2025. Frequency of generalized tonic-clonic seizures, comprehensive neuropsychologist assessment, and caregiver burden will be measured before and one year after fenfluramine initiation. Outcomes include fenfluramine-related non-seizure benefits, measured in terms of cognition (via Bayley Scales of Infant and Toddler Development (Bayley-IV), or The Wechsler Intelligence Scale adapted to age), adaptive behavior (via Vineland Adaptive Behavior Scales (VABS-III)), sleep (via Sleep Disturbance Scale for Children (SDSC)), quality of life (via Quality of Life in Children with Epilepsy (QOLCE-55)), and additional behavioral aspects (via the Behavior Rating Inventory of Executive Function (BRIEF), Aberrant Behavior Checklist (ABC), Social Responsiveness Scale (SRS-2), and Strengths and Difficulties Questionnaire (SDQ)). EEG data, treatment dosages, and efficacy will be extracted from medical records. Caregiver burden will be assessed via the Depression, Anxiety, and Stress Scale (DASS-21), Parental Stress Scale (PSS), International Trauma Questionnaire (ITQ) for post-traumatic stress, and Perceived Control-VAS (PC-VAS).

Results: To date, 2 pediatric patients (aged 4-6 years, 1 female) and 5 adult patients (aged 24-46 years, 2 females) have been enrolled and completed pre-fenfluramine evaluations. Preliminary cognitive data for 2 children (3-6 years), and 2 adults (32-36 years) (severity: normal (n=1), mild (n=1), severe (n=1), profoundly severe (n=1)) were markedly below population norms, and in line with a Swedish fenfluramine-naïve cohort (mean (SD) scores: Adaptive behavior composite: 46.3 (30.9); Communication ability: 46.8 (31.0); Daily functioning skills: 45.0 (29.6), Social ability: 49.0 (35.4)).

Conclusions: Once assessed overall, these findings will provide valuable insights regarding impact of fenfluramine treatment on daily life and function in patients with Dravet syndrome and their caregivers.

ABSTRACTS

Topic: Neurometabolic Disorders

EPNS25_424 - Brown-Vialetto-Van Laere Syndrome due to a heterozygous SLC52A3 variant with an autosomal dominant inheritance: a case report and review of the literature

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Objectives

Brown-Vialetto-Van Laere (BVVL) syndrome is a neurodegenerative disorder due to mutations in the *SLC52A2* and *SLC52A3* genes. It typically presents with sensorineural hearing loss and progressive ponto-bulbar palsy, accompanied by peripheral neuropathy and possible respiratory compromise. While most cases follow an autosomal recessive (AR) inheritance pattern, less than 30 cases to date have shown an autosomal dominant (AD) transmission.

Methods

We report a novel case of pediatric-onset BVVL due to a heterozygous *SLC52A3* variant and review available literature on AD BVVL.

Results

An 18-year-old female presented at age 15 with acute bilateral hearing loss followed by progressive cranial neuropathies and bulbar symptoms. Instrumental evaluations (brain MRI, EMG/ENG, EEG and evoked potentials) were inconclusive. Plasma acylcarnitines were normal. CSF analysis showed a slightly elevated protein count. Genetic testing revealed a novel heterozygous *SLC52A3* variant (c.1151G>A), classified as a VUS. The variant was inherited from her mother, who shows dysphonia and is awaiting audiological testing. Riboflavin supplementation (up to 70 mg/kg/day) led to significant clinical improvement in the patient and, along with her characteristic clinical findings, helped support the pathogenic role of this variant. A literature review identified 26 previously reported heterozygous BVVL cases. Phenotype is similar to AR cases; the 8 cases with treatment data available all responded to riboflavin (10 to 40 mg/kg). At least one unaffected relative was seen in all patients, although additional symptomatic family members were seen in 13/16 cases.

Conclusions

Our case and literature review confirm that BVVL may be transmitted in an AD pattern. We confirm an incomplete penetrance of the disease and a variable expressivity: indeed, the clinical spectrum of AD cases ranges from hearing loss only to severe respiratory compromise. Diagnosis can be challenging: acylcarnitine profiles (often abnormal in AR BVVL) appear normal in all AD cases and laboratory findings (such as CSF protein count) can mimic acquired inflammatory CNS diseases. Our findings reinforce the necessity of early treatment, since BVVL is progressive and riboflavin is an effective therapy. Thus, in individuals with a strong clinical suspicion but inconclusive genetic findings, a trial with riboflavin should always be initiated, to aid the diagnostic process and potentially improve outcomes.

ABSTRACTS

Topic: Neuromuscular Disorders

EPNS25_425 - Dysphagia in SMA1: phenotype and assessment tools

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Objectives

The study aims to describe the common dysphagia phenotype in SMA1 treated patients and compare available assessment tools, suggesting a clinical approach to test swallowing. The relationship between swallowing function, motor function and clinical features was also assessed.

Methods

Data of SMA1 children assessed as outpatients between September 2021 and December 2024 were retrospectively reviewed. The swallowing evaluation protocol included Mealtime Assessment Scale (MAS), Oral and Swallowing Abilities Tool (OrSAT), Food Intake LEVEL Scale (FILS) and Paediatric Functional Oral Intake Scale (p-FOIS). Motor function was assessed through the Children’s Hospital of Philadelphia Infant Test of Neuromuscular Disorders (CHOP-INTEND) scale and the motor milestone module of the Hammersmith Infant Neurological Examination (HINE-2). Correlation was used to compare clinical features, swallowing and motor function.

Results

50 SMA1 children were included in the study. All swallowing scales showed a strong correlation among them (r_S = 0.733-0.964; p-values <0.001). Swallowing efficiency correlated with CHOP-INTEND and HINE-2 ($p<0.05$). A statistically significant difference between “sitters” and “non-sitters” subgroups was found among all swallowing scales. Furthermore, a significant difference in swallowing abilities was also found when comparing pharmacological therapies and SMA1 subtypes.

Conclusions

The typical dysphagia phenotype was outlined, highlighting the need for a swallowing screening in all SMA1 treated children. Mealtime assessment should be performed in all children showing potential signs of dysphagia. Motor function correlated with swallowing efficiency, but not with swallowing safety. Symptom onset, pharmacological therapies and disease management impact swallow abilities.

ABSTRACTS

Topic: Neurometabolic Disorders

EPNS25_426 - NDUFS6 related Leigh Syndrome receiving off-label "precision medicine" treatment with sildenafil: evidence from a case study

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Objectives Leigh syndrome (LS) is a rare complex progressive neurodegenerative condition usually with onset in the first years of life. The genetic background is heterogeneous, with a poor genotype–phenotype correlation. LS encompasses more than 100 separate monogenic disorders associated with enormous clinical and biochemical heterogeneity and Mitochondrial Complex I deficiency is one of the most frequently observed abnormalities. Pathogenic variants in the NDUFS6 gene have been associated with autosomal recessive Mitochondrial complex I deficiency, nuclear type 9 (MC1DN9). MC1DN9 is a rare, early onset, and often lethal disease presenting with severe neonatal lactic acidemia. To date, only a few patients were reported with NDUFS6 pathogenic variants.

Methods Herein, we provide the clinical and molecular description of a new patient, bearing known and novel NDUFS6 variants, presenting with a slightly milder phenotype, compatible with Leigh syndrome. We present the individual experience of this patient receiving phosphodiesterase 5 (PDE5) inhibitor sildenafil as off-label precision therapy.

Results By the first month of life, central hypotonia and esotropia of the left eye was noticed and the patient was referred to physiotherapy. Brain Magnetic Resonance Imaging (MRI) at 7 months of age was reported as normal. At 11 months, she exhibited acute neurological deterioration with respiratory failure and stupor requiring admission to the Intensive Care Unit (ICU), where she remained for a duration of 32 days. At this time, her brain MRI raised the possibility of a leukodystrophy-type metabolic disease, and this was confirmed by genetic testing. Sequence analysis identified a heterozygous splice region, intron variant *NDUFS6* c.309+5G>A, and a heterozygous frameshift variant *NDUFS6* c.250del, p. (Val84*). Besides standard therapeutic measures, a trial of off-label therapy with sildenafil was initiated, with the aim to offer clinical benefit by promoting restoration of mitochondrial biogenesis based on animal studies and previous observational data.

Conclusions Following one year on treatment the patient remains stable with no adverse events. The management of Leigh disease relies on the timely establishment of the correct diagnosis, application of symptomatic treatment and non-specific application of antioxidants or co-factors, if the respiratory chain or oxidative phosphorylation is compromised. PDE5 inhibitors hold promise as a targeted treatment in patients with Primary Mitochondrial Disorders.

ABSTRACTS

Topic: Neurometabolic Disorders

EPNS25_427 - Improved developmental outcomes with early initiation of cerliponase alfa treatment in children with CLN2 disease

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Objectives

Neuronal ceroid lipofuscinosis type 2 (CLN2 disease) is a rare, neurodegenerative disorder caused by deficient TPP1 enzyme activity. CLN2 disease typically presents between the ages of 2 and 4 years and is rapidly progressive. Intracerebroventricular (ICV) infusion of cerliponase alfa (rhTPP1) slows decline in language and motor function in patients with CLN2 disease. Here, we present data on developmental outcomes among children treated with cerliponase alfa in a cohort that included children who initiated treatment <2 years of age, prior to the typical age of symptom onset (NCT02678689).

Methods

Study participants received ICV cerliponase alfa biweekly for at least 144 weeks; dose was based on age. Attainment of developmental milestones, assessed using the Denver II Developmental Screening Test, was evaluated as an exploratory endpoint. The Denver II Test assesses skills in 4 domains: fine motor adaptive, gross motor function, language, and personal social; developmental age equivalent scores in each domain were assessed at baseline and every 12 weeks until study completion.

Results

Overall, 14 participants were enrolled in the study (57% female), with mean (SD) age at baseline of 3.1 (1.5) years. Among participants <2 years of age at baseline (n=5), the majority showed developmental age equivalent scores at baseline at or above participant age at assessment, with mean (SD) age equivalent scores at baseline of 22.2 (6.6), 31.6 (9.8), 25.6 (9.7), and 30.2 (8.1) months in fine motor adaptive, gross motor, language, and personal social domains, respectively. Scores in all domains increased over the study, with a mean (SD) increase in score of 41.0 (16.7), 33.4 (13.6), 35.6 (18.0), and 25.4 (17.0) months, respectively. Among participants ≥2 years of age at baseline (n=9), mean (SD) developmental age equivalent scores at baseline were 25.2 (12.3), 33.8 (8.8), 31.3 (10.7), and 31.0 (15.3) months in fine motor adaptive, gross motor, language, and personal social domains, respectively. Scores in this age group showed little change over the study, with a mean (SD) change from baseline of 0.0 (6.7), -6.0 (20.3), -0.4 (15.0), and -0.1 (13.7) months, respectively.

Conclusions

Results show age-appropriate attainment of developmental milestones in participants younger than 2 years of age at baseline, suggesting that early initiation of cerliponase alfa treatment, prior to symptom onset, may result in improved developmental outcomes in children with CLN2 disease.

ABSTRACTS

Topic: Infectious and Inflammatory Diseases/ Neuroimmunology

EPNS25_428 - Distinguishing Dual Positivity in Anti-MOG and Oligoclonal Band Patients: Insights into Overlapping Clinical Profiles

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Objectives

This study aimed to investigate the clinical and imaging characteristics of patients with dual positivity for anti-myelin oligodendrocyte glycoprotein (anti-MOG) antibodies and oligoclonal bands (OCBs), exploring potential overlaps between multiple sclerosis (MS) and MOG-associated disease (MOGAD).

Methods

We conducted a retrospective cohort analysis of 45 patients from three medical centers, stratified into two groups: 30 with isolated anti-MOG positivity and 15 with dual positivity. Clinical and imaging parameters were compared using Fisher's Exact Test and Benjamini-Hochberg correction for multiple comparisons.

Results

The mean age at onset was significantly lower in the isolated anti-MOG group (10 ± 7 years) compared to the dual-positive group (28 ± 17 years, $p = 0.001$). No significant differences were observed in cerebrospinal fluid (CSF) pleocytosis, protein levels, or opening pressure. Optic nerve findings, including enhancement ($p = 0.0038$) and thickening ($p = 0.0017$), were more frequent in the isolated anti-MOG group, alongside a trend toward pre-chiasmatic lesions ($p = 0.06$). Papilledema was also more prevalent in this group ($p = 0.014$). The dual-positive group exhibited higher rates of polyfocal presentation ($p = 0.013$), more frequent attacks ($p = 0.002$, HR = 10.2, 95% CI: 2.19–49.23), and a greater number of brain lesions ($p = 0.0063$).

Conclusions

Our findings highlight significant clinical and imaging distinctions between isolated anti-MOG positivity and dual positivity, suggesting dual-positive cases may represent either an inflammatory variant of MOGAD or a subtype within the MS spectrum. Further prospective studies are essential to clarify these distinctions and refine diagnostic and therapeutic strategies.

ABSTRACTS

Topic: Miscellaneous

EPNS25_429 - Evaluation of Chat GPT's performance on the Pediatric Neurology Specialty Certificate Examinations

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Objectives

The dynamic technological progress has contributed to significant advancements in the field of Artificial Intelligence (AI). Its potential is being utilized in many aspects of human life, including medicine. Our work focuses on analyzing the effectiveness of AI-based language models in the context of solving the polish State Specialization Examination (SSE) in pediatric neurology.

Methods

The study evaluated the effectiveness of 2 language models: Chat GPT 3.5 and 4.0 in solving two past papers of SSE in pediatric neurology: spring and autumn 2023. For the study, questions were divided into 6 thematic groups. The point scores of both models were compared with the results of physicians taking the SSE in the given sessions. The results obtained by the language models for individual questions were also compared against the difficulty index of the questions.

Results

Chat GPT 4.0 achieved a passing score (60%) in both examination sessions. Considering the total points obtained in both examination sessions, Chat GPT 4.0 achieved similar scores (72%) to physicians (74%). Significant differences were also demonstrated between the results achieved by the older (48%) and newer (72%) versions of Chat GPT. Chat GPT 4.0 performed best in the questions connected with 'Metabolic disorders and other rare diseases' and 'Headaches and CNS tumors', while doctors achieved the highest scores in all other categories. There was no significant correlation between the difficulty coefficient and the scores of both language models.

Conclusions

Chat GPT 4.0 outperformed its predecessor, probably due to significant enhancements, such as more advanced contextual understanding, greater language fluency, and a much larger base of learned information. Variations in the Chat GPT's performance in different categories may be a result of inadequate modeling by the engineers and the differences in availability of specialty-specific materials in the training database. Nevertheless, the results presented in our work may indicate the potential utilization of artificial intelligence in the practice of pediatric neurologists. However, despite promising results, the use of AI in medicine poses ethical and practical challenges for physicians. Our poster emphasizes the importance of further research on the use of AI in pediatric neurology and the need for continuous assessment and development of these technologies, raising issues regarding their potential applications and challenges associated with their implementation in clinical practice.

ABSTRACTS

Topic: Neuropsychiatric Disorders / Functional Neurological Disorders

EPNS25_430 - Mentalizing abilities and Somatic Symptom and Related Disorders in a pediatric cohort: a single center cross-sectional study

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Objectives

Many children and adolescents report physical symptoms such as headaches, abdominal pain, or motor difficulties, significantly affect their quality of life. When these symptoms lack organic causes, they are classified as Somatic Symptom and Related Disorders (SSRD) per DSM-5. Dysfunctional relationships may impair mentalization, potentially leading to psychosomatic symptoms as a defense mechanism against internal distress. PediatricSSRD admissions have risen post-SARS-CoV2 pandemic. This study explores mentalization in the post-pandemic pediatric SSRD population and examines risk factors like parental reflective functioning, somatic symptom perception, and demographics.

Methods

Inclusion criteria: patients aged 8-18 years, hospitalized for non-organic physical symptoms, SSRD diagnosis (DSM-5), and fluency in Italian. Exclusion criteria: age under 8 years, undefined diagnosis, or organic causes. Mentalization was assessed using the Reflective Functioning Questionnaire (RFQ). Secondary outcomes were assessed using the Parenting Reflective Functioning Questionnaire (PRFQ), Child Behavior Checklist (CBCL), SAFA (anxiety/somatic symptoms), Parental Stress Index (PSI), Children's Somatization Inventory (CSI), and demographic analysis.

Results

The sample included 29 patients (72% female, median age 12): 55% conversion disorder, 28% somatic symptom disorder, and 17% brief somatic symptom disorder. The most common symptoms were limb pain/tremor, walking difficulties, and headaches; 58% reporting symptoms for at least 2 months. Patients underwent an average of 3 diagnostic tests, with 79% normal results. RFQ scores revealed a positive correlation between uncertainty of mental states and distress perception ($r = 0.566$, $p = 0.004$). Significant differences in CSI scores emerged among children, mothers, and fathers, with fathers scoring highest (58.17). PRFQ scores showed no significant differences between mothers and fathers or correlations with somatic symptom perception.

Conclusions

Early identification of emotional issues in SSRD is vital to reduce physical suffering and prevent psychological difficulties from evolving into psychiatric disorders. Fathers' heightened perception of somatic symptoms may stem from emotional processing or caregiving roles, influenced by cultural or social expectations, rather than differences in mentalization abilities. Children's greater uncertainty about mental states correlates with higher symptom distress, emphasizing the importance of mentalization in managing psychosomatic symptoms. Interventions should focus on enhancing children's reflective capacities and providing psychoeducational programs for parents to improve understanding of the mind-body connection, optimize care, and reduce unnecessary medical investigations.

ABSTRACTS

Topic: Epilepsy: Medical and Surgical treatment

EPNS25_431 - Use of Fenfluramine and Cannabidiol in Daily Practice: A Retrospective Analysis of German Prescription Claims

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Objectives

To describe use of fenfluramine (FFA) versus cannabidiol (CBD) in Germany, based on age and gender distribution, prior anti-seizure medication (ASM) use, dosage, and medication persistence, in patients with Dravet syndrome (DS) and Lennox-Gastaut syndrome (LGS).

Methods

This was a retrospective analysis of German prescription claims from March 2020-October 2023. Patient index was date of first FFA or CBD prescription. Patients with stiripentol (STP) and without felbamate (FLB) or rufinamide (RUF) at any time during study period were assigned to DS group; those with FLB or RUF and without STP were assigned to LGS group. Prior ASMs were analyzed for 9 months prior to index. Persistence was analyzed up to 36 months after index; patients lost to follow-up due to end of database records were censored. Data were extrapolated to the German statutory health-insured population.

Results

379 FFA (26.1% DS; 10.6% LGS; 63.3% undefined) and 1,918 CBD (4.6% DS; 17.2% LGS; 78.2% undefined) patients were identified in the database (with extrapolation). At index, FFA patients had a mean±SD age of 15.0±12.9 years; 40.9% male, 34.3% female, 24.8% unknown. Patients with CBD had a mean±SD age of 19.4±15.7 years; 37.8% male, 34.8% female, and 27.4% unknown. 93.7% of FFA patients and 85.5% of CBD patients received prior ASM(s). Mean±SD FFA dosage/day was 18.2±35.2 mg and mean±SD CBD dosage/day was 559.8±718.2 mg. Persistence after 12, 24, and 34 months was 73.7%, 65.6%, and 61.5% for FFA, and 52.1%, 37.1% and 32% for CBD, respectively. Results by DS or LGS will be presented.

Conclusions

Despite limitations (indication assignment, dosage calculation without patient weight), this analysis suggested that FFA and CBD recommended dosages/day were not exceeded. The proportion of FFA patients with prior ASMs was numerically higher compared to CBD. The overall (not indication-specific) medication persistency was numerically higher for FFA vs CBD patients.

ABSTRACTS

Topic: Neurometabolic Disorders

EPNS25_432 - Age and Biomarkers as Predictors of Cerebral Adrenoleukodystrophy Onset: A Multi-Center Retrospective Cohort Study

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Objectives: Among children with X-linked adrenoleukodystrophy (ALD), the risk of cerebral demyelinating lesion (cerebral ALD; cALD) in X-linked adrenoleukodystrophy peaks in the middle of the first decade, which has shaped clinical monitoring guidelines. By comparison, the age-related risk of cALD in adolescence and adulthood remains poorly understood, highlighting a critical gap in clinical practice. We hypothesized that specific age ranges, onset of other ALD-related symptoms, and plasma C26:0 lysophosphatidylcholine (LPC) levels would correlate with an increased risk of cALD onset.

Methods: We are conducting a multi-center, retrospective cohort study. Inclusion criteria are: (1) male patients, (2) aged 12 years or older, (3) with a confirmed diagnosis of X-linked adrenoleukodystrophy (ALD), and (4) availability of at least one brain MRI report. Statistical analyses were performed using IBM SPSS, with t-tests for mean comparisons and chi-square tests for percentage analysis. We defined the onset of cALD as the date cerebral lesions were detected on MRI and used the Kaplan-Meier method for time-to-event analysis. We compared distributions using the likelihood ratio chi-square test. To account for the time of entry, we employed left truncation and included censored data in the survival analysis.

Results: Preliminary findings include data from two of six participating research sites with data collection from the remaining four sites expected within the next five months. The preliminary dataset consists of 143 patients, of whom 36 developed cerebral lesions. Survival analysis without cerebral lesions reveals a progressively increasing risk of cALD onset with age. A marked rise in lesion incidence is observed between the ages of 30 and 40, followed by stabilization after the age of 60. Between ages 12 and 60, approximately 40% of our cohort had developed cerebral lesions. Analysis of initial symptoms and plasma C26:0 LPC levels are pending.

Conclusions: Our preliminary findings suggest that age may be a critical risk factor for cALD onset in adolescent and adult ALD males. Additional data collection and analysis are needed to validate these results. These findings underscore the importance of routine monitoring in ALD males, potentially influencing clinical guidelines and enabling earlier therapeutic interventions to prevent lesion progression in cALD.

ABSTRACTS

Topic: Neuromuscular Disorders

EPNS25_433 - Barriers to Implementation of Spinal Muscular Atrophy Newborn Screening Program in Singapore

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Barriers to Implementation of Spinal Muscular Atrophy Newborn Screening Program in Singapore

Objectives
Spinal Muscular Atrophy (SMA) is a genetic progressive neuromuscular disorder affecting 1 in 10,000 newborns a year. With the advent of gene modifying treatments, implementation of newborn screening (NBS) is a critical part of improving outcomes of children with this treatable disease. In Singapore, NBS for metabolic diseases is available, with high uptake of >90% newborns, but is paid out of pocket by parents. At present, genetic screening tests also require pre-test counseling and consent taking. A pilot study was performed to screen 100 newborns in a single center and to evaluate any barriers for effective implementation of a nationwide NBS program.

Methods
100 babies were screened with 3 dried blood spots for DNA extraction and quantitative PCR of *SMN1* gene at National University Hospital from April – July 2024 via sequential convenience screening. 110 parents and 10 healthcare professionals (HCPs) were surveyed about their knowledge and perception regarding NBS.

Results
No positive cases were found in this small pilot study. While 91% (n=100) parents were agreeable for NBS screening, only 67% were willing to pay up to SGD$70 (50 euros) for the screening test and 81% were willing to pay up to SGD$300 (212 euros) for post-screening confirmatory tests. 45% (n=50) of parents preferred to have patient education about SMA in their prenatal visits. Key concerns for parents were the need for extra blood collection, psychological stress of a positive diagnosis, insurance implications and cost for testing and treatment. HCPs also had some concerns about pre-test counselling as about half had average or below average knowledge about SMA prior to the study and found that it was time-consuming to educate parents about SMA. 90% HCPs felt that SMA NBS education should be done during prenatal visits. 32% felt that SMA NBS education should be done by geneticist/counsellor, 25% by the neonatologist and 16% by the obstetrician.

Conclusions
Implementation of universal SMA NBS may be challenging because of the cost considerations as parents have to pay out of pocket for testing. Pre-natal education about SMA is required to improve parental awareness so as to facilitate pre-test counselling.

ABSTRACTS

Topic: Epilepsy: Medical and Surgical treatment

EPNS25_435 - Efficacy and tolerance of Cenobamate in children with drug-resistant epilepsy in a french multicenter retrospective cohort of 44 patients

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Objectives

Cenobamate (CNB), a GABAergic agonist and sodium channel blocker, is a new anti-seizure medication approved for the treatment of focal seizures with or without secondary generalization in adults. Makridis (2022) reported 16 pediatric patients with drug-resistant epilepsy, with 31% achieving seizure freedom. We present a retrospective, multicenter pediatric series of patients who received CNB for drug-resistant epilepsy.

Methods

CNB was administered as an add-on therapy, with informed consent from patients and parents regarding off-label use. Only patients with at least six months of follow-up were included.

Results

The study included 44 patients with a mean age of 13.6 years (range: 2–18 years). Twenty patients had epilepsy onset before the age of one, and 20 experienced more than one seizure per day at CNB initiation. The cohort comprised 20 patients with non-idiopathic focal epilepsy (FE), 18 with Lennox-Gastaut syndrome (LGS), and 6 with non-idiopathic generalized epilepsy (NIGE). Thirteen patients had normal MRI findings, while 20 had abnormal MRIs. Six patients had failed epilepsy surgery, and 8 had a known genetic etiology. CNB was introduced at a mean age of 13.4 years, with an average dose of 2.2 mg/kg/day. At six months, 30 patients (66%) experienced a seizure frequency reduction of more than 50%: 80% of those with NIGE, 77% with LGS, and 65% with FE. Seven patients (16%) achieved seizure freedom. Among 23 patients who completed 12 months of treatment, 4 patients (17%) are seizure-free and 8 patients (34%) maintain a seizure frequency reduction of more than 50%. Eleven patients (47%) have reduced their co-medication by at least one ASM.
Reported side effects included sedation (4), fatigue (5), diplopia (1), dizziness (2), and mood changes with suicidal ideation (1), skin allergy (1), and seizure worsening in 2 patients.

Conclusions

The response to CNB in this highly refractory pediatric population is promising and appears to be sustained over time. Tolerability appears to be comparable to that observed in adults.

ABSTRACTS

Topic: Epilepsy: Medical and Surgical treatment

EPNS25_436 - Development and results of the epilepsy surgery in a developing country

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Objectives: The purpose of the study is to highlight the possibility of implementing an integrated solution design with efficient outcomes in management of lesional and non-lesional drug-resistant epilepsy with surgical intervention. The study aims to present a statistical review of efficacy of surgical management of epilepsy, based on our experience with the national epilepsy surgery program, commenced in 2016. Retrospective assessment of the results of the cohort, showcases the relevance of the model of the program.

Methods: Our cohort consisted of 50 patients with lesional and one with non-lesional drug-resistant focal epilepsy. All patients underwent 3T MRI and Video-EEG monitoring (VEM). 18F-FDG PET scan of the brain was performed in 24 patients. Three patients underwent stereoelectroencephalography (SEEG). Eighteen patients underwent preoperative neuropsychological examination. Three patients had multiple pathologies, with surgical intervention targeting only epileptogenic zones.

Results: The majority of the patients benefitted from surgery, with 47 (92.2%) being free of disabling seizures (Engel class I) at the time of the report. Four patients (7.8%) did not improve substantially (Engel class IV), with one of them on post-surgical follow up turning out to be having a genetic mutation resulting in Chromosome 15q11.2 deletion syndrome. Our study also reports the statistical significance of post-surgical pharmacotherapy-dependancy. Eighteen patients (35.3%) are currently ASM-free, fifteen (29.4%) are on monotherapy, fourteen (27.5%) are receiving dual therapy and four (7.8%) are on polytherapy. In 25 patients (49%) pharmacotherapy was stopped completely or one of the ASMs was withdrawn.

Conclusions: In conclusion, the study exhibits the applicability of our model in managing lesional and non-lesional drug-resistant epilepsy, with more than 90% positive outcome value. Thus, based on our experience, we strongly believe the suitability of our model of the epilepsy surgery program to be implemented in the developing countries.

ABSTRACTS

Topic: Cerebrovascular Disorders

EPNS25_437 - Evaluation of Perinatal Arterial Ischemic Stroke Patients: Underlying Etiologic Factors and Long-Term Prognosis

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Objectives

Perinatal arterial ischemic stroke (PAIS) is a significant cause of long-term neurological impairments, including epilepsy, cerebral palsy, and poor cognitive outcomes. Understanding the etiologic factors and prognostic indicators is critical for improving patient care and outcomes. This study aimed to investigate the underlying etiologic factors, clinical features, and long-term outcomes of children with PAIS, with a particular focus on the development of epilepsy and functional prognosis.

Methods

A retrospective, single-center analysis was conducted on 44 children diagnosed with PAIS between 2008 and 2024. Clinical, neuroimaging, and EEG data were reviewed to identify predictors of poor outcomes, including epilepsy and modified Rankin Scale (mRS) scores. Statistical analyses were performed to evaluate associations between clinical variables and outcomes.

Results

Of the 44 patients, 20.5% were diagnosed with neonatal arterial ischemic stroke (NAIS) and 79.5% with presumed perinatal arterial ischemic stroke (PPAIS). The mean age of symptom onset was 4.85 months, and 81.8% of patients initially presented with hemiparesis or focal motor deficits. Cortical involvement and EEG background slowing were significant predictors of epilepsy and poor functional outcomes. MCA-M1 branch occlusion and epileptiform discharges were strongly associated with epilepsy diagnosis. Favorable mRS scores (0–2) were observed in 55.8% of patients, while 44.2% had poor outcomes (mRS 3–6).

Conclusions

This study underscores the critical role of early diagnostic tools, such as neuroimaging and EEG evaluations, in predicting long-term outcomes and identifying high-risk patients with PAIS. While the findings provide valuable insights, the retrospective design and small sample size emphasize the need for multicenter studies to validate these results and guide targeted interventions aimed at improving neurodevelopmental outcomes.

ABSTRACTS

Topic: Epilepsy: Diagnosis and Investigations

EPNS25_439 - Untargeted Metabolomics Reveal Key Metabolic Alterations in Pediatric Epilepsy: Insights into Tryptophan Metabolism and the Gut-Brain Axis

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Objectives

Biochemical changes in ictogenesis and epileptogenesis are poorly understood, with no clear biomarkers for prognosis or prediction. Untargeted plasma metabolomics offers an unbiased avenue to understand the pathomechanisms of epilepsy.

Methods

This study applies untargeted plasma metabolomics through liquid chromatography-mass spectrometry in a pediatric epilepsy cohort. Blood samples were taken prospectively from 19 epileptic patients and 11 healthy controls. Data was processed using multivariate statistical analyses and pathway analysis.

Results

We found 21 key endogenous metabolites with VIP score >1 and adjusted p-value <0.05. In epileptic patients compared to healthy controls, significant decreases were observed in tryptophan, 5-HIAA, gut microbiota-derived metabolites (indole, indoxyl sulfate, p-Cresylsulfate), and niacin metabolism end-products (2PY and 4PY). Other key findings included the decrease of tricarboxylic (TCA) cycle intermediates, an increase of fatty acids derivatives, and an increase of N-Acetylneuraminic acid. The patient group's most significantly altered metabolic pathways were the TCA cycle, Vitamin A and C metabolism, prostaglandin formation, and D4&E4-neuroprostanes formation.

Conclusions

The disruptions in tryptophan metabolism point to the gut-brain axis, suggesting that gut microbiota-derived metabolites may contribute to epileptogenesis or ictogenesis. Additionally, circulatory metabolic markers indicating an energy crisis and oxidative stress provide evidence for the detectable systemic effects of seizures.

ABSTRACTS

Topic: Neuromuscular Disorders

EPNS25_441 - Design and objectives of clinical program for assessing the efficacy and safety of once-daily mexiletine prolonged release in myotonic dystrophy types 1 and 2: HERCULES and ATLAS Phase 3 studies

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Objectives: Myotonic dystrophy (DM) is a heterogeneous group of hereditary, rare diseases, classified as DM1 and DM2, with a common and defining symptom of myotonia, resulting in impairment across many different domains of patients' quality of life (QoL). Current DM management relies on off-label symptomatic treatment, and mexiletine has been used off-label as an effective antimyotonic for several decades. While physicians and patient groups support mexiletine use, limited study data exist and myotonia remains mainly untreated. Regulatory approval of mexiletine is needed to ensure optimal use in clinical practice. A new once daily (QD), prolonged release (PR) formulation has been developed as a powder for reconstitution to allow for improved swallowability, tolerability and patient compliance.

Methods: HERCULES is a randomized, double-blind, placebo-controlled, multicentre, prospective study to investigate efficacy and safety of QD mexiletine PR 500 mg for 26 weeks' treatment in adolescents (≥16 years) or adults with genetically confirmed DM1 or DM2. The aim is to generate efficacy/safety data of an improved mexiletine PR formulation in the DM population in a well-controlled study.

HERCULES is conditionally powered for 1) >90% significance on primary endpoint using dynamometer-measured handgrip myotonia (relaxation time) at week 26 for DM1, and 2) >90% for a statistical significance for ≥1 secondary endpoint: locking domain of individualised neuromuscular QoL questionnaire and myotonia behaviour scale set at type-1 error at a 2-sided 0.025 and visual analogue scale for stiffness, 10 meter-walk and DM1-Active-c at a type-1 error at a 2-sided 0.05 level. Interim analysis once 40 DM1 patients complete/early terminate HERCULES is planned to confirm the initial sample size of 80 DM1 patients, or to inform the sample size re-estimation needed to sufficiently power the study. 16 DM2 patients will be analysed separately. Primary safety endpoints: cardiac safety, adverse events.

Results: The study is ongoing across 12 centres in 5 EU countries and the UK. All patients completing HERCULES will be offered to participate in an 18-month open-label extension (ATLAS study).

Conclusions: The HERCULES study will inform on the efficacy and safety of 26-weeks' treatment with a new QD oral mexiletine PR, in addition to providing an understanding on how symptomatic treatment of myotonia improves a patient's QoL in DM.

ABSTRACTS

Topic: Epilepsy: Medical and Surgical treatment

EPNS25_442 - Use of oral cannabis in a drug-resistant epilepsy: A five-year single center experience

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Objectives

Purified cannabidiol (CBD) has been approved by the Korean government as a treatment for drug-resistant epilepsy (DRE) since 2019. We aimed to investigate the long-term efficacy, tolerability, and predictors of favorable initial outcome of pediatric DRE patient with CBD.

Methods

We included 96 pediatric patients treated with CBD (including 40 children who tapered-off) who visited the Department of Child Neurology from March 2019 to July 2024. Data from patient follow up was collected until CBD discontinuation or up to 36 month duration. CBD efficacy was assessed by seizure frequency (categorized into seizure-free, >50% reduction, <50% reduction, and no effect) and successful reduction of the number or dosage of ASMs. Patients were evaluated for any treatment-emergent adverse effects to determine safety of CBD.

Results

The median (Q1, Q3) age at CBD initiation was 9.7 (6.4, 14.7) years, with its median treatment duration of 18.3 (5.1, 37.6) months. The proportions of children who used CBD for more than 12, 24, and 36 months were 57.3%, 41.7%, and 26.0% respectively. The proportion of children who achieved seizure free or a >50% reduction at 12 month was 43.8%, while the proportions at 24 and 36 months were 34.4% and 24.0%, respectively. During the period of CBD use, 10% of the children reduced the number of ASMs, and additional 9.4% reduced the dosage of their ASMs. The most prevalent reasons for tapering off CBD was poor efficacy (26/40), followed by gastrointestinal symptoms (5/40) and somnolence (4/40).

Conclusions

In pediatric patients with DRE, CBD may be a useful treatment option that allows the reduction or reducing concomitant ASMs. CBD was also shown to be able to be used safely long-term. Proper monitoring of adverse effects and tailored dosage modification should be accompanied.

ABSTRACTS

Topic: Neurometabolic Disorders

EPNS25_444 - Assessing Lesion Progression in X-Linked Adrenoleukodystrophy: A Multi-Center Study on Imaging Techniques, Biomarkers, and Cerebral Lesion Regions

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Objectives: This study investigates cerebral lesion prevalence and progression patterns in adolescent and adult X-linked adrenoleukodystrophy (XALD) patients, focusing on brain region differences between stable and progressive lesions, the predictive value of diffusion restriction versus gadolinium enhancement for tracking progression, and the role of plasma C26:0 lysophosphatidylcholine (LPC) and Neurofilament Light Chain (NfL) levels. We hypothesize that specific brain regions are more prone to progression, diffusion-weighted imaging (DWI) is a viable alternative to gadolinium for lesion activity tracking, and LPC and NfL levels correlate with lesion type and progression.

Methods: We are conducting a multi-center, retrospective cohort study. Inclusion criteria are: (1) male patients, (2) aged 12 years or older, (3) with a confirmed XALD diagnosis, and (4) at least two brain MRI reports. Plasma C26:0 LPC levels were measured at baseline, and NfL levels at baseline and follow-up. Preliminary analysis compared stable vs. progressive lesions based on MRI findings, LPC levels and NfL levels. Brain regions were categorized as parieto-occipital, frontal, frontopontine, cerebellar white matter, or combined. Statistical analyses used IBM SPSS, with descriptive analysis, Cox proportional hazards regression for lesion development, and ANCOVA to adjust for age-related NfL differences.

Results: Preliminary findings include data from two participating research sites, with four additional sites expected to contribute within five months. The dataset consists of 143 patients, 36 of whom developed cerebral lesions. Progressive lesions are more common in parieto-occipital and frontopontine regions, while stable lesions are observed in cerebellar and frontal areas. Progressive lesions develop earlier and more rapidly, with a notable incidence peak between ages 30 and 45, while stable lesions develop gradually. The association between C26:0 LPC or NfL levels and lesion progression, as well as the predictive value of diffusion restriction compared to gadolinium, remains under analysis.

Conclusions: Preliminary findings suggest specific brain regions are associated with progressive lesions, which develop earlier and more rapidly. Further data are needed to validate these results and explore NfL and C26:0 LPC as biomarkers for disease monitoring and DWI as an alternative progression tracker to gadolinium. Insights could refine clinical guidelines and prevent lesion progression in cALD patients.

ABSTRACTS

Topic: Neuromuscular Disorders

EPNS25_445 - Mexiletine Paediatric Investigation Plan, PIP4 study: safety and pharmacokinetic findings in children with myotonia

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Objectives

The PIP (Pediatric Investigation Plan) explores safety of mexiletine treatment in children with myotonic disorders.

Methods

PIP4 (EudraCT2019-003757-28) was a 12-week open-label exploration of mexiletine in sequential cohorts. Cohort 1: 12–<18y; Cohort 2: 6–<12y. Design: 4 weeks' screening; 4 weeks' mexiletine 62, 83 or 167mg once-daily titrated to maximum 3-times-daily; 4 weeks' maintenance (best-tolerated dose). Primary endpoints: Safety, pharmacokinetics (PK), tolerability, adverse-event (AE) profiling including ECG, baseline–end of study (EOS).

Results

Cohort 1: N=7 (mean age 13y; 4 female); cohort 2: N=5 (mean age 8y; 3 female). In paediatric patients, recommended mexiletine dose is dependent on body weight: maximum daily maintenance dose range, 187 mg (20-30kg/age ~6–10y) to 500 mg (≥60kg/age 16<18y). Mexiletine exposure, ≥53 days (all subjects continue in PIP7 ≥24-month extension). ECGs were normal excluding one abnormal baseline assessment (not clinically significant). Mexiletine was well tolerated. All AEs and TEAEs were mild; most resolved without intervention and were unrelated. No subjects reported dose modifications. TEAEs were reported in n=6(86%) Cohort 1, n=1(20%), Cohort 2: overall N=7(58%). No deaths, serious TEAEs, or TEAEs leading to study discontinuation were reported. Most frequent TEAEs: abdominal pain and nausea. Physical examinations and haematological, biochemical, and muscle-function assessments revealed no clinically significant changes. PK data confirm paediatric mexiletine exposure, consistent with well-established adult posology. PK modelling adequately described oral mexiletine concentration data (all N=12 subjects), showing good agreement between observed and predicted concentrations. Paediatric doses required to achieve mexiletine concentrations are similar to adult doses. Bootstrap analysis (comparing population PK parameters with final PK model) indicates the model is robust.

Conclusions

No unexpected safety findings were observed in the PIP4 study of oral mexiletine administration in children with myotonic disorders. Mexiletine's safety profile was consistent with the NaMuscla® SMPC, 2023. No events resulted in mexiletine discontinuation. PK analyses confirm paediatric mexiletine dosing.

ABSTRACTS

Topic: Neuropsychiatric Disorders / Functional Neurological Disorders

EPNS25_446 - Predicting Treatment Response in Female Adolescents with Non-Suicidal Self-Injury Using Neurophysiological Biomarkers and Machine Learning

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Objectives

This study explores the utility of quantitative EEG (qEEG) features combined with clinical data to predict treatment response in female adolescents with non-suicidal self-injury (NSSI).

Methods

A total of 104 female adolescent inpatients (mean age: 15.95 ± 2.77) participated. EEG data were recorded under three conditions: eyes-closed, eyes-open, and during a mental arithmetic task. Preprocessing included artifact removal using independent component analysis (ICA), re-referencing, and filtering (1–100 Hz). qEEG features were extracted, including absolute and relative power across frequency bands (delta: 1–4 Hz, theta: 4–8 Hz, alpha: 8–12 Hz, beta: 12–30 Hz, gamma: 30–50 Hz), power ratios, and phase-amplitude coupling metrics. Treatment response was evaluated using pre- and post-admission scores of clinical scales, including the Health of the Nation Outcome Scales (HoNOS), Clinical Global Impression-Severity/Improvement (CGI-S/I), World Health Organization Disability Assessment Schedule (WHODAS), and Global Assessment of Functioning (GAF). Predictive models were developed using the XGBoost algorithm, incorporating qEEG features and medication data (e.g., equivalent doses of antidepressants and antipsychotics). Leave-One-Subject-Out (LOSO) cross-validation was applied, and SHapley Additive exPlanations (SHAP) analysis assessed feature importance.

Results

The models achieved excellent performance across all clinical measures, with correlation coefficients exceeding 0.9 and mean squared error (MSE) values as low as 0.02. Among these, predictions based on CGI-S improvement demonstrated the highest accuracy (correlation: 0.98; MSE: 0.02), followed by WHODAS scores (correlation: 0.96; MSE: 2.61) and GAF improvement (correlation: 0.97; MSE: 0.76). Key predictive qEEG features included relative low-beta power at the Pz electrode, absolute theta power at Fp1, and the ratio of delta to beta power at Cz. Pre-admission clinical scores, particularly CGI-S and HoNOS, also significantly contributed to predictive accuracy. SHAP analysis confirmed the importance of qEEG-derived features in explaining individual variability in treatment outcomes.

Conclusions

This study demonstrates the potential of qEEG features and machine learning in predicting treatment response across multiple clinical measures in female adolescents with NSSI. These findings support the use of neurophysiological biomarkers to enhance personalized therapeutic strategies and improve treatment outcomes in this population.

ABSTRACTS

Topic: Neurogenetics

EPNS25_448 - Serum Neurofilament Light Chain Levels in Rett Syndrome

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Objectives

Rett syndrome is a rare neurodevelopmental disorder primarily affecting females and caused by pathogenic variants in the MECP2 gene. Despite progressive loss of skills, particularly in language and hand function, neuropathological studies suggest an absence of neurodegeneration. To investigate this further, we analyzed serum neurofilament light chain (sNfL) levels, a sensitive marker of neuronal injury, across various age groups in a cohort of individuals with Rett syndrome.

Methods

This cross-sectional study included females with Rett syndrome and confirmed pathogenic MECP2 variants. Serum sNfL levels were measured using a single-molecule array (Simoa) assay and converted to age-adjusted z-scores. These scores were analyzed in relation to MECP2 variant types and clinical characteristics, including motor and hand function.

Results

The study cohort consisted of 77 patients with a mean age of 14 years. The median sNfL level was 6.8 pg/mL. Compared to age-matched healthy females, sNfL z-scores were significantly elevated in the Rett cohort (median z-score 0.92, IQR -0.5 to 1.7; $p<0.001$). Elevated sNfL levels were primarily observed in patients with pathogenic variants affecting the NCoR interaction domain ($p<0.001$). In contrast, patients with C-terminal deletions or missense mutations outside this domain did not show significantly elevated sNfL levels. Functional impairments were also associated with higher sNfL z-scores: patients unable to walk independently and those without residual hand function significantly had higher levels compared to those with retained motor abilities ($p=0.03$ and $p=0.04$, respectively). No correlation was found between sNfL z-scores and patient age.

Conclusions

Our findings demonstrate elevated sNfL levels in individuals with Rett syndrome, independent of age, suggesting ongoing neuronal damage. Notably, this elevation was primarily observed in patients with severe MECP2 variants affecting the NCoR interaction domain. These results imply a potential neurodegenerative component in certain Rett syndrome cases. sNfL could emerge as a valuable biomarker for assessing disease progression and evaluating therapeutic interventions in this population.

ABSTRACTS

Topic: Neuromuscular Disorders

EPNS25_449 - Development and validation of the Myotonia Symptom Checker

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Objectives

The non-dystrophic myotonias (NDM) are rare muscle disorders (reported prevalence, 0.75−1.7 per 100,000 population). Public awareness of NDM (including potential treatment options) can be low. Even in affected families, patients may endure symptoms without seeking help. Where there is no family history, non-specialist clinicians may not consider NDM in diagnostic examination. Suboptimal NDM awareness/management mean that it may take years to obtain a diagnosis and appropriate treatment. With rare or ultra-rare disorders including NDM, which have nonspecific, overlapping or unusual symptoms, finding useful information online, communicating effectively with clinicians and achieving prompt, accurate diagnosis can be challenging for families. We sought to understand how people seek information on NDM and its key symptom, myotonia. We also sought to develop a new tool, to raise myotonia awareness among the general public and non-specialist clinicians.

Methods

In 2022, neuromuscular specialists and NDM advocates discussed barriers to diagnosis/accessing care. Next, NDM-related internet search behaviours in patients/caregivers (N=5) and NDM-naïve subjects (N=3) were investigated. An online NDM screening tool (unMASC NDM Myotonia Symptom Checker) with 9 core questions was conceptualised in English, French and Spanish. In 2023, format, usability and perceived value of the Checker were established in a prospective, real-world, international validation using SurveyMonkey®. Data (presented as n[%]) were reviewed by specialists and advocates, and the Checker was revised.

Results

The Checker is a rules-based online form, targeted at family members of those with NDM or symptomatic people with no knowledge of myotonia. Validation (N=32) confirmed the Checker was easy to use (93%), quick to complete (90%) and easy to understand (85%): 75% said that symptoms and personal experiences were adequately covered. Most respondents had not used a symptom checker before but were willing to share downloadable results with clinicians. The revised Checker (expanded to 12 core questions) was launched in 2024.

Conclusions

unMASC NDM Myotonia Symptom Checker is a simple, novel, online tool that helps people to characterise symptoms suggestive of myotonia and encourage them to seek medical advice; its results can guide clinicians toward appropriate specialist referral. Principles used to develop the Checker may be of interest to those seeking to create screening tools for other rare/ultra-rare disorders.

ABSTRACTS

Topic: Infectious and Inflammatory Diseases/ Neuroimmunology

EPNS25_451 - Dynamics of MOG-specific B cells in children with MOGAD

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Objectives

MOG antibodies are an important biomarker for diagnosing patients with MOG antibody associated diseases (MOGAD). In around 40% of children a conversion to MOG antibody seronegativity is observed. Our aim was to investigate MOG-reactive B cells in patients with persistent serum MOG antibodies, compare them with patients who have lost MOG IgG in their serum, and analyze the correlation between MOG-reactive B cells in peripheral blood, serum MOG antibodies, and clinical outcomes in children**.**

Methods

In this retrospective study, we differentiated blood-derived B cells in vitro into antibody-secreting cells via engagement of toll-like receptors (TLR) 7/8 and assessed autoantibodies produced from those cells. We compared 16 children (mean age 11 ± 5 years) with persistent serum MOG Abs and 7 children (mean age 12 ± 5 years) who lost their specific Abs over time. In our longitudinal study, we have followed up serum reactivity for up to 7 years. MOG Abs in serum and cell culture supernatants were measured with a live cell based assay. For three group comparison a Fisher´s exact test was performed.

Results

MOG-specific B cells in peripheral blood did not show a correlation with serum MOG antibody levels. Paediatric patients who were positive for serum MOG antibodies had a significantly higher number of MOG-specific B cells in their blood compared to those who had seroreverted. MOG-specific B cells were found in 69% (11 of 16) of children with MOG antibodies in their serum, while only 14% (1 of 7) of seroreverted children had detectable MOG-specific B cells.

Conclusions

Overall, assessing the role of MOG antibodies and autoreactive B cells provides novel insights into the disease pathogenesis, important for treatment decisions.

ABSTRACTS

Topic: Neurogenetics

EPNS25_454 - MED13L-related intellectual disability: A Single Center Case Series

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Objectives

MED13L encodes a component of the Mediator complex, which regulates transcription via interactions between upstream transcriptional factors and the basal RNA polymerase II initiation machinery, and, as such, plays a role in the control of cell growth, repression of cell cycle target genes, and cell cycle inhibition. MED13L genetic variants cause impaired intellectual development and distinctive facial features with or without cardiac defects.

Methods

Herein, three children with different variants in the MED13L gene, one of which is a novel variant, are presented.

Results

The ages of our patients were 6,7 and 13 years, two of them were boys. All MED13L variants are de novo and are listed as **:** c.5920C>T (p.R1974*) (Heterozygous) (Pathogenic) (Missense variant), c.4532-1G>A (Heterozygous) (Novel variant) (Likely pathogenic) (Splice site variant), c.5588+1G>T (IVS24+1G>T) (Splice site variant). All patients had neurodevelopmental impairment, dysmorphic findings, and epilepsy. Cardiac abnormality was not found in any of the patients. The patient with the novel mutation had mild frontal atrophy and insignificant T2 hyperintensity in the frontoparietal white matter on cranial MRI, while the other patients had normal MRI. One patient with epilepsy has no seizures with a single medication, while two patients are being followed up with drug-resistant epilepsy. The patient with novel mutation had syndactyly between the second and third toes on both feet.

Conclusions

We describe a a novel variant in MED13L gene which broaden the genetic spectrum. Additionally, three cases with MED13L syndrome were discussed in detail to draw attention to this syndrome.

ABSTRACTS

Topic: Neuromuscular Disorders

EPNS25_455 - Prenatal and postnatal diagnostics of spinal muscular atrophy: a case report and overview of therapeutic possibilities.

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Objectives This case report indicates the impact of early prenatal diagnosis on the management of spinal muscular atrophy (SMA), evaluates the effectiveness of early gene therapy with onasemnogene abeparvovec in improving clinical outcomes for SMA patients and the role of the Newborn Screening Program in enabling early diagnosis and treatment of SMA.

Methods A 41-year-old woman with a family history of spinal muscular atrophy (SMA) presented for prenatal diagnostics after the death of her previous child from SMA. Amniocentesis at 17 weeks revealed potential SMA in the fetus. At birth, the newborn was assessed with an Apgar score of 10 and a CHOP INTEND score of 47. Genetic testing confirmed a deletion in the SMN1 gene and two copies of the SMN2 gene.

Results He was later diagnosed with SMA and urgently started on gene therapy with onasemnogene abeparvovec at 9 days of life. Post-therapy, the child showed mild elevations in troponin and liver enzymes, but no abnormalities were found in cardiac or abdominal exams. At two months, the CHOP-INTEND score improved to 53, indicating a positive response to treatment. The child demonstrated normal muscle strength and tone and met motor milestones, including head control. Early intervention resulted in a promising prognosis and development.

Conclusions Gene therapy offers a promising treatment for genetic diseases, especially when initiated before symptoms appear. The inclusion of spinal muscular atrophy (SMA) in Poland's Newborn Screening Program enables early diagnosis and timely treatment, often before symptom onset. This case highlights the importance of early prenatal diagnosis and personalized treatment planning, allowing for the early initiation of gene therapy and improved prognosis. Although prenatal screening for SMA is not widely recommended, it could benefit high-risk groups, such as carriers or those with a family history of SMA. The multidisciplinary approach in this case contributed to a successful outcome, offering the child a high chance of normal psychomotor development and improved quality of life.

ABSTRACTS

Topic: Neuromuscular Disorders

EPNS25_456 - Efficacy of Nusinersen Treatment in Type 1, 2, and 3 Spinal Muscular Atrophy: Real-World Data from a Single-Center Study.

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Objectives Spinal muscular atrophy (SMA) is an inherited neuromuscular disease characterized by progressive muscle weakness and atrophy due to the absence of the survival motor neuron 1 (*SMN1*) gene. SMA is classified into types 0 through 4 based on the age of symptom onset and the severity of motor function decline. Recent advances in SMA treatment, including nusinersen, onasemnogene abeparvovec, and risdiplam, have significantly improved the prognosis of SMA patients. This study evaluated the safety and efficacy of nusinersen in pediatric patients with SMA types 1, 2, and 3 in a real-world clinical setting.

Methods This prospective observational single-center study assessed the treatment effects of nusinersen in 23 pediatric patients with genetically confirmed SMA over a 22-month observation period. All the participants received intrathecal loading doses of 12 mg of nusinersen on days 1, 14, 28, and 63, followed by maintenance doses every four months. Functional assessments were conducted using the CHOP-INTEND scale. Data were collected during routine patient visits, including clinical laboratory tests and vital sign parameters, and adverse events were recorded. The inclusion criteria were defined by the national reimbursement program for nusinersen treatment in Poland.

Results Initially, 37 patients ranging from 1 month old to 18 years old were included, but 23 were ultimately observed due to changes in treatment regimens or assessment scales. The patients showed significantly improved CHOP-INTEND scores over the 22-month period. At 6 months, the average increase was 4.2 points, continuing to 17.8 points at 22 months. By the end of the study, 100% of patients showed either stabilization or improvement, with significant clinical improvements observed in several patients. Nusinersen was generally well-tolerated, with post-lumbar puncture headache and lower back pain being the most common adverse events.

Conclusions Nusinersen treatment significantly enhances motor function in pediatric patients with SMA types 1, 2, and 3. This study demonstrates the importance of early and sustained treatment, with most patients showing the continuous improvement or stabilization of motor function. These findings support the use of nusinersen as an effective therapy for SMA; however, further research is needed to understand the long-term outcomes and optimize treatment strategies.

ABSTRACTS

Topic: Neurodevelopmental Disorders / Developmental Neuroscience

EPNS25_460 - NTNG2-associated Developmental Dyskinetic Disorder with Further Clinical and Genetic Delineation

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Objectives

NTNG2 encodes Netrin-G2, a key protein in neuronal circuit development, synaptic organization, and diversification. Bi-allelic variants in *NTNG2* are associated with a neurodevelopmental disorder characterized by severely impaired intellectual and motor development, hypotonia (often with inability to walk), and significant behavioral abnormalities, including features of autism spectrum disorder reminiscent of Rett syndrome. However, the full phenotypic spectrum, including movement disorders and milder ambulatory individuals, has not yet been fully described. We aim to further characterize the clinical and genetic spectrum of *NTNG2*-associated neurodevelopmental disorder.

Methods

We retrospectively collected clinical information and molecular genetic data from 13 unpublished individuals with bi-allelic variants in *NTNG2* from 10 unrelated families at multiple institutions worldwide. Clinical exome or whole exome sequencing was performed to detect variants. All variants were segregated in the affected families.

Results

Ultra-rare, bi-allelic, previously unreported variants in *NTNG2* were identified in 13 individuals (6 females, mean age 6.7±3.4 years), frequently homozygous (11/13, 85%). Motor delay, severe to profound cognitive impairment, autistic behaviors, stereotypies (e.g., hand clapping, bruxism), and a non-progressive course were present in all. Neurological findings included axial hypotonia (13/13, 100%), diminished deep tendon reflexes (6/13, 46%), progressive microcephaly (3/13, 23%), and spasticity/contractures (2/13, 15%). Hyperkinetic movement disorder was characterized by generalized and focal dystonia (5/13, 38%) and dyskinesia (7/13, 54%) with episodes of intense choreiform movements. The mild to moderate phenotype with ambulatory function, social smiling, and intense eye contact was observed in two (2/13, 15%), whereas the severe to profound phenotype (non-ambulatory) was present in eleven (11/13, 85%) individuals. Epilepsy was uncommon, with only two individuals (2/13, 15%) exhibiting temporal epileptiform discharges on EEGs. Cranial MRI demonstrated cerebral atrophy and posterior periventricular white matter signal changes. With only

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one recurrent variant, three variants (3/11, 27%) were likely pathogenic and eight (8/11, 73%) were of unknown significance.

Conclusions

The presence of hand clapping stereotypies, autistic features, severe developmental delay, and areflexia contributes to the identification of bi-allelic *NTNG2* deficiency as a Rett-like syndrome. Dyskinesia with chorea and dystonia are more prominent than in Rett syndrome. The full spectrum of the disease may include ambulatory individuals. The features of the neurodevelopmental disorder and the hyperkinetic movement disorder overlap, suggesting that *NTNG2*-associated disease is also a developmental and dyskinetic encephalopathy.

ABSTRACTS

Topic: Neuromuscular Disorders

EPNS25_463 - Dystrophin and Neurodevelopment: Exploring the Link Between Duchenne Muscular Dystrophy and Autism Spectrum Disorder

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Objectives

Duchenne muscular dystrophy (DMD) is a severe X-linked disorder characterized by progressive muscle degeneration. Beyond motor impairments, DMD is associated with neuropsychiatric comorbidities, including autism spectrum disorder (ASD). This study explores the hypothesis that the association between DMD and ASD is not incidental but may be driven by specific dystrophin isoform deficiencies affecting brain function.

Methods

We retrospectively analyzed 74 patients with DMD or Becker muscular dystrophy (BMD) from a tertiary pediatric neurology clinic. Clinical and genetic data were reviewed, focusing on five patients with a confirmed ASD diagnosis using standardized tools. Genetic analysis assessed dystrophin isoforms affected in each case (Dp427, Dp140, Dp71). Findings were compared with existing literature and ASD prevalence in the general population (1–2%).

Results

The prevalence of ASD in the cohort was 6.75%, significantly higher than the general population prevalence (1–2%). In four of the five cases with ASD, Dp140 isoform deficiency was identified, supporting a potential role of this isoform in neurodevelopmental impairments. No consistent associations were observed with Dp427 or Dp71. Neurobiological hypotheses suggest that dystrophin deficiency contributes to excitatory/inhibitory imbalances in the brain, particularly affecting glutamatergic and GABAergic pathways.

Conclusions

This study supports the hypothesis that the association between DMD and ASD is mediated by dystrophin isoform deficiencies, particularly Dp140, rather than being coincidental. Future research should aim to elucidate these mechanisms and develop targeted interventions to improve outcomes.

ABSTRACTS

Topic: Epilepsy: Medical and Surgical treatment

EPNS25_464 - Ketogenic diet and mTOR inhibitors combined therapy in patients with tuberous sclerosis complex

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Objectives

In patients with tuberous sclerosis complex (TSC), the ketogenic diet (KD) is one of recommended options for treatment of drug-resistant epilepsy, while mTOR inhibitors (mTOR-I) are also used to inhibit tumour growth. There is some evidence that KD may act synergistically with mTOR-I by influencing the mTOR pathway through carbohydrate restriction. In some cases, a combination of these therapies is needed. However, little is known about the possible benefits and risks of combination therapy with KD and mTOR-I in children with TSC. The aim of this study was to determine the treatment efficacy, safety and adverse events profile in patients with TSC-associated epilepsy treated with a ketogenic diet and mTOR-I compared to patients treated with KD alone.

Methods

We retrospectively analyzed the impact on seizures and tumours associated with TSC in children who were treated with the KD without or together with an mTOR-I between 2016 and 2025.

Results

Thirty-three patients with TSC received KD. Sixteen of them (48.5%) were treated with KD and concomitant mTOR inhibitor. The median duration of combined KD and mTOR-I therapy was 19.3 months (range 0.2-92.9 months). Seven patients (43.8%) continued on KD and three of these (42.9%) continued on combination therapy, while three patients (17.6%) withdrew KD and continued on mTOR-I therapy alone. The most common adverse events reported by patients during combined treatment were lipid profile abnormalities in eight patients (50%), gastrointestinal problems in two patients (12.5%), and two patients (14.3%) had no adverse events. Adverse events in patients treated with KD alone were gastrointestinal problems in seven patients (41.18%), weight loss in two patients (11.76%), nephrolithiasis in one patient (5.88%) and six patients (35.29%) had no adverse events. There was an improvement in seizure control or complete resolution of seizures in eleven patients (68.8%) receiving mTOR-I and KD compared with ten patients (62.5%) on KD alone. No new tumour growth was reported on combination therapy.

Conclusions

Combination therapy with KD and mTOR-I was well tolerated and effective in the treatment of TSC manifestations. The side effect profile of combination therapy was different from that of the KD alone.

ABSTRACTS

Topic: Neurorehabiltation

EPNS25_465 - Impact of Early Neurorehabilitation Interventions on Paediatric Stroke Recovery: A systematic review and meta analysis

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Objectives

This systematic review and meta-analysis aimed to evaluate the effectiveness and safety of early neurorehabilitation interventions in improving motor, cognitive, and language outcomes in pediatric stroke patients. Secondary objectives included assessing the impact of intervention timing, safety profiles, and broader benefits such as quality of life improvements.

Methods

A comprehensive search of PubMed, Embase, Cochrane Library, Scopus, and Web of Science was conducted to identify studies evaluating early neurorehabilitation interventions in children aged 0–18 years with ischemic or hemorrhagic stroke. Inclusion criteria encompassed randomized controlled trials, cohort studies, and case-control studies reporting outcomes such as motor function, cognitive recovery, and language development. Risk of bias was assessed using validated tools, and data were synthesized through narrative review and random-effects meta-analysis.

Results

Twelve studies comprising 435 participants were included. Early neurorehabilitation significantly improved motor function (HR: 0.9; 95% CI: 0.8–1.0), cognitive outcomes (HR: 0.9; 95% CI: 0.8–1.2), and language recovery (HR: 1.2; 95% CI: 0.9–1.32). Heterogeneity across studies was low to moderate (I^2 = 4.36–11.32%). Secondary outcomes indicated that early interventions were safe, with minimal adverse events, and provided additional benefits such as enhanced quality of life and caregiver-child interactions. Timing was critical, with interventions initiated within three weeks post-stroke yielding the greatest benefits compared to delayed rehabilitation.

Conclusions

Early neurorehabilitation interventions significantly enhance recovery outcomes in pediatric stroke patients, particularly when initiated promptly. These findings underscore the need for timely, targeted, and multidisciplinary approaches to maximize recovery potential and improve quality of life. Future research should explore long-term outcomes and optimize intervention protocols to further refine clinical practices.

ABSTRACTS

Topic: Epilepsy: Medical and Surgical treatment

EPNS25_467 - Onset and Duration of Adverse Events in Patients Treated With Fenfluramine in the Lennox-Gastaut Syndrome Clinical Trials

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Objectives: This post-hoc analysis describes the time of onset and duration of treatment-emergent adverse events (TEAEs) reported in the fenfluramine (FFA) randomized controlled trial (RCT, NCT03355209) and open-label extension (OLE, NCT03355209) study in patients with Lennox-Gastaut syndrome (LGS).

Methods: In the RCT, patients were randomized to FFA 0.2 mg/kg/day or FFA 0.7 mg/kg/day (maximum 26 mg/day) or placebo. After 14 weeks of titration and maintenance in the RCT, patients could enroll in the OLE. FFA was started at FFA 0.2 mg/kg/day for 1 month, then was flexibly titrated to effect and tolerability during Month 2–Month 6. Incidence of TEAEs occurring in ≥10% of patients by week of first onset, median time to onset of TEAEs and percent of patients experiencing resolution of TEAEs in the RCT and OLE are reported; duration of TEAEs in the RCT will be described. Time to onset is measured from FFA initiation in either study. Descriptive statistics were used.

Results: TEAEs occurring in ≥10% of patients in the RCT were diarrhea, vomiting, fatigue, pyrexia, decreased appetite and somnolence. Of the RCT FFA treatment groups (FFA 0.2 mg/kg/day [n=89], FFA 0.7 mg/kg/day [n=87], placebo [n=87]), earliest median time to onset of first occurrence of these TEAEs was reported in patients on FFA 0.7 mg/kg/day who experienced somnolence (n=15; median 6 days; range 1-95). Resolution of first occurrence of these TEAEs occurred in 45.2%-100% of FFA treatment patients; first occurrence of pyrexia (n=9) and vomiting (n=12) resolved in all patients treated with FFA 0.2 mg/kg/day.

In the OLE (N=247), of TEAEs occurring in ≥10% of patients (decreased appetite, fatigue, nasopharyngitis, seizure), decreased appetite exhibited the earliest median time to onset (n=40; median 51.5 days; range 1-397) and 72.5%-100% of patients experienced resolution of the TEAEs reported by ≥10% of patients.

Conclusions: These results provide insight on time of onset and duration of TEAEs associated with FFA in the LGS clinical trials. Incidence of first onset of TEAEs was most common during the RCT titration phase and flexible dose phase in the OLE. These data further highlight that long-term FFA is generally well tolerated, which may contribute to health-related quality of life outcomes in patients with LGS.

ABSTRACTS

Topic: Headache / Migraine

EPNS25_468 - High Prevalence of OCD, ADHD, and Autism in Children and Adolescents with Headache

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Objectives

To assess the prevalence and symptom severity of Obsessive-Compulsive Disorder (OCD), Attention-Deficit Hyperactivity Disorder (ADHD), and Autism Spectrum Disorder (ASD) in children and adolescents attending a headache clinic compared to healthy controls.

Methods

This cross-sectional, case-control study recruited patients with headache were recruited from the Headache Outpatient Clinic, Department of Pediatrics and Adolescents, Copenhagen University Hospital - Herlev and Gentofte, Denmark (October 2018 to April 2021). Patients were classified according to the International Classification of Headache Disorders-III criteria. Healthy controls were recruited from schools (November 2022 - January 2024) and divided into those with and without headache. Symptoms of OCD were assessed using the Obsessive-Compulsive Inventory Revised, ADHD using the Attention-Deficit Hyperactivity Disorder Rating Scale Extended, and ASD using the Social Responsiveness Scale 2. Prevalence was defined by participants either having a prior diagnosis or exceeding the cut-off value on the respective questionnaires.

Results

343 patients (86 with migraine, 101 with TTH, 81 with both migraine and TTH, one with cluster headache, 21 with secondary headache, and 53 with unclassified headache) and 130 controls were included. Among controls, 72 had headaches and 58 did not, comprising the control group with and without headache. Patients with migraine had more severe OCD symptoms (8.1 [2.0-9.0], p=0.015) and ADHD symptoms (12.9 [5.0-17.0], p=0.020) than controls without headache (4.1 [1.0-6.0] and 10.0 [4.0-16.0], respectively). Patients with TTH had more severe ASD symptoms (49.2 ± 5.9, p=0.028) than controls without headache (45.9 ± 5.0). Controls with headache had more severe symptoms of OCD (10.7 [2.0-16.0], p<0.001), ADHD (13.4 [5.0-18.0], p=0.010), and ASD (48.3 ± 6.1, p=0.035) compared to controls without headache. A strong association was found between headache frequency and all comorbidities in the control group. The prevalence of OCD was 20.8% in all cases, 27.8% in controls with headache, and 1.7% in controls without headache. ADHD prevalence was 17.3% in all cases, 18.8% in controls with headache, and 7.0% in controls without. ASD prevalence was 10.1% in all cases, 4.4% in controls with, and 1.8% in controls without headache.

Conclusions

Both patients and controls with headache exhibited severe symptoms and a high prevalence of psychiatric comorbidity compared to the general population. In the controls, symptoms increased with headache frequency. Headache and psychiatric comorbidities were associated regardless of whether the child sought medical attention. Healthcare professionals should implement a screening for OCD, ADHD, and ASD in the management of headache in childhood.

ABSTRACTS

Topic: Neurometabolic Disorders

EPNS25_469 - Effects of atidarsagene autotemcel gene therapy on peripheral nerves in late-infantile metachromatic leukodystrophy

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Objectives

This study evaluated the efficacy of ex vivo autologous hematopoietic stem cell gene therapy (atidarsagene autotemcel, "arsa-cel") in reducing the severity and progression of peripheral neuropathy, assessed by nerve conduction velocity (NCV), in individuals with late-infantile metachromatic leukodystrophy (LI-MLD).

Methods

A post-hoc analysis was conducted on pre-symptomatic LI-MLD patients treated with arsa-cel as part of prospective, open-label, single-arm interventional trials or expanded access programs. Longitudinal nerve conduction studies (NCSs) assessed motor (ulnar [UN], deep peroneal [DPN]) and sensory (median [MN], sural [SN]) nerves. Results were compared to those from untreated control patients (NHx) evaluated using the same standardized protocol. The study analyzed the impact of baseline characteristics (age at treatment, pre-treatment NCV Z-scores) and post-treatment arylsulfatase A (ARSA) enzyme activity in myeloid CD15+ cells on treated patients' NCVs. The primary endpoint was NCV, reflecting the severity of demyelinating neuropathy. Dermal nerve histopathology in skin biopsies served as an exploratory outcome.

Results

The analysis included 15 treated and 16 NHx patients, with a median treatment age of 13 months (IQR 9.1–14.5). At 36 months of age, treated patients demonstrated higher estimated NCVs across all nerves compared to age-matched NHx patients (~15 m/s difference in motor nerves). Peripheral neuropathy was evident in most treated patients prior to therapy (ages 7.3–17.4 months). However, pre-treatment neuropathy severity did not affect NCV outcomes at two years post-treatment or the rate of subsequent NCV slowing. Younger treatment age was associated with higher NCVs in the motor UN and sensory MN nerves at two years post-treatment. Elevated ARSA activity in CD15+ cells was associated with higher NCVs in motor DPN at two years post-treatment and slower NCV decline in the DPN, UN, and MN nerves.

Conclusions

Peripheral neuropathy assessed by NCV is significantly ameliorated in pre-symptomatic LI-MLD patients treated with arsa-cel compared to untreated patients of similar age. Earlier intervention and higher ARSA levels were associated with better preservation of peripheral nerve function. These findings suggest arsa-cel may exert a stronger effect on NCV than allogeneic hematopoietic stem cell transplantation, likely due to enhanced ARSA expression.

ABSTRACTS

Topic: Neurometabolic Disorders

EPNS25_471 - Tyrosine supplementation as a therapeutic strategy for TyrRS/YARS1 deficiency

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Objectives

Autosomal-recessive aminoacyl-tRNA synthetase (ARS) type 1 deficiencies cause an impaired charging of tRNA with their respective amino acids in the cytosol. ARS enzymes are named according to the amino acids they attach; for example, tyrosyl-tRNA synthetase (TyrRS, encoded by *YARS1*) couples tyrosine to its tRNA. Clinically, TyrRS/*YARS1* deficiency is characterized by impaired neurological development and growth. Additional typical features include liver failure, pancreatic insufficiency, and anemia. Case reports have described that supplementation of the respective amino acids can improve growth and neurological development in isoleucyl-, leucyl-, seryl-, phenylalanyl-, and methionyl-tRNA synthetase deficiencies. Whether L-tyrosine supplementation could improve outcome in TyrRS/YARS1 deficiency has not yet been explored.

Methods

Five children homozygous for p.(Arg367Trp), and two children with [p.(Ile59Thr), p.(Asp61Asn)] & [p.(Gly542Val), p.(Arg367Trp)] received L-tyrosine with or without high-protein diet for 1–2 years as a compassionate approach to improve outcome. To test the effect of low or high tyrosine concentrations on TyrRS enzyme activity, we measured aminoacylation activity at 100, 250 and 500 µM L-tyrosine in fibroblasts of patients.

Results

Children with dystrophy significantly gained weight since onset of treatment. According to teachers, occupational, and physical therapists, speech, attention, and fine motor skills improved in all children homozygous for p.(Arg367Trp) (aged 2, 9, 10, 12, and 18 years). Those two children with compound-heterozygous variants showed comparatively less developmental progress. In vitro, the TyrRS activity in fibroblasts from three p.(Arg367Trp) children was significantly reduced under physiological blood concentrations of L-Tyrosine (100 µM: 0-9%). Under supra-physiological tyrosine concentration (500 µM), TyrRS activity of p.(Arg367Trp) significantly increased, even surpassing the activity of the control measured at physiological concentrations of L-tyrosine. In contrast, the TyrRS activity of the [p.(Ile59Thr), p.(Asp61Asn)] individual was reduced to 49% only, and did not increase at higher concentrations of L-tyrosine, in line with the reduced treatment response.

Conclusions

Supplementation with L-tyrosine, an inexpensive and safe compound, may improve growth and neurological development in patients with TyrRS deficiency. Further clinical studies are needed to confirm the benefits of this approach.

ABSTRACTS

Topic: Miscellaneous

EPNS25_472 - Demographic and Temporal Analysis of Child Neurology Residency Programs in Brazil

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Objectives: Since the establishment of the first child neurology residency program in 1972, the number of such programs in Brazil has grown steadily. This study aims to analyze the demographic distribution of child neurology residency programs and practicing child neurologists in Brazil, as well as their evolution over the past five decades.

Methods: Data were collected from official online sources, including the Federal Council of Medicine (Conselho Federal de Medicina, CFM), the Brazilian Institute of Geography and Statistics (Instituto Brasileiro de Geografia e Estatística, IBGE), and the Ministry of Education (Ministério da Educação, MEC). Categorical variables were analyzed using proportions and percentages.

Results: The number of child neurology residency programs increased from three in the 1980s to seven in 2000, 19 in 2010, and 27 in 2022. Of these, 78% are concentrated in the Southeast and South regions, while the first program in the North was established in 2020. Currently, approximately 80 child neurologists graduate annually from the 27 active residency programs. Nationwide, there are 1,401 registered child neurologists, with 48% based in the Southeast region and 72% holding pediatrics as their primary medical specialty. The national density of child neurologists is 0.68 per 100,000 population, with higher rates in the Southeast (0.82), South (0.91), and Federal District (2.2). In contrast, the North and Northeast regions have lower densities, averaging 0.50 and 0.47, respectively.

Conclusions: The number of child neurology residency programs in Brazil has significantly increased over the last five decades, extending to remote and economically disadvantaged regions. However, the distribution of training centers and practicing child neurologists remains predominantly concentrated in economically developed areas. The average density of child neurologists in Brazil aligns with rates observed in other developing countries.

ABSTRACTS

Topic: Neurogenetics

EPNS25_473 - A Retrosepctive review of a series of patients with Spino-cerebellar Ataxia 7 at a quartenary care hospital in South Africa

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Objectives: To describe the clinical profile of a series of patients with genetically confirmed Spino-cerebellar Ataxia 7 at a quaternary care hospital in South Africa

Methods: Retrospective/ Descriptive

Results: We identified five children (4 males, 1 female) with a confirmed diagnosis of SCA7. The children ranged between 19 months and 12 years of age at the time of presentation. All patients were of African indigenous ancestry. All patients presented with developmental delay. Two patients had visual symptoms at presentation. Two patients had a confirmed (genetic) family history of SCA7. Two patients had co-morbid HIV-1 infection and one patient had ocular myasthenia gravis. All patients had cerebellar and corticospinal signs at presentation. Four patients had evidence of pigmentary retinopathy on fundoscopy. Of the 4 patients who had MRI scans of the brain and spine- 4 had cerebellar atrophy, 2 had cortical atrophy and 3 had spinal cord atrophy. All our patients presented at an advanced stage of the disease with severe disability. Two patients demised and 1 did not return for follow-up.

Conclusions: Clinicians should have a high index of suspicion for SCA7 in children presenting with visual symptoms and developmental delay combined with cerebellar and corticospinal signs. Co-morbid HIV-1 infection may affect the presentation and clinical course. Clinical suspicion is essential in resource-limited settings where genetic testing may be unavailable. These patients should be referred for prompt genetic testing if available so they can be appropriately counselled and managed.

ABSTRACTS

Topic: Movement Disorders/ Cerebral Palsy

EPNS25_474 - Modelling Spinocerebellar Ataxia Type 29 (SCA29) in Human Induced Pluripotent Stem Cell (hiPSC)-Derived Cerebellar Organoids: From Clinical Cohorts to Disease Models

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Objectives. Spinocerebellar ataxia type 29 (SCA29), Gillespie syndrome (GLSP), and severe pontine / cerebellar hypoplasia (PCH) are early-onset ataxia disorders caused by pathogenic variants in the *ITPR1* gene. *ITPR1* encodes the type 1 inositol 1,4,5-triphosphate (IP3) receptor (IP3R1), a calcium channel predominantly expressed in cerebellar Purkinje cells. Based on the largest, multinational cohort of patients with *ITPR1* missense variants, pathogenic variants cluster in three functional regions of the IP3R1 protein with both dominant negative (DN; ~90% of known variants) and gain-of-function (GOF; ~10% of known variants) mechanisms, but the pathophysiological impact of these mutations is poorly understood. Furthermore, disease models that accurately recapitulate SCA29 disease mechanisms are urgently needed to enable therapeutic testing. Our objective was to model the DN and GOF mechanisms of SCA29 in human induced pluripotent stem cell (hiPSC)-derived cerebellar organoids to study SCA29 pathogenesis downstream of dysregulated calcium signaling.

Methods. Isogenic hiPSC lines with DN and GOF variants in the ITPR1 gene were generated from a control (healthy) hiPSC line through CRISPR/Cas9-mediated genome editing. Cerebellar organoids were produced using established protocols and characterized by calcium imaging at day 63 and bulk RNA sequencing (RNAseq) at day 90.

Results. Cerebellar organoids from all hiPSC lines demonstrated similar growth rates and comparable expression levels of quality control marker genes across the differentiation protocol. At day 63, IP3 stimulation of cerebellar organoid-derived 2D neuronal cultures generated reduced calcium signals in the DN neurons while the calcium signals were increased in the GOF neurons. RNAseq at day 90 revealed ~1000 differentially expressed genes, most of which were downregulated in the ITPR1 mutant organoids. Upregulated genes that were enriched in the mutant organoids were involved in postsynaptic specialization and signaling pathways.

Conclusions. Detailed characterization of the spectrum of genotype-phenotype variation in rare diseases is crucial to ensure that new disease models accurately replicate the full range of disease mechanisms at play. Here, calcium imaging and RNAseq in hiPSC-derived cerebellar organoids reveal new insights into the disease mechanisms of SCA29, providing a reproducible system for testing potential treatment modalities.

ABSTRACTS

Topic: Neuromuscular Disorders

EPNS25_477 - Real-World Experience With Gene Therapy for Duchenne Muscular Dystrophy: Experince from Qatar

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Objectives
To describe Qatar experience with delandistrogene moxeparvovec in 8 DMD patients.

Methods
A retrospective chart-review of genetically confirmed children with DMD who received GT. treatment Protocol: 8 patients received delandistrogene moxeparvovec gene therapy following a well-defined protocol designed to maximize efficacy and minimize adverse effects. Patients were closely monitored for side effects and clinical improvement. Laboratory results, including serum CK, ALT, AST, and Troponin I levels, were recorded pre- and post-infusion. Biomarker levels were monitored weekly for the first 12 weeks.

Results

We observed distinct patterns in the response of AST, ALT, CK, Troponin I and GGT and other parameters. The distinct biomarker trends observed between age groups emphasize the importance of age-specific management strategies in gene therapy for DMD:

Younger Patients: The stable biomarker responses in younger patients indicate that early gene therapy intervention, paired with supportive care, may be more effective in stabilizing muscle and cardiac health, potentially slowing disease progression with minimal adverse effects.

Older Patients: The variability in biomarker trends in older patients highlights the need for individualized follow-up, with more frequent monitoring of muscle, cardiac, and hepatic markers. Tailoring supportive therapies, such as adjusting corticosteroid doses or infusion protocols, may further optimize outcomes and minimize side effects in this group.

Conclusions

We explored the physiological responses to gene therapy in a cohort of 8 DMD patient. This study demonstrated age-related differences in response to gene therapy in DMD, underscoring the need for tailored protocols based on patient age. Younger patients exhibited more stable biomarker trends, indicating that early intervention might be beneficial in slowing disease progression. Older patients showed greater variability, particularly in muscle and liver biomarkers, suggesting a need for more vigilant and individualized follow-up to optimize safety and therapeutic effectiveness. Our findings support the safety and efficacy of gene therapy in DMD when paired with a structured protocol involving antibody screening, corticosteroid use, physiotherapy, and regular cardiac and hepatic monitoring. Further studies with larger sample sizes and extended follow-up are recommended to validate these age-specific trends and refine protocols for broader application in DMD GT. This study has demonstrated age-related differences in response to gene therapy, underscoring the need for tailored protocols. Younger patients exhibited more stable biomarker trends, indicating that early intervention might be beneficial in slowing disease progression. Older patients might require closer liver function monitoring. Our findings support the safety and efficacy of gene therapy in DMD.

ABSTRACTS

Topic: Epilepsy: Diagnosis and Investigations

EPNS25_481 - Sleep Related Epilepsy in Children (Etiology, Semiology and EEG Characteristics)

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Objectives to study SRE, etiology, semiology, electroencephalogram (EEG) characters and to determine their outcome regarding seizure control on properly selected anti- seizure medication (ASMs).

Methods One hundred patients who fulfilled the inclusion criteria were enrolled in this study. All of them were submitted to history taking, full examination, seizure semiology analysis, inter-ictal EEG recordings and some of them underwent magnetic resonance- imaging (MRI).

Results Patients with self-limited epilepsy with centro-temporal spikes (SeLECTS) were the most common epilepsy syndrome (52%) followed by sleep related hyper motor seizures (SHE) (33%) then patients with self-limited epilepsy with autonomic symptoms (SeLEAS). Our results showed that 79% of the patients had sleep seizures while 21% had seizures during sleep and wakefulness, also oxcarbazepine (OXC) was the most used first ASM in 62% of our patients followed by levetiracetam (LEV) that was used in 28% of the patients. School performance was affected in 35% of our patients.

Conclusions SeLECTS or benign Rolandic epilepsy, SHE, and SeLEAS are three of the most frequently implicated epilepsy syndromes occurring during the sleep state. Oxcarbazepine was the most effective drug to control seizures. Poor school performance tends to be more notable with symptomatic etiology, occurrence of seizures during sleep and wakefulness, prolonged period of active seizures, poor response to ASMs and when EEG shows frontal spikes.

ABSTRACTS

Topic: Neurogenetics

EPNS25_482 - Assessment of Clinical and Genetic Characteristics of Channelopathies with novel mutations in a Tertiary Pediatric Neurology Clinic

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Objectives

To evaluate the clinical and genetic features of channelopathies in the Pediatric Neurology Department at Aydın Adnan Menderes University.

Methods

Patients genetically diagnosed with a channelopathy between 2019 and 2024 were included in the study. Data collected included age, gender, clinical phenotypes, inheritance patterns, the pathogenicity of the variants, and whether the variants had been previously reported.

Results

The study group consisted of 29 patients (17 males and 12 females). The median age was 4 years (IQR: 3.5), and the median age at the first clinical symptom(s) was 1 year (IQR: 2.75). Fourteen different variants were identified, including 5 novel variants found in 7 patients. The most frequently detected variants were in the *SCN1A*, *SCN2A*, and *ADGRV1* genes. The most common presentations were genetic epilepsy with febrile seizures plus (GEFS+) and self-limited infantile epilepsy.

Conclusions

The accumulated genetic and clinical data on channelopathies will enhance our understanding of their frequency and common presentations.

ABSTRACTS

Topic: Neurogenetics

EPNS25_483 - WDR37-Associated Neurooculocardiogenitourinary Syndrome (NOCGUS): A Case Report of Multisystem Involvement.

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Objectives

To describe a 16-year-old male with WDR37-associated neurooculocardiogenitourinary syndrome (NOCGUS), a recently described syndrome. The WDR37 pathogenic variants are associated with a multisystem phenotype, including neurodevelopmental, ophthalmological, cardiac, genitourinary, and musculoskeletal abnormalities.

Methods

We Describe the findings including cerebellar vermis hypoplasia, bilateral colobomatous microphthalmia, micropenis, left inguinal orchidopexy, Seizures, bilateral vesicoureteral reflux, solitary right kidney, bilateral hip dislocations, and faltering growth.

Results

Whole genome sequencing (WGS) identified a pathogenic variant in the WDR37 gene, confirming NOCGUS

Conclusions

This case highlights the critical role of WGS in diagnosing rare genetic syndromes, particularly in patients with complex multisystem involvement. WDR37-associated NOCGUS presents a distinct phenotype, including neurodevelopmental, ophthalmological, urogenital, and musculoskeletal abnormalities. This case adds to the limited literature on NOCGUS. Further research is needed to define the full spectrum of WDR37-related phenotypes.

ABSTRACTS

Topic: Miscellaneous

EPNS25_484 - Post-graduate training in pediatric neurology: don't forget outpatient care

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Objectives: Although the expansion of neurologic critical care and the emergence of novel innovative treatments have increased the complexity of inpatient cases and, a significant part of neurology practice takes place in outpatient services. The aim of this project was to explore the exposure of pediatric neurology residents to outpatient clinics and discuss their educational perspectives.

Methods: We distributed via email a 20-item anonymous survey to pediatric neurology residents in the United Kingdom during the period February 2023-February 2024. Open-ended questions were also included. Descriptive statistical methods were used to analyse the results.

Results: The survey was emailed to 50 residents and we received 35 complete responses (70% response rate) with 34.3% of the respondents having already completed ≥ 1 year of training in pediatric neurology. Most residents joined 1 or 2 neurology clinics per month (48.6% and 37.1%, respectively) and on a typical clinic day 57.1% would see 3 and 14.3% 4 patients. The majority of the respondents (94.2%) found general pediatric neurology clinics to be helpful in improving their clinical skills and 71.4% felt that clinics help them develop therapeutic relationships with patients/families. Nevertheless, 26.5% of participants expressed concerns about lack of protected time during clinics and 20% did not feel that they received adequate feedback from the supervising consultant regarding specific skills to work on these accordingly. Although the kind of patients seen in general neurology clinics were representative of patients seen in everyday practice, a significant number of responders (31.4%) felt that the number of follow-up patients they see in general neurology clinics is not adequate for their training purposes. The majority (51.5%) were doubtful about the contribution of virtual clinics to their professional development. In open-ended questions many respondents mentioned that neurological disorders encountered in the inpatient and outpatient settings are different from each other and highlighted that outpatient clinics incorporate elements both from ward-based activities and from ambulatory care.

Conclusions: Outpatient pediatric neurology clinics contribute to the professional development of residents and our study has identified them as a valuable educational resource. Protected time, appropriate ratio of new and follow-up patients and constructive feedback from consultants are areas needing improvement. Re-designing pediatric neurology residency programs across Europe and placing learning at the centre of everyday clinical practice are essential steps to maximise the educational potential of clinics.

ABSTRACTS

Topic: Neurogenetics

EPNS25_485 - Biallelic Variants in Alkaline Ceramidase 3 Cause Infantile and Early Childhood Onset Neurodegeneration with Progressive Leukodystrophy

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Objectives

The alkaline ceramidase 3 (*ACER3*) gene codes for a member of the ceramidases, *ACER3*, an enzyme, regulating the levels of bioactive lipids such as ceramides, sphingosine, and sphingosine 1-phosphate. Maintaining a balance between these bioactive lipids is essential for cellular viability. Biallelic variants in *ACER3* have previously been linked to early-onset progressive leukodystrophy/leukoencephalopathy in three case reports describing five families with seven patients. Our study delineates the clinical phenotype and molecular spectrum of *ACER3*-related disease by characterizing 64 patients from 59 independent families (57 patients are from 54 newly reported unrelated families).

Methods

Exome sequencing, data sharing, screening the genetic databases of several international genetic laboratories, and GeneMatcher were used to identify the patients here. ACER3 enzyme activity, lipidomics in patient fibroblasts, mutagenesis, functional assays, and protein modeling were performed.

Results

Premature death at the mean age of 5.8±4.2was observed in 30% of cases and the mean age of the alive patients is 6.6±4.9. The disease presents with predominantly infantile-onset (86%), moderate (52%) and rapidly (39%) progressive neurological deficit manifesting with global developmental delay (71%) or developmental regression (98%)/stagnation (83%) commonly resulting in limbs spasticity (93%), limb dystonia (72%) and axial hypotonia (73%), feeding difficulties (62%), and joint contractures (42%), scoliosis 17/48 (35%), and epileptic seizures 12/39 (31%). Dysmorphology assessment revealed a consistent facial gestalt, consisting of a long face with high anterior hairline, prominent but narrow forehead, full lower lip, and a broad or pointed chin. Neuroimaging analysis revealed invariable posterior gradient white matter signal changes and diffuse cerebral volume loss (73%). Using biochemical assays of wild-type ACER3 and clinically relevant mutants, we show that diverse patient-derived variants limit the activity of ACER3 to hydrolyse ceramide, implying the phenotype observed is due to ACER3 dysfunction. Biochemical analysis of mutants further reveals hot spots in the enzyme essential for function. Consistent with the identified alleles being pathogenic, in vitro ceramidase enzyme activity assays determined a dramatic decrease for each allele individually, while studies of patients derived fibroblasts determined that total alkaline ceramidase activity ranged from 2-40% normal. Further analysis of the patient fibroblasts by lipidomic analysis determined a 50% increase in the ACER3 substrate ceramide and its upstream metabolite sphingomyelin and a corresponding decrease in the ACER3 product sphingosine

Conclusions

Biallelic variants in ACER3 are associated with infantile and childhood-onset neurodegeneration with progressive leukodystrophy.

ABSTRACTS

Topic: Headache / Migraine

EPNS25_486 - Gain-of-function SCN1A variants result in Familial Hemiplegic Migraine (FHM3) with Elicited Repetitive Daily Blindness (ERDB) and demonstrate response to sodium channel blockers

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Objectives: Published case series report two families symptomatic of Familial Hemiplegic Migraine (FHM3) co-segregating with Elicited Repetitive Daily Blindness (ERDB). Pathogenic variants in the alpha subunit of voltage-gated sodium channel Nav1.1 were found in both families (SCN1A:Gln1489His in proband 1; and SCN1A:Phe1499Leu in proband 2).

This study aims to functionally characterise the pathogenic variants reported in two families with FHM3 and ERDB previously reported in the literature.

We aim to collate the clinical characteristics, genetic variants, and treatment response in four new families presenting with co-segregation of Familial Hemiplegic Migraine 3 (FHM3) and Elicited Repetitive Daily Blindness (ERDB) associated with SCN1A mutation.

Methods: Electrophysiological patch-clamp data were obtained for variants SCN1A: Gln1489His and SCN1A:Phe1499Leu, using the wild-type as a control.

Clinical assessment of the proband in four new families (families 3-6) was undertaken before and after treatment with carbamazepine. In addition, electronic case notes were reviewed recording symptomatology, family history, genetic testing, and the results of investigations.

Results: In variants SCN1A:Gln1489His and SCN1A:Phe1499Leu, changes to the functional properties of the Nav1.1 voltage-gated sodium channel result in an overall gain-of-function effect.

Four new families are described with symptoms of FHM3 and ERDB. The proband in each family reports daily episodes of bilateral visual loss, lasting for 3-30 seconds at a time. Events occur at random, or with predictable triggers such as orthostasis, change in environmental light or applied orbital pressure. Probands report typical hemiplegic migraines unrelated to the episodes of visual loss. Family members are also reported to have hemiplegic migraines with an apparent autosomal dominant pattern of inheritance. Not all family members with FHM3 report ERDB. Magnetic Resonance Imaging, electroencephalogram and electroretinogram testing did not reveal other aetiologies in probands.

We describe 3 novel variants in the SCN1A gene: Ala1343Ser (proband 3), Val1784Phe (proband 4) & SCN1A: Ala1669Val (probands 5 and 6). Each of these variants is predicted to result in a gain-of-function.

Probands 3-6 were commenced on the sodium channel blocker carbamazepine (commenced at 1.5mg/kg/day and titrated to response). This resulted in a reduction in episodes of hemiplegic migraine, and reduced episodes of visual loss by up to 90% in frequency.

Conclusions: FHM3 with ERDB is the result of gain-of-function SCN1A mutations. Symptoms respond to sodium channel blockade with carbamazepine.

ABSTRACTS

Topic: Neuromuscular Disorders

EPNS25_487 - Fluoroscopic guidance for intrathecal delivery of nusinersen in pediatric patients with spinal muscular atrophy and complex spines

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Objectives: The introduction of nusinersen revolutionized the treatment of spinal muscular atrophy (SMA). However, nusinersen is administered by interlaminar intrathecal injection which is challenging in patients with severe scoliosis, a common comorbidity of advanced SMA. Objectives: This study evaluated the technical benefits of fluoroscopic guidance of intrathecal nusinersen administration in complex SMA patients with or without a fixation device.

Methods: The cohort included 12 patients aged 10-20 years (total 124 injections) identified by retrospective database review.

Results: Demographic characteristics were diverse. Mean age at first injection was 14.2 years. Mean duration of radiation exposure was 77 seconds; mean dose area product was 2.32Gycm2; and mean cumulative air kerma was 20.91mGy. Adverse events included post-dural-puncture headache (4.8% of procedures), mostly mild and self-limited, and one allergic reaction. Treatment was discontinued in 2 patients because of difficult intrathecal access, and in 2 for reasons unrelated to the injection technique.

Conclusions: Fluoroscopy-guided nusinersen administration is a feasible option for patients with SMA and complex access. Success depends on proper patient positioning and expertise of the interventional radiologist. Radiation exposure is lower than with other techniques, with lower radiation exposure seen especially in patients with transpedicular fixation devices. Larger prospective studies are needed to confirm these findings.

ABSTRACTS

Topic: Neurogenetics

EPNS25_489 - Tuberous Sclerosis Complex in Greece. Clinical characteristics and rare manifestations.

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Objectives: Tuberous Sclerosis Complex (TSC) is a rare neurocutaneous disorder that usually presents with various symptoms early in life. This study aims to describe the characteristics of TSC patients in Greece, focusing on clinical manifestations, neuroradiological findings, genetic data, and rare manifestations.

Methods: A cohort of 115 patients was assembled, primarily through pediatric neurologists. For additional information, patients and/or their parents were interviewed.

Results: Our cohort consisted of 115 patients, (60 males, 55 females), with ages ranging from 0.7 to 61.5years (mean 18.5 years). The average age at symptom-onset was 2.3 years(0-18), while the average age at diagnosis was 4.9years (0-43). The predominant presenting symptom was seizures, observed in 81 patients (79.4%), with 104 patients (90.4%) developing epilepsy. Seizure-onset types included infantile spasms in 37 patients(35.5%), focal seizures in 36 patients (34.6%), complex partial seizures in 20 patients (19.2%), generalized tonic-clonic seizures in 7 patients (6.7%) and status epilepticus in 4 patients (3.8%). Skin manifestations were the second most common presenting symptom, seen in 13 patients (11.3%), followed by cardiac symptoms in 6 patients (5.2%), lumbar pain in 1 patient(0.9%), and hypotonia in 1 patient (0.9%). Four patients were diagnosed incidentally through other tests, and 9(7.8%) were diagnosed due to a symptomatic family member. Mental retardation was identified in 57 patients(49.6%), autism spectrum disorder in 22,6%, attention deficit disorder in 9.6%, and behavioral issues in 20.9%. Brain abnormalities were noted in 112 patients, including cortical tubers(93.9%), subependymal nodules(92.2%), subependymal giant-cell astrocytoma (20%), migratory lines (15.7%), cerebellar atrophy in 3 patients and Chiari I malformation in 2. Renal manifestations were found in 68 patients (59.1%), with angiomyolipomas in 56(82.3%), cysts in 27(39.7%), and renal-cell carcinoma in 1 patient. Cardiac involvement was noted in 33%. Skin involvement was observed in all patients, including hypomelanotic macules(97.4%), angiofibromas(39.1%), confetti lesions(14.8%), shagreen patches(27.8%), ungual fibromas(13%) and

ABSTRACTS

poliosis 1.7%). Dental manifestations were noted in 6,1%, and eye manifestations in 17.4%. Genetic testing was conducted in 67 patients, revealing 16 with *TSC1* mutations, 46 with *TSC2* mutations, and five negative tests. Rare manifestations included glioblastoma, renal-cell carcinoma, pancreatic neuroendocrine tumor, diffuse lipomatosis, rectal polyps, and breast cancer.

Conclusions: Our findings align with existing literature, reinforcing the importance of continuous monitoring in TSC patients. The occurrence of rare manifestations, underscores the need for lifelong vigilance to ensure timely management and prevention of potential complications.

ABSTRACTS

Topic: Fetal and Neonatal Neurology

EPNS25_490 - Neonatal subpial hemorrhage: padua experience and systematic review

Claudio Ancona[1], Cristina Impieri[2], Benedetta Bortolatto[2], Irene Laghetto[2], Sofia Galzignato[2], Margherita Nosadini[1 3], Irene Toldo[1], Ignazio D'Errico[4], Giulia Calignano[5], Maria Elena Cavicchiolo[6], Elena Cavaliere[1], Stefano Sartori[1 3 7]
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Objectives

Subpial hemorrhage (SPH) is a rare subtype of intracranial hemorrhage, often associated with cortical-subcortical infarction in the adjacent parenchyma and predominantly affecting term neonates. We described the epidemiology of neonatal SPH by analyzing cases referred to our hospital and concurrently conducting a systematic review of the cases reported in the literature. We also illustrated factors associated with adverse outcomes.

Methods

A retrospective study was conducted on neonates with SPH referred to our hospital from 2013 to 2023 (cohort 1). Additionally, a systematic literature review on neonatal SPH was performed using PubMed, Scopus, Cochrane, and Web of Science up to April 2024 (cohort 2). Cohorts 1 and 2 were pooled for combined analysis. In a subset of patients (cohort 3), including those in cohort 1 and cohort 2 with available individual patient data (IPD), Pearson's correlation coefficients (r) were calculated to assess linear relationships between variables and to identify clinical and neuroradiological factors correlated with severe outcomes (death or neurological impairment).

Results

A total of 173 cases were analyzed, 10 original cases (cohort 1) and 163 literature cases (cohort 2). Ninety-two percent were term/late preterm neonates (59% male). Clinical presentations included seizures (36%), apnea (36%), and encephalopathy (18%). Ninety-four percent were diagnosed with brain magnetic resonance imaging and/or cranial ultrasound. Lesions were located in the temporal lobe in 60%, with parenchymal infarctions adjacent to SPH in 90%. Sixteen percent died, 53% was diagnosed with neurological impairment, and 8% with epilepsy. IPD were available for 67 patients (cohort 3): 10/10 from cohort 1, 57/163 from cohort 2. In cohort 3 low birth weight, seizures, neonatal infections, and adjacent parenchymal hemorrhage were significantly associated with adverse outcomes.

Conclusions

This is the first systematic literature review on SPH. Although neonatal SPH is rare, understanding and characterization of the condition are expanding. SPH is predominantly located in the temporal lobe, and we identified a distinctive clinical presentation, including apnea (potentially of ictal origin) and seizures. Neurologic sequelae are common, with adjacent parenchymal hemorrhage showing a strong correlation with neurological impairment in our study.

ABSTRACTS

Topic: Epilepsy: Diagnosis and Investigations

EPNS25_491 - Assessing Sleep Problems for Patients with Drug-resistant Epilepsy Using Caregiver-reported Survey Data

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Objectives

This research aimed to evaluate the quality of life in patients with early-onset epilepsy, genetically confirmed, through the Brief Quality of Life in Childhood Epilepsy Questionnaire (QOLCE-16) and to assess sleep problems using the Sleep Disturbance Scale for Children (SDSC), relying on responses provided by caregivers.

Methods

The inclusion criteria required patients to 1) take two more antiseizure medications diagnosed with drug-resistant epilepsy and 2) complete all required questionnaires by parents. The exclusion criteria specified if patients achieved seizure-free states over 1 year. Sleep questionnaires could be required on patients over 4 years, so all included patients were above 4 years old.

Results

We included 63 drug-resistant epilepsy patients (male, N= 39). The average age was 8.0 (SD +-3.7) years old, and their median seizure onset was 1.1 (IQR 0.3-2.9) years. Among them, 30 patients (48.4%) had brain structural abnormalities, and 43 patients (68.3%) revealed genetic backgrounds. The mean total score on QOLCE-16 was 49.3 (SD +- 16.9). The SDSC total score was 51.8 (SD+-16.9), substantially higher than the reference score of 35.1, reflecting severe sleep problems. Patients getting older have higher SDSC scores in patients with drug-resistant epilepsy.

Conclusions

This study provided meaningful insights into the quality of life and sleep disturbances in patients with drug-resistant epilepsy by caregiver survey. These findings highlight that these patients experience significantly poor quality of life and severe sleep problems. Future research is warranted to explore specific variables contributing to these outcomes and develop targeted treatment strategies to improve their daily life.

ABSTRACTS

Topic: Neurorehabiltation

EPNS25_492 - Clinical profile and long-term fine motor outcome in pediatric patients of GBS

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Objectives: To study the long-term outcome in terms of fine motor movements and dexterity affection in children with GBS.

Methods: All diagnosed cases of GBS were enrolled, offered acute care, and then followed up on an OPD basis for the next 1-year post-discharge. Disability was assessed quantitatively by ONLS (overall neuropathy limitation scale score) and GBS Disability Score, applied at discharge, at 6 months, and at 1 year. SPSS 26.0 was used for statistical analysis.

Results: Fifty-two patients with GBS were admitted with a mean age of 8 years (1y-17y). The male: female ratio was 2.25:1. 46.15% (n=24) of patients required ventilatory support. The average duration of hospital stay was 30 days and 8 days for ventilated and non-ventilated patients respectively. The GBS disability score ≥4 (loss of ambulation) was present in 55.7% (n=29) while it reduced to 9.6% (n=5) at 6 months. The score of ≥4 was present in only 3.8% (n=2) patients at 1 year of follow-up. The arm score >2 of the ONLS was present in 46.1% (n=24), 26.9% (n=14), and 8%(n=4) patients at discharge, at 6 months, and at 1year follow-up respectively while leg score of >2 was seen in 86.5% (n=45), 19.2% (n=10) and 9.6% (n=5) respectively. There was a significant improvement in the GBS Disability score and the ONSS at discharge, 6 months, and 1 year of follow-up in both AMAN and AIDP variants ($p<0.05$).

Conclusions: GBS affected patients have long term fine motor disability affecting the dexterity of child, although most of them will have normal breathing and ambulation. Thus, a routine assessment of the fine motor functional capability is of utmost importance to realize the long-term outcome of this disease. MRI can be a useful tool for diagnosis as well as for guiding immunotherapy to improve the functional ability of these children.

ABSTRACTS

Topic: Neurogenetics

EPNS25_493 - Genetic and acquired pediatric cerebellar disorders and their phenotypic heterogeneity- the PEDIATAX study

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Objectives. Improvements in the diagnostic yield of next generation sequencing (NGS) studies in pediatric cerebellar disorders (PCDs) causing ataxia have stalled during the last decade. Additionally, population-specific differences in the distribution of PCDs exist. To further describe the epidemiology of PCDs, we performed a cohort study entitled PEDIATAX to evaluate the epidemiology, etiologies, and clinical and neuroradiological characteristics of PCDs, with a specific focus on genetic etiologies.

Methods. PEDIATAX is a longitudinal population-based cohort study of children with a movement disorder or a cerebellar malformation (diagnosis ≤16 years; study period 1970-2022). The genotype-to-phenotype associations were compared with those of 1007 individuals with matching monogenic etiologies, identified through a literature search. The pathogenicity of a variant of unknown significance (VUS) in *KIF1C* was assessed using a multidisciplinary team (MDT) approach including functional assays.

Results. A total of 107 individuals with a PCD were included (cumulative incidence 21.9 per 100,000 live births). A defined etiology was identified for 59 individuals, including monogenic (66%), chromosomal (12%), or non-genetic (22%) etiologies. Ataxia was the most common movement disorder. Friedreich's ataxia was uncommon in the study population, while certain other monogenic ataxias were overrepresented. Cerebellar atrophy (CA) was the most common imaging finding (n=12/49), while progressive CA was accompanied by progressive ataxia in only 40% of cases. The overall diagnostic yield was 55%, and 65% for NGS in ataxia. The most frequent clinical features were ataxia, developmental delay, seizures, hypotonia and abnormalities in brain MRI, while hearing loss, sensory neuropathy, and microcephalia were associated with fewer etiologies. Functional assays supported the pathogenicity of the *KIF1C* variant.

Conclusions. PCDs are a heterogeneous disease group. The diagnostic yield of NGS has increased over time. Age of onset and certain clinical features (i.e., hearing loss, sensory neuropathy, and microcephalia) may help to distinguish between different genetic etiologies. An MDT approach is necessary for confirming the pathogenicity of VUS findings. Our dataset expands the clinical spectrum of PCDs and helps clinicians to recognize them, their co-morbidities, and genetic etiologies. Further natural history data is essential for future clinical trials.

ABSTRACTS

Topic: Infectious and Inflammatory Diseases/ Neuroimmunology

EPNS25_494 - FINCA is a childhood-onset multi-organ neurodevelopmental disorder with deficient immune response

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Objectives

FINCA disease (OMIM 618278) is caused by recessive variants in NHL repeat containing protein 2 (NHLRC2). Since the initial characterisation, 33 patients from various ethnic backgrounds have been reported with different combinations of recessive pathogenic variants in NHLRC2 broadening the phenotypic spectrum of the disease. The molecular function of NHLRC2 protein is still largely unknown. We have generated the first NHLRC2 knock-in mouse and cell culture models to study pathophysiology of the FINCA disease.

Methods

We analysed the behavioural and immunological phenotype of the FINCA mice and studied the molecular pathways affected by p.Asp148Tyr in NHLRC2 using mouse and human-derived cell culture models. We analyzed differentially expressed genes of FINCA and Nhlrc2 knockout mouse embryonic stem cells by RNA sequencing and compared them to putative interacting partners identified from human embryonic kidney cells by proximity-labeling mass spectrometry.

Results

The FINCA mice displayed mild hyperactivity and deficient early immune response when challenged with LPS leading to altered cytokine responses. By comparing gene expression and putative interaction partners affected by p.Asp148Tyr, we identified Rho GTPase signalling as the common pathway.

Conclusions

FINCA disease is a clinical spectrum of Fibrosis, Infection susceptibility, Immunodeficiency, Intellectual disability, Neurodevelopmental disorder, Neurodegeneration, Chronic Anaemia, and Cerebral Angiomatosis. The pathogenic NHLRC2 variants lead to altered neurodevelopment and defective immune response in our mouse model and indicate the primary manifestations of FINCA disease.

ABSTRACTS

Topic: Epilepsy: Medical and Surgical treatment

EPNS25_495 - Effectiveness of Vagus Nerve Stimulation in Children with Drug-Resistant Epilepsy: A Single-Center Experience

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Objectives: Vagus nerve stimulation (VNS) is a non-pharmacological treatment modality for patients with drug-resistant epilepsy. The aim of this study is to evaluate the long-term effectiveness and potential side effects of VNS in children and to share our findings.

Methods: This study included 23 patients who underwent VNS implantation at our center and were followed for at least one year; 16 of the patients were male. Patient files were retrospectively reviewed to analyze changes in seizure frequency, adjustments in antiepileptic drugs (AEDs), and recorded side effects following VNS implantation.

Results: The etiologies of epilepsy among the included patients were structural in 10 cases (43%), genetic in 4 cases (17%; including Dravet syndrome, Ring 20 chromosome, and protocadherin mutation), and infectious in 1 case (4%). The mean age at VNS implantation was 10 years (range: 6–16 years). Seizure semiology was generalized tonic-clonic in 5 patients (22%) and focal onset in the remainder. Post-implantation, a reduction in seizure frequency of over 50% was observed in 43% of patients, while 26% experienced a reduction of less than 50%, and 26% showed no change. Notably, seizure frequency increased in only 1 patient (4%). During follow-up, the number of AEDs was successfully reduced in 8 patients (35%). Side effects were observed in 35% of patients, including hoarseness (n=2), cough (n=4), headache (n=1), and bradycardia (n=1).

Conclusion:VNS is an effective and beneficial treatment option for children with drug-resistant epilepsy. The associated side effects are mild and manageable, underscoring its utility as a safe therapeutic approach in this population.

ABSTRACTS

Topic: Neurodevelopmental Disorders / Developmental Neuroscience

EPNS25_496 - Overview of Sleep Disorders in Children with Angelman syndrome

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Objectives: Angelman syndrome (AS) is a rare congenital neurodevelopmental disorder characterized by developmental delay, epilepsy, lack of speech, movement impairment, and an apparent happy demeanor. Moreover, up to 80% of children suffer sleep problems, with a high impact not only on patients' quality of life, but also in their families. Interestingly, the loss of the maternal Ube3a copy of the gene results in abnormal functioning of the superchiasmatic nucleus, involved in the circadian clock regulation. The aim of the present study was to investigate the main sleep disorders in a pediatric population with AS, and to objectively assess circadian rhythms disorders in the same study population.

Methods: Families of children with AS follow-up in two reference centers of our country were invited to participated in this observational study. Inclusion criteria were: 1-18 years old, both sexes, and confirmed diagnosis of AS. Parents completed a validated sleep questionnaire (the Sleep Disturbance Scale for Children (SDSC)), and an actigraphy was placed in the non-dominant hand for at least one week to assess circadian rhythm.

Results: Overall, 11 children and adolescents with AS were enrolled. The mean age was 6.4±3.6, years, 54% were female. Up to now, according to the SDSC none of participants screened positive for global sleep disorders, the higher T-score was for onset and maintenance sleep problems, and a long sleep latency (>30 minutes) was found in 20% of the study population. Objective assessment of sleep/wake rhythms based on actigraphy data showed that total sleep time, according with the recommendations of the National Sleep Foundation per age, was decreased in all cases a mean of 3 hours per night. Moreover, delayed sleep phase was present in the different range age groups, but especially in toddlers and teens.

Conclusions: While sleep problems can be subtle in children with AS, insufficient sleep and delayed sleep phase should be considered in this rare genetic disorder, especially in toddlers and adolescents. Moreover, objective assessment in children with AS and a high suspicious of sleep disorders is recommended to improve the quality of life of these children and their families.

ABSTRACTS

Topic: Infectious and Inflammatory Diseases/ Neuroimmunology

EPNS25_499 - Detecting Cognitive Decline in Pediatric MS: The Significance of Personal Measures for High-Achievers

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Objectives

To explore the need for a personal measure of cognitive decline (Personal Cognitive Decline, Personal-CD), in individuals with Pediatric Onset Multiple Sclerosis (POMS), focusing on declines relative to estimated previous abilities rather than the normative standards. We explored the significance of both Personal-CD, defined as a decline in cognitive performance relative to individual's estimated premorbid abilities, as well as Cognitive Impairment (CI), defined as performance below -1.5 SD of the normative means.

Methods

A cohort observational study included 31 POMS patients (20 females, mean age 15.8 years) recruited from a pediatric neuroimmunology clinic, with a 94% consent rate. Participants underwent neuropsychological assessments across six cognitive domains and psychological questionnaires on anxiety and depression. A high rate of participants who showed academic excellence (n = 11) was found, who were compared to those with typical academic performance (n = 20).

Results

CI was identified in 26% of participants, primarily in those with typical academic performance, and was associated with disease-related disability (p = .02). In contrast, 45% showed Personal-CD, particularly in the excellence group (73%), found associated with depression (p = .01), but not with disease severity.

Conclusions

Personal-CD uncovered subtle cognitive decline overlooked by the use of standard CI measures, especially in high-achieving patients. These cognitive changes were associated with psychological distress rather than disease severity. Thus, albeit supporting the use of CI as associated with disease severity, the use of Personal-CD highlights also the role of psychological distress in coping with POMS.

ABSTRACTS

Topic: Infectious and Inflammatory Diseases/ Neuroimmunology

EPNS25_502 - Factors Determining Residual Impairments in Opsoclonus Myoclonus Ataxia Syndrome (OMAS) Treated with an Escalating Protocol

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Objectives

The study was performed to identify factors determining residual impairments in cognition, behaviour, motor functions and language in children with OMAS who received immunomodulation for atleast 12 months.

Methods

The study design was a single-centre, prospective, descriptive, and cross-sectional study. Eighty-four children were screened, and forty-two children were enrolled. All except three were treated with an escalating protocol with baseline two drugs. Clinical details at the onset of OMAS were reviewed from the records. Intellectual Quotient (IQ) or IQ equivalents, behavioural screen, OMAS severity score, and Scale for the Assessment and Rating of Ataxia (SARA) score were assessed. A maximum of two subjective problems reported by parents were noted.

Results

At a median follow-up of 42 months, twenty-five children (60%) had normal cognitive outcomes (IQ ≥85). Seventeen children (40%) had poor cognitive outcomes (IQ <85). The mean IQ ± SD was 89 ± 16, and the median IQ (IQR) was 89 (76–101), ranging from 60–120. Those with monophasic OMAS had a higher mean IQ than relapsing OMAS (97 ± 13 vs 82 ± 15, p=0.004). Poor cognitive outcomes (IQ < 85) were predicted by the younger mean age at onset (16 months vs 22 months, p=0.041), higher mean OMAS scores at baseline (13 vs 10, p=0.038), higher median number of relapses (one vs nil, p=0.012), and higher median Mitchell and Pike score at the last follow-up (two vs one, p<0.001). No significant predictor of poor cognitive outcomes was identified with multivariate analysis using binary logistic regression. Eleven patients (26%) had screened positive on the behavioural scales. All of them had a course of relapsing OMAS (p=0.006). Problems concerning the parents were misarticulation (N=24, 57%), language delay (N=6, 14%), and behavioural issues (N=7, 17%). Those reporting problems were more likely to have children with IQ < 85 (50% vs 10%, p=0.031) and lower mean IQ scores (86 ± 16 vs 98 ± 12, p= 0.022), than those who did not report any problem. At the last follow-up, both the median OMAS severity score and the median SARA score were one. None of the children had residual motor deficits.

Conclusions

The cognitive outcome in children with OMAS treated with an escalation protocol with baseline two drugs is favourable and is influenced by the occurrence of relapses and the initial severity. Speech therapy should be considered a crucial component of therapy in the long-term management of children with OMAS.

ABSTRACTS

Topic: Neuromuscular Disorders

EPNS25_503 - Pediatric Neuromuscular Diseases and Sleep-Disordered Breathing: A National Study from Latvia

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Objectives
Children with neuromuscular diseases (NMD), such as Duchenne muscular dystrophy (DMD) and spinal muscular atrophy (SMA), are highly vulnerable to sleep-disordered breathing (SDB), which contributes to premature mortality and cognitive decline. This study aimed to assess the utility and effectiveness of spirometry and respiratory polygraphy combined with transcutaneous capnography (PG + trCO2) in diagnosing respiratory dysfunction in children with DMD and SMA.

Methods
A retrospective cohort study was conducted, involving 72 pediatric patients with DMD and SMA. Data were collected on pulmonary function tests (PFTs), including spirometry and peak expiratory flow (PEF), as well as PG + trCO2 assessments. The study evaluated the detection of respiratory abnormalities and monitored the progression of sleep-related respiratory disturbances over time.

Results
Of the 72 patients analyzed. Only 36% underwent PG + trCO2, of which 77% exhibited significant respiratory abnormalities during sleep. PFTs were conducted in 63% of patients, revealing: 38% had normal spirometry results; 47% showed restrictive respiratory patterns; 15% were unable to complete PFTs due to lack of cooperation. PG + trCO2 identified significant respiratory dysfunction in three patients with normal PFT results, prompting the initiation of non-invasive ventilation therapy. Longitudinal sleep studies in 11% of patients revealed progression in sleep-related respiratory disturbances, with some developing notable nighttime respiratory changes, such as sleep apnea and hypoventilation, despite normal PFT outcomes.

Conclusions
This study underscores the importance of comprehensive respiratory evaluations in children with NMD. PG + trCO2 demonstrated significant value in detecting SDB, particularly in patients with normal PFT results. These findings highlight its critical role in early diagnosis and management of respiratory dysfunction, emphasizing the need for integrated respiratory monitoring in this high-risk pediatric population.

ABSTRACTS

Topic: Infectious and Inflammatory Diseases/ Neuroimmunology

EPNS25_504 - Navigating Treatment Challenges in pediatric GAD65-Antibody-Mediated Encephalitis

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Objectives

GAD65 autoantibodies are associated to autoimmune diseases, including several neurological disorders. Among them: GAD65 autoimmune encephalitis, a neuroinflammatory disorder characterized by a broad spectrum of symptoms including cognitive impairment, behavioral changes and autoimmune-associated drug-resistant epilepsy (DRE).

Methods

We present a complex case of a 15-year-old previously healthy boy who was admitted to our hospital after experiencing generalized and focal onset motor seizures that were refractory to treatment with valproic acid, clobazam, and lamotrigine.

Results

CSF analysis showed pleocytosis, elevated protein levels, and type 2 oligoclonal bands. Immunofluorescence analysis by tissue-based assay revealed a neuropil signal and by cell-based assay we detected high titer GAD65 antibodies in CSF and serum. The patient's EEG showed focal epileptic discharges and brain MRI demonstrated a voluminous and signal-altered right hippocampus. We diagnosed a GAD65 antibody-mediated encephalitis with DRE and episodes of confusion and amnesia. Immunotherapy with intravenous methylprednisolone and immunoglobuline resulted in transient resolution of seizures and EEG abnormalities. Within weeks, seizures recurred, along with a worsening of psychological symptoms. Due to persistent GAD65 antibodies and changes in the morphological structure of the controlateral amygdala and hippocampus we intensified treatment with further methylprednisolone pulses, immunoadsorption, various antiepileptic drugs (cenobamate, perampanel, cannabidiol and oxcarbazepine), and finally, with the second-line therapy with rituximab.

Conclusions

This case 1) illustrates the role of antineuronal autoantibodies in the etiology of drug-resistant epilepsies, 2) emphasizes the importance of prompt and aggressive immunotherapy in GAD65-mediated neurological disorders, 3) highlights the limited knowledge regarding symptom progression over time and the response to immunotherapy in patients with GAD65 antibody-mediated encephalitis, and 4) emphasizes the need to establish a pediatric patient cohort to assess the long-term outcomes and establish a standardized treatment pathway.

ABSTRACTS

Topic: Neuromuscular Disorders

EPNS25_506 - Impact of vamorolone, prednisone and placebo on linear growth in the VISION-DMD study, as measured by changes in height over 24 weeks (Encore)

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Objectives: Corticosteroids are recommended as standard of care for patients with Duchenne muscular dystrophy (DMD). However, children with DMD are on average shorter than the general population by the age of 5 years, and daily dosing with prednisone or deflazacort leads to further stunting of growth (Bello et al. 2015 PMID: 26311750; Stimpson et al. 2022 PMID: 35073949). In the Phase 2b VISION-DMD study (NCT03439670) height percentile (adjusted by age using US CDC growth charts) was shown to decline from baseline to month 6 in patients treated with prednisone, but not in those treated with the dissociative corticosteroid vamorolone at 6 mg/kg/day (Guglieri et al. 2022 PMID: 36036925). Here we further study the impact of vamorolone or prednisone vs placebo on linear growth in the VISION-DMD study by reporting unadjusted changes in height (cm) and patient-level changes in height over the course of 6 months.

Methods: The design of the prospective VISION-DMD study has been reported previously. Boys aged 4 to <7 years were randomised to placebo, prednisone 0.75 mg/kg/day, vamorolone 2 mg/kg/day or vamorolone 6 mg/kg/day. Height was recorded at baseline and at 12-week intervals. This analysis included 118 participants in the safety population.

Results: At baseline, median height ranged from 106 to 111 cm across the treatment groups. After 6 months of treatment, median height increases were lower in the prednisone group (n=30, 2.60 cm) than in the placebo group (n=28, 3.55 cm, p=0.03) or vamorolone 6 mg/kg/day group (n=26, 3.50 cm, p=0.009). There were no significant differences in median height increase between either vamorolone group and placebo (p>0.1). In the prednisone group, 30.0% of children showed reductions in height z-score ≥0.2 standard deviations after 6 months, compared with 18.5% in the vamorolone 2 mg/kg/day group, 10.7% in the placebo group and 0 children in the vamorolone 6 mg/kg/day group.

Conclusions: In patients with DMD aged 4 to <7 years, absolute height (cm) values after 6 months of treatment showed similar increases with vamorolone and placebo, while significantly less growth (i.e. growth stunting) was observed with prednisone.

Data first presented at the 2024 Muscular Dystrophy Association (MDA) Clinical & Scientific Conference.

ABSTRACTS

Topic: Neuromuscular Disorders

EPNS25_507 - Evaluation of behavioural problems using PARS III in the VISION-DMD study of vamorolone vs prednisone in Duchenne muscular dystrophy (DMD) (Encore)

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Objectives: Psychiatric adverse effects during systemic corticosteroid therapy are common and well documented. Here we report the frequency of behavioural problems in the Phase 2b VISION-DMD study (NCT03439670) using the PARS III scale, a validated index of youth psychosocial adjustment in Duchenne muscular dystrophy (DMD).

Methods: Patients were prospectively randomised to placebo, prednisone 0.75 mg/kg/day, or vamorolone at 2 or 6 mg/kg/day. PARS III subscales assessed by parents were normalised as z-scores using historical data. Clinically relevant worsening in PARS III subscales was defined as a shift from normal baseline adjustment score (z-score <1) to an abnormal score (z-score ≥1) at Week 24.

Results: Moderate or severe behaviour adverse events (BAEs) were more frequent in the prednisone group (22.6%) than in any other arm (≤3.4% in all other groups). One patient on prednisone discontinued due to a severe BAE. Clinical worsening in hostility was more frequent with prednisone (26.1%) than vamorolone 6 mg/kg/day (15.4%), 2 mg/kg/day (9.1%) or placebo (8.0%). Clinical worsening in dependency and productivity was reported in >20% of patients with prednisone (24.0% and 26.9%, respectively) compared with <10% in any other group.

Conclusions: Vamorolone 6 mg/kg/day was associated with an increase in mainly mild BAEs compared with placebo, but with a lower frequency and severity of BAEs reported compared with prednisone. PARS III subscales showed a reduced risk for psychosocial adjustment/functioning in hostility, dependency, and productivity with vamorolone compared with prednisone.

Data first presented at the European Academy of Neurology congress 2024.

ABSTRACTS

Topic: Movement Disorders/ Cerebral Palsy

EPNS25_508 - Expanding the genetic and phenotypic spectrum of patients with dystonia related to DYT-VPS16

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Objectives

DYT-VPS16 is a recently identified form of early-onset, isolated dystonia caused by heterozygous variants in the *VPS16* gene. This study aimed to further delineate the clinical and genotypic spectrum of DYT-VPS16 in a large, international cohort of patients.

Methods

Exome sequencing was performed to investigate patients with early-onset dystonia suspected to have a genetic etiology, across multiple international medical centers. RNA sequencing or cDNA analysis was conducted in four patients to assess splicing abnormalities. Comprehensive clinical evaluations and a review of the literature were also undertaken.

Results

We report 16 novel dystonic patients from 10 different countries, harboring heterozygous variants in *VPS16*. Dystonia onset occurred at a mean age of 12 years (IQR 6.0–18.8) initially affecting the limbs (n=10), neck (n=4), face and tongue (n=2). Patients with initial leg involvement had an earlier age at onset than those with involvement of other regions (6.4 years compared to 19.6 years). Progression was noted in 15/16 cases, leading to generalized (50%) or focal/segmental forms (50%). On the last evaluation, dystonic symptoms caused speech difficulties (62.5%), jerky dystonic hand tremor (37%), bulbar dysfunction (19%) and gait loss (19%). Dystonia was isolated in 12 cases or accompanied by

ABSTRACTS

pyramidal, cerebellar, or psychiatric features in four cases. Two early-treated young patients showed significant improvement with *globus pallidus* internus deep brain stimulation.

Our 16 patients harbored 11 different *VPS16* variants, of which 10 had not been reported previously (two missense, two nonsense, three small deletions/insertions and four splice region/site changes). Investigation of blood-derived *VPS16* mRNA revealed alternatively spliced transcripts, consistent with loss-of-function effects, including an exonic splice-altering variant previously interpreted as a missense change (c.1475A>G), and a near-splice-site variant (c.1368-11G>A). We identified six asymptomatic heterozygote individuals in 13 families (6/22 individuals tested, 27%), suggesting that penetrance for this disorder (73%) could be lower than previously suggested.

Conclusions

We expanded the phenotypic and mutational spectrum of VPS16-related dystonia (DYT-VPS16), highlighting it as a relatively frequent and treatable cause of dystonia in childhood and adolescence.

ABSTRACTS

Topic: Infectious and Inflammatory Diseases/ Neuroimmunology

EPNS25_509 - Miller Fisher Syndrome: A single center retrospective clinical experience

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Objectives Guillain-Barré syndrome (GBS) is an acute immune-mediated inflammatory polyneuropathy typically characterized by symmetric and ascending weakness. Miller Fisher syndrome (MFS) is a rare variant of GBS defined by the triad of external ophthalmoplegia, areflexia and ataxia. Approximately 85-90% of patients with MFS are positive for the anti-GQ1b IgG antibody.

Methods In this study, we present a retrospective analysis of five pediatric cases diagnosed with MFS in our clinic.

Results The male to female ratio among the children diagnosed with MFS was 4:1. The age range of the patients was from 3 years and 10 months to 10 years. All cases had a history of infection within the previous two weeks. Three patients had acute gastroenteritis and two had upper respiratory tract infections. Serum creatine kinase (CK) levels were measured in four patients, one of whom had elevated levels (CK=238). Anti-GQ1b antibodies were positive in 80% of patients.

Case 1: A patient diagnosed with MISC after presenting with fever, fatigue and rash during a one-week course of antibiotics was treated with IVIg, steroids and aspirin. Three days after discharge, the patient developed double vision and headache; examination revealed bilateral restricted upward and outward gaze.

Case 2: A patient presented with double vision and weakness one week after experiencing diarrhea and fever. The light reflex was absent, suggesting a second cranial nerve involvement. Subsequently, ataxia and ophthalmoparesis developed. The patient was treated with repeated IVIg and plasmapheresis and was discharged on day 21.

Conclusions In MFS, diplopia is often the initial symptom, with ataxia and areflexia appearing at different times. Longitudinal assessment is crucial for diagnosis. Anti-GQ1b IgG antibodies have been reported in MFS, GBS, Bickerstaff brainstem encephalitis and patients with acute ophthalmoplegia. In cases where the classic MFS triad is absent but atypical features are present, measurement of ganglioside antibodies may aid diagnosis.

ABSTRACTS

Topic: Neurogenetics

EPNS25_510 - Diagnostic yield of WES for unclear neurological patients in Kazakhstan

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Objectives The use of whole exome sequencing methods has allowed many countries to study genes and detect mutations that lead to genetic diseases. Clarifying the molecular basis of neurogenetic diseases associated with damage to the central and peripheral nervous systems of the population of the Republic of Kazakhstan is of great scientific interest, since at the moment the genetic features of neurological diseases characteristic of this region have not been studied yet . The identification of precise genetic mutations provides, in some cases, the opportunity to choose drug therapy, thereby favorable clinical outcomes and contributes to clinically important carrier testing and prenatal diagnosis.

Methods in 2024 we observed 99 patients with unclear neurological disorders with involvement of the central or peripheral nervous system and provided them with WES.

Results As a result of the analysis of patients who underwent whole exome sequencing (WES) shows 43% of positive genetic results with identification of pathogenic gene mutations, 19% had uncertain significance and 38% were negative. The following disease groups were identified: metabolic disorders, specifically mitochondrial diseases, neuromuscular diseases (including DMD in girls carriers), neurodegenerative diseases like Huntington's chorea and spinal-cerebellar ataxias, epilepsies and developmental encephalopathies, connective tissue diseases

Conclusions The diagnostic yield of this method was 43%, which exceeds the global average. This shortens the "diagnostic odyssey", increases the accuracy of diagnoses and allows us to choose the optimal way of patient management. Timely appropriate performance of this technology helps to choose the most effective therapy, reducing the risk of disability and becoming a promising tool for improving the diagnosis, treatment, and quality of life of patients with neurological disorders, offering new opportunities for personalized medicine and disability prevention, especially in middle income countries such as Kazakhstan.

ABSTRACTS

Topic: Neuromuscular Disorders

EPNS25_511 - Growth velocity changes in boys with DMD treated with vamorolone, prednisone, deflazacort and placebo – a post hoc analysis vs external comparators (Encore)

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Objectives: Vamorolone, a corticosteroid with a chemical structure distinct from classic corticosteroids, is approved for the treatment of patients with DMD in the US (in patients aged ≥2 years) and in Europe (in patients aged ≥4 years). One of the major side effects of traditional corticosteroids is stunting of normal growth in the setting of chronic treatment with corticosteroids. Here, we performed a post-hoc analysis of growth velocities on data from recently concluded studies with vamorolone and an external comparator study, using the FDA guidance on growth evaluation in pediatric patients treated with corticosteroids.

Methods: In this post hoc, cross-study comparison, data were analysed from two randomised, double-blind studies [FOR-DMD (NCT01603407) and VISION-DMD (NCT03439670)] and one open-label study (VBP15-LTE; NCT03038399). The individual slopes for the mean change in growth velocity and differences between cohorts were calculated with linear regression (VISION-DMD: baseline, Week 12, Week 24, Week 48; VBP15-LTE: baseline, Months 3–30) and were analysed with ANCOVA, using baseline height and age as covariates per FDA 2007 guidance.

Results: In patients with DMD aged 4 to <7 years, growth velocity changes in patients treated with vamorolone were similar to those seen in patients who received placebo. The vamorolone-treated groups showed significant changes in growth velocities (favoring growth) when compared to groups treated with prednisone and deflazacort.

Conclusions: These results suggest that vamorolone may not affect linear growth as much as prednisone or deflazacort.

Data first presented at the European Muscle Conference (EMC) 2024.

ABSTRACTS

Topic: Epilepsy: Medical and Surgical treatment

EPNS25_512 - Zorevunersen demonstrates potential as a disease-modifying therapy in patients with Dravet syndrome through durable seizure reduction and improvements in cognition, behavior, and functioning with up to 24 months of continued dosing in open-label extension studies

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Objectives: Dravet syndrome (DS) is a severe developmental and epileptic encephalopathy caused primarily by *SCN1A* variants resulting in $Na_V1.1$ haploinsufficiency. Patients with DS experience prolonged, refractory seizures, and developmental and cognitive impairments. Zorevunersen is an investigational antisense oligonucleotide designed to upregulate $Na_V1.1$ by leveraging the *SCN1A* wild-type copy. Clinical effects and safety of zorevunersen in patients with DS are presented.

Methods: In the MONARCH/ADMIRAL (NCT04442295 [US]; 2020-006016-24 [UK]) Phase 1/2a studies, 81 patients on best available antiseizure medications (ASMs) received single/multiple doses of zorevunersen (≤70mg). At the end of Phase 1/2a studies, 74 patients transitioned to the SWALLOWTAIL/LONGWING (NCT04740476 [US]; 2021-005626-14 [UK]) open-label extension (OLE) studies and received zorevunersen (≤45mg) every four months. Convulsive seizure frequency (SF), adaptive behavior (Vineland-3), and clinical status were evaluated.

Results: As of 28 June 2024, 565 total doses of zorevunersen were administered; patients received ≤12 doses for ≤3 years. Six months after the last dose in MONARCH/ADMIRAL, patients administered single (N=8) or multiple (N=11) doses of 70mg zorevunersen experienced 57.3% (n=7) and 73.6% (n=9) median SF reductions relative to naïve baseline, respectively. Seizure reductions were sustained through Month 24 of the OLEs. Estimated improvements (95% confidence interval) in Vineland-3 subdomain growth scale values from OLE baseline to Month 24 were 3.791 (0.855–6.727) and 5.216 (2.928–7.504) for Expressive and Receptive Communication, respectively, in all enrolled patients. Substantial clinical status improvements were also observed. Single/multiple doses of ≤70mg zorevunersen were generally well tolerated. Increased cerebrospinal fluid protein was the most common drug-related treatment-emergent adverse event (11/81 and 20/74 patients in MONARCH/ADMIRAL and SWALLOWTAIL/LONGWING, respectively), with no associated clinical manifestations observed.

Conclusions

Substantial and durable clinical improvements were observed in patients with DS receiving best available ASMs. These findings support further evaluation of zorevunersen in Phase 3 trials.

Funding: Stoke Therapeutics

ABSTRACTS

Topic: Cerebrovascular Disorders

EPNS25_513 - Paediatric post-pump chorea: a clinical and imaging study

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Objectives. To describe clinical and imaging features of paediatric post-pump chorea, a rare complication of cardiac surgery procedures with cardio-pulmonary bypass (CPB), scarcely reported so far.

Methods. This monocentric retrospective study included consecutive paediatric patients (<18 years of age) who had cardiac surgery with CPB in a tertiary care institution between 2014 and 2023, and focused on those with identified post-pump chorea. Data were retrieved from local databases and electronic charts. We collected parameters concerning demographics, clinical presentation and timing of onset, imaging, and outcomes.

Results. During the 10-year inclusion period, among 7,059 cardiac surgery procedures with CPB performed, 11 patients (0.15%) presented with post-pump chorea: five boys and six girls, at a median age of 5.7 years [range 0.45-9.9]. The median delay between surgery and post-pump chorea onset was 20 days [4-64]. Six/11 patients (55%) had a cyanotic cardiac condition. Six patients (55%) had a history of previous cardiac surgery with CPB, without complication, including abnormal movements. The CPB and ICU hospitalization median durations (132 min [64-362], and 6 days [1-186], respectively), and levels of inflammatory markers were similar with patients without post-pump chorea. Median BMI in affected patients was significantly low (14.8 [11.9-17.4]). Abnormal movements, e.g. chorea, always involved the face (100%), and frequently involved the limbs (upper 91%, lower 82%), usually bilaterally (82%). Brain imaging did not display significant ischemic injury in any patient. Six patients (55%) received pharmaceutical treatments, including tetrabenazine (n=2), IV immunoglobulins (n=1), oral corticosteroids (n=1), L-Dopa (n=1), and cyamemazine (n=1). Abnormal movements disappeared after a median 44 days [3-181], but chorea lasted for more than 6 months in one patient.

Conclusions. Post-pump chorea is a very rare condition, with a possible delayed onset of days to weeks after surgery. Outcomes seems favourable, with no permanent ischemic injury. Pathophysiology remains unsolved and therapeutic management may be diverse.

ABSTRACTS

Topic: Movement Disorders/ Cerebral Palsy

EPNS25_514 - Genetic Mimics of Cerebral Palsy: A Single-Center Experience

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Objectives

Cerebral palsy (CP) is defined as a group of permanent disorders of movement and posture, leading to activity and mobility limitations caused by non-progressive disruptions in the development of the fetal or infant brain. Many genetic and metabolic disorders may exhibit a clinical presentation similar to CP. Clarifying the etiology in this patient group is of great importance in terms of treatment possibility, predicting prognosis and genetic counseling.

Methods

Patients were followed up in our clinic between 2006-2024 who presented with a clinical presentation that mimicked CP and were subsequently diagnosed with a genetic disorder were retrospectively evaluated. Patients who did not show clinical progression and had normal or only minor non specific findings on brain MRI were included in the study.

Results

Thirty-one patients meeting the criteria were included in the study. The mean age of symptom onset was 11.03 months (range 2-24 months), and the mean age at diagnosis was 73.67 months (range 12-208 months). 17 (54.83 %) of the patients had consanguineous marriage of parents and 10 (32.25 %) the patient had a family history of similar diseases. Thirteen patients exhibited features similar to spastic CP, while two showed dyskinetic features, seven presented with ataxic characteristics, and nine displayed features resembling mixed-type CP. The spastic group was largely composed of hereditary spastic paraplegias (HSPs) and contained a wide variety of genes. Ataxic CP mimics included NKX6-2, SLC2A1, ALDH5A1, MECP2 genes, dystonic CP mimics included TH, GCDH genes and mixed CP mimics included ADSL, SLC18A2, KCNJ10, GNB1, GJC2, CYP7B1, GBA2, SPG11 genes. 17 (54.83%) patients were diagnosed by whole exome sequencing (WES). Seven patients received etiology-directed treatment.

Conclusions

Due to the high diagnosis rate, next-generation sequencing may be considered as the first stage of genetic workup in patients with idiopathic CP. Identifying a genetic cause may provide the opportunity for treatment in some cases.

ABSTRACTS

Topic: Infectious and Inflammatory Diseases/ Neuroimmunology

EPNS25_518 - Frequency and spectrum of psychiatric symptoms in children with NMDA-R Encephalitis

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Background and Objective: N-Methyl-D-Aspartate Receptor (NMDAR) encephalitis is an autoimmune disorder of the CNS with antibodies against the GluN1 subunit of the NMDA receptor. The disease is characterised by psychiatric and neurological symptoms at onset which contribute to the long-term morbidity.
To investigate the frequency and spectrum of psychiatric symptoms as well as cognitive outcome in children with NMDA-R encephalitis at onset and at follow-up.

Methods: Children with autoimmune encephalitis who tested positive for serum NMDAR abs, had characteristic clinical features, underwent an MRI and were followed up by the GENERATE Junior Network were included prospectively and retrospectively. A questionnaire-based assessment regarding psychiatric symptoms will be performed using the Child Behaviour Checklist (CBCL/4-18) and the subsequent CASCAP-2-test.

Results: 68 children (51 female, 17 male) with NMDA-R encephalitis and a median age at onset of 13,5 years (range: 0.9 – 20.1 years) have been included so far. At diagnosis, psychiatric symptoms were present in 58/68 children. The most common symptoms were changes in character (22/68), hallucinations (16/68) and aggressiveness (22/68) in addition to disorders of higher cognitive function (51/68). Neurological symptoms consisted of epileptic seizures (47/68), impaired consciousness (42/68) and memory disorders (31/68).

38/64 children had a follow-up examination to date with a median follow-up of 21,5 months (range: 1-142 months). A median mRS of 1 (range 0-4) was reported. At the follow-up, 28/38 children still displayed symptoms. 13/28 children showed cognitive impairments consisting of difficulties with concentration, attention or memory. 5/28 children exhibited speech disorders and 3/28 children had headaches. 14/28 children exhibited behavioural problems consisting of impulsivity, affect instability or mood swings. A detailed description of the frequency and spectrum of psychiatric symptoms obtained by the abovementioned questionnaire is pending. So far 6 children have been investigated by CBCL and 7 patients by CASCAP-2.

Conclusions: Most children have good clinical outcomes, but many experience long-term behavioural and cognitive problems. Regular follow-ups with MRI and neurocognitive testing at defined intervals are recommended to monitor these sequelae, with an emphasis on implementing a standardized assessment to ensure consistent and comparable evaluation.

ABSTRACTS

Topic: Neurodevelopmental Disorders / Developmental Neuroscience

EPNS25_519 - Prevalence and clinical characteristics of some neurodevelopmental disorders among children at alexandria university children's hospital

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Objectives

Neurodevelopmental disorders (NDD) are conditions that occur during the early developmental period. They manifest early and are characterized by developmental deficits that produce impairments of personal, social, academic, and occupational functioning. Estimates of the prevalence of NDDs are critical in pediatric medicine. The estimates typically influence medical welfare policy decisions and provide the foundations for pediatric research advancement. This study aimed to identify the prevalence and clinical characteristics of a cohort of children with some neurodevelopmental disorders attending the outpatient neurology clinic of Alexandria University Children's (AUCH).

Methods

This retrospective study included medical records of all patients with neurodevelopmental disorders including Attention Deficit Hyperactivity Disorder ADHD, Autism Spectrum Disorder ASD, intellectual disability ID, and global developmental delay GDD who attended the Outpatient Neurology Clinic in AUCH from the 1st of January 2017 till the 31st of December 2021. data were collected from the medical records of children diagnosed with at least one neurodevelopmental disorder including ADHD, ASD, ID, or GDD according to DSM-5 diagnostic criteria attending the outpatient neurology clinic at AUCH during a period of 5 years. The following data was retrieved from patients' files: Demographic data, family history data, Prenatal, natal, post-natal data, developmental data, and school-related data.

Results

The prevalence of NDDs is 42.17% with a male-to-female ratio of 2.19: 1 (501 out of 1188 children). The most frequently diagnosed NDD was ADHD, followed by GDD, ID, and ASD. While the majority of NDD cases received single diagnosis (470 out of 501), mixed diagnosis was reported in only 31 patients (2.6%).

Conclusions

The most frequently diagnosed NDD is ADHD followed by GDD, ID, and ASD. The most important risk factor for NDD was genetic predisposition, represented by a high incidence of family history. There was a lag in the diagnosis from the first presentation.

ABSTRACTS

Topic: Neurodevelopmental Disorders / Developmental Neuroscience

EPNS25_521 - Impact of an Early Educational Protocol on the Oral Language of Formerly Preterm Children Exhibiting Phonological Fragility: A.Multicenter Randomized ClinicaTrial

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Objectives

Evidence of the benefits of early intervention in children formerly born preterm to prevent learning disabilities (reading, writing, and arithmetic) remains limited.

We hypothesized that in a population of children born prematurely, that is, before 33 weeks of gestation, with phonological fragility (but not dysphasia)) we would observe minimal motor disorders that, according to the motor theory of speech perception and the sensorimotor prerequisites of language, could hinder the development of phonology (i.e., the organization of sounds during speech).

Methods

The LAMOPRESCO study was a multicenter, prospective, randomized, open-label, interventional study.

We conducted a six-center, prospective, randomized, open-label trial to assess whether an early standardized educational protocol provided from 42 to 48 months of age improved the progression of oral language and phonological development in children born preterm. A total of 552 children were included in this study. Children with phonological fragility were randomized to receive the educational protocol (guided arm, n = 87) or not (non-guided arm, n = 78). In the guided arm, oral language development used a short “say and do” type educational protocol designed to maintain visual attention and train the developmental phonology/lexicon/morphosyntax structural links. In contrast, a conservative approach was used in the non-guided arm. A total of 70 guided and 73 non-guided children completed the study. After six months, educated children showed a non-significant increase in their phonology score (p = 0.37), while variations in the scores of the production lexicon (secondary endpoints) were significantly improved (p = 0.0008)

Results

Children with phonological fragility were randomized to receive the educational protocol (guided arm, n = 87) or not (non-guided arm, n = 78). In the guided arm, oral language development used a short “say and do” type educational protocol designed to maintain visual attention and train the developmental phonology/lexicon/morphosyntax structural links. In contrast, a conservative approach was used in the non-guided arm. A total of 70 guided and 73 non-guided children completed the study. After six months, educated children showed a non-significant increase in their phonology score (p = 0.37), while variations in the scores of the production lexicon (secondary endpoints) were significantly improved (p = 0.0008)

Conclusions

We conclude that short, standardized stimulation of the sensorimotor aspects of language in children formerly born very preterm increases the production lexicon. This protocol improves the language of premature children, especially those with minimal motor skills, with more significant improvement in phonological scores.

ABSTRACTS

Topic: Infectious and Inflammatory Diseases/ Neuroimmunology

EPNS25_523 - Evaluating the Necessity of Extensive Neurological Assessments in Neonates with Enterovirus or Human Parechovirus CNS Infections

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Objectives: The purpose of the study is to describe clinical , neuroradiological , neurophysiological and laboratory features of a group of infants with confirmed Enterovirus (EV) or Human Parechovirus (HPeV) infection of the central nervous system (CNS) occurred in the neonatal period.

Methods: This study was conducted retrospectively, collecting clinical data on study outcome variables between 2016 and 2024 from neonates admitted to ASST Ospedale Metropolitano Niguarda, Milan, Italy. Patients were included if they had confirmed cerebrospinal fluid (CSF) positivity at molecular testing for EV or HPeV. Exclusion criteria included the presence of congenital malformations or a positive CSF culture for bacteria or fungi. General assessment consisted of clinical examination, neurophysiological evaluation, laboratory tests including CSF analysis, and cranial ultrasound (cUS). In some cases, brain magnetic resonance imaging (MRI) was also performed, as well as auditory evoked potentials (AEP) testing after 3 months of age. Clinical outcomes were reassessed after 3 months of follow-up.

Results: Overall, 11 patients with EV (10; 90,9%) or HPeV (1; 9,1%) CNS infection were included. The mean age of patients was 19,6 days of life (range 5–30). Fever (11; 100%), irritability (5; 45,4%) and hyporeactivity (2; 18%) were more frequently reported. Pleocytosis, defined as ≥5 WBC/mm3 in CSF, was detected in 2 cases (18%). MRI and cUS were not altered in any of the infants affected by EV infection. The case affected by HPeV infection showed on brain MRI unilateral single punctate lesions in the left frontal deep white matter, characterized by altered signal with heterogeneous T2 hypointensity, T1 hyperintensity, and water diffusivity restriction on DWI, consistent with acute inflammation. AEPs were normal in all patients. All infants underwent EEG recording, but none showed specific patterns, focal abnormalities as frequent or occasional spikes and sharp waves were observed in 4 cases (36%).

Conclusions: Among this cohort, none of the patients exhibited severe clinical manifestations. Comprehensive evaluations revealed no significant neurological abnormalities. MRI findings were unremarkable in most patients, except for one case. Considering clinical risk stratification could aid in identifying which neonates with confirmed EV or HPeV CNS infections might benefit from extensive diagnostic assessments. While our findings offer valuable insights, the relatively small cohort size remains a limitation of the study. Further investigations involving a larger number of patients may help to confirm the validity of our hypothesis.

ABSTRACTS

Topic: Epilepsy: Diagnosis and Investigations

EPNS25_524 - Safety, Tolerability, Pharmacokinetics, and Efficacy of Fenfluramine in Combination With Cannabidiol: Results From a Phase 1 Study

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Objectives

Dravet syndrome (DS) and Lennox-Gastaut syndrome (LGS) are lifelong developmental and epileptic encephalopathies. Fenfluramine and cannabidiol are approved for the treatment of seizures in DS and LGS in the US, Europe, Israel, and Australia. Cannabidiol's CYP450 inhibitory activity overlaps substantially with fenfluramine-metabolizing CYP450 enzymes. This study assessed the safety, tolerability, pharmacokinetics, and efficacy of fenfluramine and cannabidiol in a small cohort of patients with DS or LGS.

Methods

A phase 1, open-label study (NCT03467113) enrolled patients 2-18 years old with DS or LGS and a stable cannabidiol dose (cannabidiol source was not controlled). Patients had a 4-week baseline phase, ≤4-week titration phase, ≤104-week maintenance phase, and ≤6-month follow-up. In the titration phase, fenfluramine was titrated from 0.2 mg/kg/day to a target dose of 0.7 mg/kg/day (maximum 26 mg/day) and continued throughout maintenance. Safety and tolerability (primary objective), pharmacokinetics, and change in seizure frequency were assessed for fenfluramine and cannabidiol combination.

Results

Nine patients (DS, n=4; LGS, n=5) were enrolled and received ≥1 dose of fenfluramine. Mean treatment duration was 552.0 days. All patients reported ≥1 TEAE; of 62 TEAEs reported, nasopharyngitis (55.6%) and somnolence (44.4%) were most common; no valvular heart disease or pulmonary arterial hypertension were observed during echocardiographic monitoring. No deaths and no discontinuations due to TEAEs were reported. Median pre-dose plasma concentrations for fenfluramine and cannabidiol were 49.7 and 26.6 ng/mL respectively, and the highest concentrations were 72.6 (4-hours post-dose) and 81.3 ng/mL (2-hours post-dose), respectively. In the titration and maintenance periods, median change from baseline in DS convulsive seizure frequency and LGS "drop" seizure frequency was -65.6% and -23.2%, respectively. During the maintenance period, ≥50% of patients were "improved", and no patients worsened according to investigator-rated CGI-I scores.

Conclusions

Fenfluramine 0.2-0.7 mg/kg/day was well tolerated when administered with cannabidiol. These data further support the safe use of fenfluramine and cannabidiol combination.

ABSTRACTS

Topic: Epilepsy: Medical and Surgical treatment

EPNS25_525 - Fenfluramine Efficacy Trajectories in Placebo or Treatment Groups From Randomized Controlled Trial to Open-Label Extension in Patients With Lennox-Gastaut Syndrome

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Objectives

Efficacy trajectories of fenfluramine (FFA) in patients with Lennox-Gastaut syndrome (LGS; a developmental and epileptic encephalopathy) who enrolled in a randomized controlled trial (RCT), were randomized to placebo or FFA during the RCT, and transitioned to FFA in the open-label extension (OLE) are described. The natural history of seizure frequency in enrolled placebo-treated patients is also described.

Methods

Trajectories of efficacy outcomes were assessed retrospectively for patients who completed the 14-week RCT and enrolled in the OLE, transitioning to FFA 0.2 mg/kg/d. Median percentage change from baseline in frequency of seizures associated with a fall (SF) and in generalized tonic-clonic seizures, number of days without SF, SF responder rates (≥50%, ≥75%), and Clinical Global Impression—Improvement (CGI-I) scale (investigator and caregiver) score were assessed.

Results

The RCT-placebo group (n=87, N=263) maintained a consistent median percent change in SF from baseline (-12.6% to -7.2%). Within Month 1 of the OLE (N=247), median percent change from baseline in RCT-placebo (n=85, -29.0%) became numerically comparable to RCT-FFA (n=156, -25.4%). RCT-placebo and RCT-FFA maintained similar SF change from baseline through the end of the OLE. In all other assessed outcomes in the OLE, RCT-placebo and RCT-FFA were numerically comparable in efficacy.

Conclusions

Patients previously randomized to placebo exhibited numerical improvements in efficacy outcomes following transition to the OLE (FFA treatment). Regression to the mean was not observed in RCT-placebo patients, suggesting that changes were not due to extreme events and could be attributed to FFA treatment. The change in SF frequency in RCT-placebo occurred during Month 1 of the OLE, confirming rapid onset of efficacy. Further analysis on time to efficacy in a larger population of patients with LGS who may have been excluded from the RCT/OLE would be beneficial.

ABSTRACTS

Topic: Neurodevelopmental Disorders / Developmental Neuroscience

EPNS25_526 - Effectiveness of a Parent Training Intervention for Children with Comorbid Autism Spectrum Disorder and Behavioral Problems in Alexandria, Egypt

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Objectives

To evaluate the effectiveness of a culturally sensitive parent training intervention for children with comorbid ASD and behavioral problems in a clinic-based setting in Alexandria, Egypt.

Methods

A quasi-experimental study with non-equivalent groups (intervention, non-intervention, 46 each) was conducted targeting parents/caregivers of children aged ≥ 3 years with ASD and having at least one behavioral problem. The intervention group participated in a multi-component group intervention including psychoeducation, parent training and brief cognitive behavioral therapy. Both groups were assessed immediately after program completion (post-1) and 3 months later (post-2). Measured outcomes included caregivers' ASD related knowledge and emotional status, and children's behavioral problems, that were assessed using: ASD knowledge self-report questionnaire, The Arabic Version of Depression Anxiety Stress Scales, The Arabic Version of Strengths and Difficulties Questionnaire, and The Arabic Version of Home Situation Questionnaire for ASD.

Results

Positive effect of the program was evidenced by significant improvement on all outcome measures at post-2. The highest percentage mean change was reported in caregivers' anxiety symptoms (-63.64), followed by caregivers' depression symptoms, child's behavioral problems and caregivers' stress symptoms (-52.63, -45.64 and -38.18, respectively). ASD related knowledge recorded the least percentage mean change (18.18).

Conclusions

The current intervention provided evidence for the effectiveness of an Egyptian group-based parent-focused multi-component intervention in addressing educational and emotional problems of caregivers of children with comorbid ASD and behavioral problems.

ABSTRACTS

Topic: Neurogenetics

EPNS25_528 - Retinal Nerve Fiber Layer Thickness in Friedreich's Ataxia: Longitudinal Observations from the Czech Observational Cohort

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Objectives

This study aimed to document longitudinal changes in retinal nerve fiber layer (RNFL) thickness among patients with Friedreich's ataxia (FA) and to assess preliminary findings related to omaveloxolone (omav) treatment. Patients were longitudinally observed as part of the standardized, multicenter FA natural history study (EFACTS/UNIFAI).

Methods

A total of 41 FA patients underwent 81 optical coherence tomography (OCT) assessments between 2022 and 2025. 70 scans were performed using the Spectralis Heidelberg system and 16 on OptoVue. In five cases, same-day measurements on both devices showed an average inter-device deviation of -0.5 µm (range: -4.5 to +2.5 µm, OptoVue minus Spectralis). The mean patient age was 33 years (range: 8–74). Four pediatric patients from this goup (8–17 years) accounted for 12 assessments, with one initiating omav treatment after reaching the approved age threshold (16+ years).

Longitudinal follow-up included 27 measurements from untreated patients and 14 assessments before and after omav initiation or across multiple treatment visits. Routine OCT follow-ups typically occurred annually. For patients who initiated omav, the first post-treatment scan occurred at a mean interval of 3.4 months (range: 1–7 months) after treatment initiation.

Results

Patients with late-onset FA, characterized by slower disease progression, exhibited relatively stable RNFL thickness with minimal thinning over time. In contrast, those with earlier onset showed ongoing RNFL thinning from childhood or adolescence. Severe visual impairment (visual acuity <0.5) was rare (4 patients) and typically associated with RNFL values of 50–77 µm (mean: 65 µm).

Among untreated individuals, RNFL thickness declined at an average rate of -1.6 µm (range: -11 to +4 µm). In contrast, patients receiving omav showed a mean RNFL change of +0.5 µm (range: -4.5 to +3.8 µm), suggesting stability or slight increases. In a statistical comparison of the Non-Omav and Started Omav groups, overall RNFL thickness did not differ significantly (p=0.789), yet a separate analysis of changes from the previous visit showed a statistically significant difference (p=0.0016), indicating that omaveloxolone may slow RNFL thinning relative to untreated patients.

Conclusions

Early-onset FA is associated with progressive RNFL thinning, whereas late-onset cases demonstrate relative preservation. While visual function remains largely stable, substantial RNFL loss is linked to reduced visual acuity. Unexpectedly, patients receiving omav exhibited stable or slightly increasing RNFL thickness, in contrast to the expected progressive decline in untreated individuals. These preliminary findings warrant further investigation into omav's potential neuroprotective effects on retinal structures in FA.

ABSTRACTS

Topic: Neuromuscular Disorders

EPNS25_529 - FIG4-Related Neuropediatric Phenotypes: Rare And Multifaceted Diagnoses Associated With Particular Protein Changes

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Objectives

Up to date, five neurological phenotypes caused by pathogenic variants affecting the *Factor-Induced Gene 4* (*FIG4*) are described. Bilateral temporooccipital Polymicrogyria and Yunis-Varon syndrome which manifest in childhood, as well as Charcot-Marie-Tooth (CMT) disease type 4J, which can occur in childhood or adulthood. So far, Amyotrophic lateral sclerosis 11 and a combination of CMT 4J and parkinsonism are only described in adults. All *FIG4*-associated diseases are classified as rare. Notably, the severity of *FIG4*-associated phenotypes has a wide range from mild clinical signs to severe disability. The FIG4 protein is localized at the vacuolar membrane and is involved in endolysomal trafficking and autophagy. Molecular markers (of pathophysiological relevance) differentiating between the various clinical manifestations are currently still lacking.

Methods

We retrospectively collected epidemiological, clinical and molecular genetic data sets of five pediatric patients from four different families harbouring biallelic *FIG4* variants. Additionally, the proteomic signature of white blood cells was studied to decipher stratification markers.

Results

Of the five children, two are monozygotic twins presenting with severe developmental delay and mild dystonic movement disorder. Similarly, our third patient demonstrates a profound developmental delay and distinct bradykinesia. Exome sequencing revealed compound heterozygous *FIG4* variants in all three patients. Interestingly, one variant (p.Ile41Thr), of the child presenting with bradykinesia, has already been associated with parkinsonism, but only in adults. In contrast, the fourth patient shows exclusively central nervous system symptoms including epilepsy and the fifth patient displays a combination of central nervous system symptoms and neuropathy, both due to biallelic variants of *FIG4*. Proteomic profiling identified distinct biochemical signatures associated with each phenotype, underscoring the variability of *FIG4* mutations.

Conclusions

With this study, we validate the wide range of clinical signs associated with *FIG4*-related disorders, particularly in childhood, and describe the first pediatric *FIG4* case with distinct bradykinesia as potential symptom of early-onset parkinsonism. Furthermore, we identified corresponding biochemical markers that not only offer valuable insights into the disease's molecular origins but may also pave the way for improved stratification of patients with *FIG4* mutations.

ABSTRACTS

Topic: Miscellaneous

EPNS25_530 - Improving accessibility to cell and gene therapy for rare diseases

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Objectives

Despite growing awareness of rare diseases, knowledge of approved cell & gene treatment (CGT) treatments and their accessibility remains limited. The administrative and logistical challenges involved in managing patient eligibility and treatment initiation also hinder CGT's broader application. Complexity of CGT, and its case-by-case individual character is another limiting factor for its wider use. We evaluated the role of processes in accelerating the access to CGT in practice, including autologous CGT, which are among the most complex treatments.

Methods

The administrative processes for 6 different cell&gene therapies in 20 diagnostic and treatment centers in Europe, from diagnosis to treatment and 2 years follow up, were mapped and evaluated. A total of 52 different processes were required from diagnosis to local treatment or cross-border treatment.

Results

133 patients were evaluated, of whom 29 were eligible for and received approved CGT, which is subject to strict eligibility criteria. Between 6 and 18 months elapsed between diagnosis and initiation of therapy, due to limited experience with CGT and de novo, intense interactions among all stakeholders. Of the 52 processes identified, 29 were specific to CGT, with 21 processes (40%) requiring more than 100 additional hours of effort to establish treatment centers. Additionally, 31 processes (60%) related to the cross-border treatment (diagnosis assessment, treatment proposal, review, and implementation). The allocated CGT team helped clarify responsibilities and coordinated all interactions to speed up processes.

Conclusions

The administrative and logistical burden associated with CGT significantly impacts the scalability of treatment. The complexity of the process, requiring coordination across multiple stakeholders (including diagnostic centers, treatment centers, and payers), increases the time and resources needed to initiate therapy. Therefore, standardization of documentation and establishment of CGT team can improve access to CGT, since effective management of these processes is essential. Where treatment centers lack dedicated CGT teams, external coordination, such as provided by Medasol, can help streamline these tasks. Ensuring proper process management from diagnosis to treatment initiation will facilitate broader access to CGT and support timely, effective treatment for rare disease patients.

ABSTRACTS

Topic: Infectious and Inflammatory Diseases/ Neuroimmunology

EPNS25_532 - Long-Term Clinical and Biological Prognostic Factors of Anti-NMDA Receptor Encephalitis in Children

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Objectives Anti-NMDAR encephalitis (NMDARE) is a severe neurological condition and recently, the NEOS score (NMDAR Encephalitis One-year functional Status) has emerged as a one-year prognostic tool. This study aimed to evaluate NEOS score and biomarkers (NfL, t-Tau, GFAP, serum cytokines) correlation

Methods In this French multicenter observational study, 104 pediatric patients with NMDARE were followed for a minimum of two years. Clinical data and serum/plasma samples were collected. Biomarker levels, measured using electroluminescence MSD S-PLEX, were compared between patients and controls and assessed for correlations with disease activity, mRS, cognitive/language impairment, and recovery status at two years.

Results At a median follow-up of 39.5 months, sixty-eight percent of patients had unfavorable recovery, and 54% had significant cognitive impairment. Both outcomes were strongly associated with younger age at diagnosis (*OR* 6.10 (1.91-27.3) $P < 0.01$ and 5.69 (1.46-27.7) $P = 0.02$, respectively). A higher NEOS score was significantly correlated with increased cognitive impairment (*OR* 2.53 (1.52-4.21), $P < 0.001$), higher mRS scores (*OR* 2.12 (1.34-3.57), $P < 0.01$), and unfavorable recovery at two years (*OR* 2.00 (1.30-3.06), $P = 0.015$). Elevated NfL levels were significantly associated with unfavorable recovery (*OR* 3.62 (1.29-10.9) $P = 0.012$) and severe cognitive impairment (*OR* 3.77 (1.38-10.9) $P = 0.012$) at two years. The combined AUC for NfL and NEOS was significantly higher than the AUCs of NEOS and NfL alone ($P = 0.01$).

Conclusions The NEOS score strongly predicts long-term outcomes in NMDARE, with its predictive value extending beyond the first year mRs prediction. NfL levels at disease onset seems to improve accuracy in predicting poor outcomes, providing valuable information for treatment decisions and future clinical trials

ABSTRACTS

Topic: Neuromuscular Disorders

EPNS25_533 - Interim results from RESPOND: study of nusinersen in children with spinal muscular atrophy previously treated with onasemnogene abeparvovec

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Objectives: RESPOND (NCT04488133) study evaluates nusinersen in children with spinal muscular atrophy (SMA) who have previously received onasemnogene abeparvovec (OA) and have suboptimal clinical status in ≥1 domains at baseline: motor function, swallow/feeding ability, respiratory function, and other. This analysis provides interim clinical, neurofilament, and safety findings.

Methods: The interim set included children who received ≥1 dose of nusinersen and had the opportunity to complete the Day (D) 302 assessment (data-cut: 18 Oct 2023). Analysis was stratified by age and *survival of motor neuron* 2 (*SMN2*) copy number. All participants who received ≥1 dose of nusinersen comprised the safety set.

Results: Of 37 children who reached D302, 21 were age ≤9 months at first nusinersen dose with two *SMN2* copies (group 1), 13 were age >9 months with two *SMN2* copies (group 2), and three were age >9 months with three *SMN2* copies (group 3). Median age at baseline in each group was 8.2, 15.9, and 34.2 months, respectively. All children were symptomatic at OA dosing. The safety set included 46 children on study for a median of 562 days.

Mean change from baseline to D302 in total Hammersmith Infant Neurological Exam section 2 (HINE-2) score was +8.7 points in group 1 and +6.9 points in group 2 (not calculated in group 3 due to small sample size). Mean D302 HINE-2 score was 11.6 and 15.2 points in each group, respectively. Of 27 children unable to sit at baseline, 14 (52%) achieved sitting by D302. Baseline plasma neurofilament light chain (NfL) levels were elevated, suggestive of active neurodegeneration at study entry (group 1 mean, 132.0 pg/mL; group 2 mean, 121.0 pg/mL). Mean NfL levels decreased from baseline to D302 by 77% and 82% in groups 1 and 2, with consistent patterns of decline by age and time from OA dose. Mean compound muscle action potential amplitudes increased from baseline to D302 for ulnar-abductor digiti minimi (mean change from baseline, +0.4 mV in both groups) and peroneal-tibialis anterior (group 1, +0.7 mV; group 2, +0.5 mV). Adverse events (AEs) occurred in 37 (80%) participants. Three (7%) children had a nusinersen-related mild AE (proteinuria). No serious AEs were considered related to treatment: all children continued to receive nusinersen.

Conclusions: Continued improvements in clinical and biomarker outcomes support the benefit of nusinersen in children with suboptimal clinical response to OA. Safety was consistent with nusinersen's safety profile.

ABSTRACTS

Topic: Epilepsy: Medical and Surgical treatment

EPNS25_536 - Twelve month review of Infantile Spasm patients treated with Combination Therapy – Time Matters

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Objectives

Infantile spasms (IS) are seizures associated with a severe developmental and epileptic encephalopathy, occurring mainly in children aged 3-18 months. Early diagnosis is key to treatment and better outcomes. We present a 12 month case review of IS patients.

Methods

This project reviews seventeen existing patients who presented with IS. We reviewed the epidemiology, aetiology, diagnosis and management of these patients, and response to treatment in a tertiary centre from January to December 2024.

Results

Seventeen patients, seven females (41%) and ten males (59%), presented with IS at a median age of 6 months ±3.43SD. At presentation, the median weight was 7.03kg ±2.03SD, and median head circumference was 43cm ±4.10SD. Fifteen (88%) patients presented with Typical Spasms, whilst two (12%) presented with Atypical Spasms.

Three (18%) patients had a family history of Epilepsy, with no other neurological background. Eleven (65%) had a background of seizures before their diagnosis of IS. Five (29%) patients had a significant adverse perinatal history (prematurity associated with hypoxic-ischemic encephalopathy (HIE), and one case of hemimegaloencephaly). All patients underwent magnetic resonance imaging (MRI), of whom eight (47%) had abnormal results. MRI revealed four patients (24%) had severe HIE. The remaining four (24%) showed significant findings, suggestive of Leigh Syndrome, Lissencephaly, Haemorrhagic Cystic Encephalomalacia, and Left Hemimegaloencephaly dysplasia. Hypsarrhythmia was identified in twelve (71%) patients, and modified hypsarrhythmia in five (29%). Fifteen (88%) patients received genetic testing, revealing variants in seven (47%) including: Mosaic PIKC3A, William Syndrome, SCN8A, KCNT1, Trisomy 21, and Leigh Syndrome.

Sixteen (94%) patients received combination therapy (Vigabatrin and Prednisolone), as per the ICISS protocol, and one (6%) was treated with Vigabatrin monotherapy. After treatment, all patients experienced resolution of clinical spasms and hypsarrhythmia. Spasms resolved immediately in twelve (71%) patients, while five (29%) took more than one week– the remaining five patients had HIE and Leigh Syndrome, and one was treated with vigabatrin monotherapy.

Conclusions

The findings highlight the importance of early IS identification for prompt treatment and optimal seizure control. This project demonstrates that combination therapy, following the ICISS protocol, is effective in achieving early seizure control.

ABSTRACTS

Topic: Epilepsy: Medical and Surgical treatment

EPNS25_539 - Why childhood absence epilepsy is not always a benign epilepsy: a multicentric retrospective study in Flanders

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Objectives

Childhood absence epilepsy (CAE) is often considered a well-treatable epilepsy syndrome with minimal long-term developmental impact. This study aimed to review clinical outcomes and experiences in four university hospitals in Flanders, Belgium.

Methods

Retrospective data were obtained from the Flemish EpiCARE register, collected and managed using REDCap electronic data capture tools hosted at KU Leuven. The cohort included patients diagnosed with CAE up to May 1, 2024, treated at the university hospitals of Antwerp, Brussels, Ghent, or Leuven. Outcome measures included age of onset, response to first-line antiseizure medications (ASM), seizure freedom (defined as no seizures for ≥6 months at the last follow-up), and neurodevelopmental functioning (education, intellectual abilities, learning problems, and neuropsychiatric comorbidities). Descriptive analyses were performed using SPSS v29.

Results

Among 2014 patients in the database, 109 (5.4%) were diagnosed with CAE, with a mean age of onset of 5.2 years. Despite standard-of-care pharmacological treatment, 28% of patients failed to achieve seizure freedom. Patients who reached seizure freedom tried an average of 2.4 different ASMs, while non-seizure-free patients were treated with 3.7 different ASMs on average. Valproate was the most prescribed ASM. Intellectual disabilities (IQ < 80) were identified in 43% of formally tested patients. Learning problems were reported in 15% of cases, and 40% of patients required adapted education with additional support. Among those receiving educational support, 63% achieved seizure freedom compared to 75% of children in regular education without support, although this difference was not statistically significant. Neuropsychiatric comorbidities, primarily autism spectrum disorder and attention-deficit/hyperactivity disorder, were observed in 15% of patients.

Conclusions

Despite its reputation as a benign epilepsy syndrome, CAE is frequently associated with significant challenges in neurodevelopmental functioning and academic achievement, even with optimal treatment. These findings highlight the importance of routine neuropsychological and psychiatric screening in children with CAE to facilitate early detection and intervention. Study limitations include referral and selection bias due to data collection in tertiary care centers and incomplete data registration.

ABSTRACTS

Topic: Neurogenetics

EPNS25_540 - Diagnostic Challenges in Pontocerebellar Hypoplasia Type 11: A Case Report

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Objectives

Pontocerebellar hypoplasias (PCHs) are a group of prenatal-onset neurodegenerative disorders that primarily affect the cerebellum and brainstem within the central nervous system. The TBC1D23 gene, which plays a critical role in intracellular endosomal vesicle trafficking, is a very rare cause of PCHs. This study presents a rare case of a patient with speech delay and gait instability diagnosed with pontocerebellar hypoplasia type 11 due to a homozygous mutation in the TBC1D23 gene.

Methods

This presentation is designed as a case report.

Results

A six-year-old male patient first presented to our clinic at the age of three years with complaints of speech delay, gait instability and frequent falls. Developmental delay was observed at all milestones. Apart from parental consanguinity, there were no other significant findings in the patient's medical history. Neurological examination revealed limited eye contact, restricted shared attention, microcephaly, dysmorphic facial features, ataxia and hyperactive deep tendon reflexes. Baseline biochemical and metabolic assessments were normal. Brain magnetic resonance imaging (MRI) revealed cerebellar hypoplasia and megacisterna magna. Genetic analysis, including karyotyping (46,XY), fragile X testing and chromosomal microarray (array-CGH), showed normal results. In addition, enzymatic assessments for neuronal ceroid lipofuscinosis (NCL) types 1 and 2 were unremarkable. Whole-exome sequencing identified a homozygous mutation c.1858C>T (p.Arg620*) in the TBC1D23 gene, confirming the diagnosis of pontocerebellar hypoplasia type 11.

Conclusions

PCHs are a group of disorders with a broad genotypic and phenotypic spectrum that may overlap with other clinical conditions. Therefore, they should be considered in the differential diagnosis of similar presentations and advanced genetic studies are recommended.

ABSTRACTS

Topic: Infectious and Inflammatory Diseases/ Neuroimmunology

EPNS25_541 - Early Identification of Individuals at Risk for Multiple Sclerosis by Quantification of EBNA1381-452-specific Antibody Titers after Primary Epstein-Barr Virus Infection

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Objectives

Multiple sclerosis (MS) is a chronic immune-mediated, demyelinating disease of the central nervous system (CNS), which occurs in approximately 3-5% of all cases in children. Currently there is no biomarker available to assess the individual risk of developing MS. Mechanisms initiated by an immune response to Epstein-Barr-Virus (EBV) are considered to play a critical role in the development of MS, since EBV encodes for the EBNA-$1_{381-452}$-region, which initiates autoreactive IgG antibody responses against distinct CNS-derived proteins.
We investigated whether EBNA-$1_{381-452}$-specific IgG antibodies in children and adults could serve as a biomarker for identification of individuals at risk for MS.

Methods

This multi-centered, retrospective case-control-study included 704 EBV-EBNA1-seropositive relapsing remitting MS patients and 5381 EBV-EBNA1-seropositive control individuals. Longitudinal follow-ups over the course of 3 years, starting from time of EBV seroconversion, were available for 324 adult MS patients and 324 controls. EBNA-$1_{381-452}$-specific IgG antibody titers were quantified from all plasma samples using a newly developed peptide-based enzyme-linked immunosorbent assay (ELISA).

Results

Adults and children with MS presented with significantly higher EBNA-$1_{381-452}$-specific IgG antibody titers at the time of MS diagnosis compared to EBNA-$1_{381-452}$ seropositive controls ($P < 0.0001$). In adults significantly increased EBNA-$1_{381-452}$-specific IgG antibody titers were detected as early as 9 months after EBV seroconversion (OR: 5,7; 95% CI: 4.1-8.1; $P < 0.0001$), which corresponds to a median of 5.4 years before the onset of the disease. Continuously high EBNA-$1_{381-452}$-specific IgG antibody titers were associated with a more rapid development of MS after EBV seroconversion (4.38 years vs. 8.33 years, $P < 0.0001$).

Conclusions

Quantification of EBNA-$1_{381-452}$-specific IgG antibody levels provides a reliable prognostic biomarker to assess an individual's risk for the development of MS. This may present the opportunity for early treatment in prodromal stages of MS, which could delay demyelination and its consequences.

ABSTRACTS

Topic: Infectious and Inflammatory Diseases/ Neuroimmunology

EPNS25_542 - Therapeutic apheresis: Immunoadsorption or plasmapheresis - which is better to choose?

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Objectives

Plasmapheresis (PEX) and immunoadsorption (IA) are two therapeutic procedures used to treat antibody-mediated diseases by removing blood components from the blood. In IA, cytokines and immunoglobulins are eliminated, while PEX involves a complete plasma exchange [1]. However, there is insufficient data to determine which of the methods should be favoured. This study therefore compares IA with PEX in terms of indication, course of therapy and outcome.

[1] Connelly-Smith L, Alquist CR, Aqui NA*, et al.* Guidelines on the Use of Therapeutic Apheresis in Clinical Practice - Evidence-Based Approach from the Writing Committee of the American Society for Apheresis: The Ninth Special Issue. J Clin Apher 2023; 38(2): 77–278

Methods

In a retrospective study, 14 children (female: 10; age: m=10,1 years, range: 4–15) were examined between the years 2004–2024 in a multi-site university paediatric centre as well as two paediatric ICUs. The first IA was carried out in July 2014. The outcome was measured using the Expanded Disability Status Scale Score (EDSS).

Results

6 children received an IA, 9 a PEX (one child was switched from PEX to IA). One patient with PEX showed positive MOG antibodies, all other patients with PEX had no detectable antibodies. In the patients with IA, five showed detectable specific antibodies, mainly MOG antibodies. Per episode, 4-8 cycles of PEX or 4-6 cycles of IA were performed. The underlying diseases were similar for both methods (MS, Guillain-Barre syndrome, ADEM, limbic encephalitis, NMOSD, MOG-AD). All patients with PEX had previously received methylprednisolone and immunoglobuline therapy, whereas only one patient with IA had previously received methylprednisolone. With regard to outcome, 5 patients with PEX and 6 patients with IA showed an EDSS of zero (=normal neurologic examination). Two patients with PEX showed an EDSS of 8–9. Zero patients with IA showed an EDSS higher than zero. One patient who had received PEX died because of his severe progressive disease. Before the disease, all patients had an EDSS score of 0. There were no complications during the PEX, one patient with the IA was suspected of having a catheter infection.

Conclusions

Immunoadsorption is a safe and effective early escalation therapy and can be used in the same way as plasmapheresis. Further multi-centre studies are needed to further clarify and improve the prognosis of the outcome and the possibilities of immunotherapies for inflammatory demyelinating diseases.

ABSTRACTS

Topic: Neurometabolic Disorders

EPNS25_543 - MCT8 Deficiency, Arginase 1 deficiency and Neurotransmitter disorders: Identifying patients through hospital coding?

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Introduction

MCT8 deficiency (MCT8), arginase 1 (ARG) deficiency and neurotransmitter disorders (NTD) such as Aromatic L-Amino Acid Decarboxylase (AADC) deficiency are treatable conditions and known cerebral palsy (CP) mimics. Clinical features overlap.

We previously identified potential NTD patients through the generation of a patient list utilising hospital Structured Query Learning (SQL) coding data and reviewing patient records [DOI:10.23937/2643-4571/1710048].

Objectives

Are patients being investigated for MCT8 deficiency and arginase 1 deficiency?

Methods

SQL coding profiled potential patients with NTD at a UK tertiary paediatric neurology centre. Patient records of a sample of 39 patients identified were reviewed to see what testing has been performed and in particular if thyroid function testing for MCT8 or metabolic testing for ARG1 had been performed as clinical features overlap with NTDs.

Results

29/39 patients had a confirmed diagnosis: 8 had a metabolic diagnosis, 8 a genetic diagnosis and 9 had cerebral palsy with a history and MRI consistent with HIE. 10 patients were 'undiagnosed'. All these patients had genetic testing and MRI brain performed. Testing for plasma amino acids was performed in 9/10, neurotransmitters in 4/10 and T3 level in 1/10. 5/10 of the 'undiagnosed' patients had a normal MRI brain but none had testing for T3 levels (0/5), 2/5 had neurotransmitters and 3 /5 had plasma amino acids tested.

Conclusions

All children with potential CP mimic are investigated with MRI brain and genetics, most for ARG1 (90%), but only a few for MCT8 (10%) and NTD (40%). No known NTD, MCT8 and ARG1 patients were identified. As the disorders are rare, our sample was too small. Furthermore, hospital coding may not detect symptoms such as autonomic dysfunction, tachycardia, and faltering growth which may point to these diagnoses.

However, we highlight that even if the MRI brain and genetics are sent, thyroid function with T3 levels, plasma amino acids and CSF neurotransmitters are inconsistently tested. This is especially important when the MRI brain is normal or non-specific with findings like delayed myelination as NTD, MCT8 and ARG1 are treatable.

ABSTRACTS

Topic: Epilepsy: Medical and Surgical treatment

EPNS25_545 - Safety and Effectiveness of Fenfluramine for the Treatment of Seizures in Lennox-Gastaut Syndrome: Results From the Final Analysis of an Open-Label Extension Study

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Objectives: To describe the final long-term safety and effectiveness data from a fenfluramine (FFA) open-label extension (OLE) study in participants with Lennox-Gastaut syndrome (LGS) (NCT03355209)

Methods: Participants started on FFA 0.2 mg/kg/day, then flexibly titrated to effectiveness/tolerability after 1 month. Relevant outcomes include incidence of treatment-emergent adverse events (TEAEs) and percentage change from baseline in seizures associated with a drop. Wilcoxon signed-rank test was used for median percent change from baseline (from Month 1–end of study) in seizures associated with a drop. Additional methods have been described [Knupp 2023 Epilepsia].

Results: 247 participants (mean age 14.3±7.6 years) were enrolled in the OLE; 158/244 completed the study, 86/244 discontinued FFA (13/86 due to adverse event), and 3 participants rolled over into a continuation study, but disposition information was not reported. Median treatment duration was 364 days (range, 19-537). 205 (83.0%) participants experienced ≥1 treatment-emergent adverse event (TEAE). Of 41 participants with ≥1 serious TEAE, 12 had ≥1 related to FFA. TEAEs reported in ≥10% of participants were: decreased appetite (16.2%), fatigue (13.4%), nasopharyngitis (12.6%), seizure (10.9%), pyrexia (10.1%). No cases of valvular heart disease or pulmonary arterial hypertension were observed. Median decrease in frequency of seizures resulting in drop over the OLE (n=241) was 29.5% (P<0.0001).

Conclusions: In this final analysis of an OLE study in participants with LGS , FFA was generally well tolerated with no new safety signals. FFA was associated with a sustained reduction in seizures associated with a drop, confirming FFA as an important treatment option for patients with LGS.

ABSTRACTS

Topic: Neurometabolic Disorders

EPNS25_546 - Tango2 deficiency disorder in a cohort of italian chidren

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Objectives

TANGO2 Deficiency Disorder (TDD) is an autosomal recessive condition first described in 2016, characterized by neurodevelopmental delay, movement disorders, epilepsy, hypothyroidism, and episodic, life-threatening metabolic crises triggered by stressors such as illness or prolonged fasting. These crises may include rhabdomyolysis and cardiac arrhythmias, which often lead to fatal outcomes. The precise function of TANGO2 remains unknown, but it is hypothesized to be involved in lipid homeostasis and endoplasmic reticulum-to-Golgi transport, with secondary effects on mitochondrial energy metabolism.

Methods

We collected data from an Italian cohort of children between June 2023 and December 2024. Information was gathered through a review of medical records.

Results

Data were collected from five patients (40% female) living across the country. The median age at the time of data collection was 8 years, while the median age at onset was 10.5 months, with the exception of a sibling who is currently asymptomatic. All patients received genetic confirmation of a 22q11.2 deletion (heterozygous deletion of TANGO2). Four out of five patients displayed phenotypic variability, ranging from progressive developmental delay, ataxia, dystonia, and speech difficulties, to metabolic crises with cardiac arrest in two patients (fatal in one, who died at 13 months of age). Two out of five patients had seizures, and three out of five patients presented with "Tango spells," which are transient and episodic symptoms including balance and coordination difficulties, ataxia, movement disorders, dystonia, exotropia, slurred speech and fatigue, often triggered by warm weather, exertion, or decreased oral intake. Brain MRI performed on three out of five patients revealed nonspecific findings such as mild diffuse ventriculomegaly, cerebral volume loss, and reduced white matter. Metabolic tests at baseline were normal, except for one patient with hypothyroidism. Management included daily supplementation with a multivitamin containing all eight B vitamins, which resulted in a reduction of metabolic crises and improvement in developmental outcomes.

Conclusions

Our experience with the Italian cohort of TDD confirms the phenotypic variability of this disorder and highlights the importance of early diagnosis and timely initiation of supportive therapies that can help to reduce mortality and to improve quality of life for theese patients. Additionally, it is crucial to consider the possibility of TANGO2 involvement in patients presenting with neurodevelopmental disorders and paroxysmal episodes, even in the absence of clear metabolic crises.

ABSTRACTS

Topic: Infectious and Inflammatory Diseases/ Neuroimmunology

EPNS25_547 - Neurological Manifestations of Gluten Sensitivity in Children and Adolescents

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Objectives

Neurological manifestations of gluten sensitivity (GS), of which gluten ataxia (GA) is the most common, are well-recognised in adults, with very limited reports in children. We present our experience in children and young people (CYP) seen with suspected GS, mainly GA, over a 5-year period.

Methods

Retrospective case note analysis was performed on clinical, serological and neuroimaging data of 21 CYP seen in our specialist ataxia referral centre with suspected GS.

Results

15 female and 6 male CYP (range: 6-15 years, median: 12 years) were referred to our specialist ataxia clinic. All 21 patients had motor coordination/balance difficulties and/or ataxia. Headaches were present in 11/21 CYP (57%), sensory neuropathic symptoms in 6/21 CYP (29%), and postural dizziness suggestive of autonomic dysfunction in 7/21 (33%). 9/21 CYP (43%) had autism spectrum disorder (ASD). Other reported problems included tremors, attention and concentration difficulties, sensory/visual/auditory processing difficulties, dyslexia and fatigue. Family history of GS was present in 8/21 CYP (38%). Serological abnormalities were present in all 21 CYP, with raised antibodies: antigliadin in 16/21 (76%), transglutaminase-6 in 12/21 (57%), transglutaminase-2 in 7/21 (33%), and endomysial in 4/21 (19%). One CYP had cerebellar atrophy. MR Spectroscopy of the cerebellum (cerebellar vermis and hemisphere) showed a reduced N-acetylaspartate: Creatine (NAA/Cr) ratio (<1) in 15/21 (71%). 5/21 (24%) had coeliac disease. 19/21 (90%) received a gluten-free diet (GFD). Only 1 CYP received immunomodulation. 14/19 (74%) of CYP reported improvement of symptoms on GFD.

Conclusions

In this series, we present the clinical, serological and neuroimaging profile of 21 children with probable neurological manifestations of GS, coexisting or independent of coeliac disease. Diagnosis should be considered in the presence of motor coordination difficulties with abnormal serology and MRS of the cerebellum. Raised antigliadin and/or transgutaminase-6 antibodies are helpful in making the diagnosis. Early diagnosis of gluten ataxia is important, as it is a treatable cause of childhood ataxia. High index of clinical suspicion and using the right serological tests and neuroimaging protocols for diagnosis is recommended. Improvement with GFD was demonstrated in the majority. Further follow-up will help in defining the natural history and neurological phenotype of GS in CYP.

ABSTRACTS

Topic: Cerebrovascular Disorders

EPNS25_549 - Associated factors, determination of etiology and neurological outcomes in neonatal and childhood haemorrhagic strokes

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Objectives

Pediatric haemorrhagic stroke is a rare condition compared to the adult age group, yet it results in mortality or causes patients to live with neurological deficits for many years. In this study, we aimed to evaluate clinically and radiologically patients diagnosed with hemorrhagic stroke in childhood.

Methods

We retrospectively reviewed the patients with haemorrhagic stroke during neonatal period and childhood diagnosed and followed-up at Hacettepe University İhsan Doğramacı Children's Hospital between 2000 and 2023. We studied demographic characteristics, neurological examination findings, risk factors, neuroradiological findings and outcome aiming to reveal clinical and radiological features that could predict prognosis and neurological outcome. Patients with prematurity, history of major trauma, central nervous system neoplasia, ischemic stroke and hemorrhagic transformation of synovenous thrombosis were excluded.

Results

In our study, 61 childhood and five neonatal cases were included. The median age at diagnosis in childhood was seven years. Patients most commonly presented with focal neurological findings (55.7%) and altered mental status (34.4%). Haematological (36.1%) and vascular risk factors (29.5%) were the most common etiological factors. Haemorrhage was frequently intraparenchymal, mostly involving the frontal lobe (32.7%). Stroke-related mortality was observed in 30.5% of patients. Cerebral oedema treatment (72.4%) was the most common treatment. Presence of a known disease, male gender, GCS <8, presence of subarachnoid haemorrhage, and increased haemorrhage size were associated with poor outcome and mortality. The median age at diagnosis in the neonatal group was 17 days. Hematological risk factors were detected in three of these patients. One patient resulted in neurological deficit, one patient developed epilepsy, and one patient died.

Conclusions

Our study revealed that patients with pediatric hemorrhagic stroke had a heterogeneous etiological profile, vascular and hematological etiology as the most common causes. Although haemorrhagic stroke is not common in the pediatric age group, it is a neurological disease with serious consequences. Timely diagnosis of stroke is of critical importance; clarification of the etiology after diagnosis will be decisive in guiding the treatment and predicting the course of the disease and recurrences.

ABSTRACTS

Topic: Epilepsy: Diagnosis and Investigations

EPNS25_553 - Comparison of Sleep Scoring with Video-Electroencephalography Monitoring and Polysomnography in a Pediatric Epileptology Unit

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Objectives

In academic research and clinical studies conducted in pediatric epileptology units, sleep assessment using polysomnography is limited due to the discomfort caused by the large number of electrodes on the patient and the time required to manually score the recordings in 30-second periods. The aim of our study is to investigate the reliability and coherence of sleep scoring using video electroencephalography (EEG) monitoring in the pediatric epileptology unit and to compare it with standard polysomnographic sleep scoring.

Methods

We calculated the agreement between two sleep scoring methods using single-night recordings with 21-electrode video-EEG or polysomnography in 30 pediatric patients admitted to our pediatric epileptology unit. Sleep recordings were scored manually by an experienced epileptologist using polysomnography and by two pediatric neurologists using video-EEG recordings, according to the American Academy of Sleep Medicine 2017 guidelines. The number and distribution of sleep cycles, total sleep time, sleep efficiency, NREM and REM sleep stage latencies, sleep latency, wake after sleep onset, and sleep stage transitions were assessed. The intraclass correlation coefficient test was used to assess inter-rater agreement.

Results

There was very good inter-rater agreement for all sleep parameters according to the interclass correlation coefficient. (0.81-1.0). While the lowest agreement was found in the N1 sleep stage (0.88), the highest agreement was observed in the N3 sleep stage (0.96).

Conclusions

Our study shows that sleep scoring with video electroencephalography (EEG) monitoring is compatible with manual polysomnography staging and suggests that video EEG may be an acceptable alternative for macrostructural sleep studies in patients hospitalised in epileptology units.

ABSTRACTS

Topic: Fetal and Neonatal Neurology

EPNS25_554 - Precision dosing of mTOR inhibitors in tuberous sclerosis complex, implications for fetal treatment of hydrops fetalis

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Objectives

mTOR inhibitors (mTORi, sirolimus and everolimus) are disease-modifying treatments in tuberous sclerosis complex (TSC). Recent case reports have noted the improvement of severe TSC fetal findings (including heart failure) with maternal treatment with mTORi. Without treatment, cardiac failure leading to hydrops fetalis may occur. Additionally, clinical trials are investigating if mTORi treatment can be a preventative for TSC. However, the optimal dosing of mTORis in the perinatal period is unknown.

Methods

mTORi dosing and blood levels were collected from two cohorts: infants treated with dosing performed via standard of care (N=13) and infants with dosing informed by pharmacokinetic dosing models (N=5). All consented to separate studies but had similar blood levels and dosing collected. Groups were compared using t-tests, ANOVA, and logistic regression as appropriate. Additionally, a case was reviewed in which precision dosing of sirolimus was used in pregnancy to reverse hydrops fetalis.

Results

In infants, precision dosing improves the time of mTORi levels in the goal range (94% vs 53%) and reduces the time to target trough level from 63.6 +/- 52.0 days to 9.8 +/- 3.8 days (p=0.05). As precision dosing improved infant treatment, we used this model in a case where a woman with twin gestation presented with fetal hydrops due to cardiac rhabdomyomas at 28 weeks gestation. The family was initially counseled about imminent fetal demise. Maternal sirolimus was started at 3 mg/m^2/day and rapidly increased per the precision model to 6 mg/m2/day. Therapeutic mTORi levels were obtained within 1 week of discovering the fetal hydrops and maintained throughout the pregnancy. Both twins were delivered with no need for support. Maternal and infant sirolimus blood levels are nearly identical at delivery (9.2 ng/ml in maternal venous blood at 1407 and 8.0 ng/ml in infant venous blood at 1556).

Conclusions

In vulnerable TSC patients, especially infants and pregnant women, time to achieving a therapeutic mTORi dose is crucial. Precision dosing of mTORis allows for obtaining target levels sooner and improves the time spent in the therapeutic range. In one case, rapid achievement of therapeutic mTORi levels was obtained and resulted in the birth of an infant without support who was thought to have irreversible heart failure. Future work will determine if precision dosing improves outcomes and if a global model can be made for widespread use.

ABSTRACTS

Topic: Epilepsy: Medical and Surgical treatment

EPNS25_555 - Experience in treating children with epileptic encephalopathy with CSWS

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Objectives The aim of our study was to evaluate the efficacy of methylprednisolone hormone therapy in children with DEE and CSWS in reducing seizure frequency and improving cognitive function.
Methods Between 2015-2024, 24 children with the CSWS pattern on EEG were observed. All children received methylprednisolone pulse therapy at a dose of 30 mg/kg for 5 days. Additionally, the patients took other anticonvulsants.
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Results The clinical picture showed: speech development disorder in 16 children (66%), cognitive development disorder in 24 (100%), autism spectrum in 9 (40%), cerebral palsy in 1 (4%), frequently resistant seizures in 14 (58%), no seizures but autism spectrum in 5 (21%), and seizures at onset with subsequent relief but persistent CSWS on EEG in 5 (25%). Structural changes were detected on MRI in 10 (42%).
All children received methylprednisolone, which demonstrated high efficacy in reducing seizures in 67% of patients. However, despite combined antiepileptic drugs and methylprednisolone, most children had persistent CSWS on EEG.
Conclusions Methylprednisolone pulse therapy was effective in controlling seizures, but EEG patterns of CSWS persisted long-term. Although seizure reduction occurred, CSWS on EEG and cognitive impairment remained..

ABSTRACTS

Topic: Basic Science

EPNS25_556 - Pathological mechanism underlying epilepsy in ZEB2 variants: neurons from induced pluripotent stem cells (iPSCs) as a reliable model

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Objectives Our research group has identified a distinctive electroclinical pattern in Mowat-Wilson syndrome (MWS), a genetic disorder caused by *ZEB2* haploinsufficiency (Ricci et al. 2021, Cordelli et al. 2012). Epilepsy in MWS appears to have a well-defined genetic origin, independent of brain malformations. So far, the pathological mechanisms underlying epilepsy in *ZEB2* variants have only been investigated using mouse models. This study aims to gain a deeper understanding of epilepsy pathophysiology in MWS by analyzing the morphology, gene expression profiles, and electrophysiological properties of neurons derived from induced pluripotent stem cells (iPSCs) of patients with pathogenic *ZEB2* variants.

Methods The study was conducted in three phases. First, iPSC lines were generated by reprogramming peripheral blood mononuclear cells (PBMCs) from four patients and two age- and sex-matched controls. Quality control assessments included morphology evaluation, loss of reprogramming factors, markers of undifferentiated state, pluripotency analysis, and genetic screening. In the second phase, neural progenitors were obtained and analyzed for their morphology and transcriptomic profiles. Finally, the differentiated neurons were evaluated in terms of morphology, gene expression profiles, and electrophysiological properties.

Results Quality control tests confirmed the reliability of our iPSC and iPSC-derived neural models. Cells with *ZEB2* variants exhibited distinct differences from control cells in both morphology and transcriptomic profiles. Notably, the expression of key epilepsy-related genes (e.g., *CACNB1, KCNN3, GABBR2*) was impaired. The severity of morphological abnormalities appeared to correlate with the degree of transcriptomic dysregulation. Electrophysiological studies are currently ongoing.

Conclusions this research provides some important preliminary data that may be useful to build more extensive studies on *ZEB2*-mutated neurons bringing us closer to possible future precision therapy hypotheses.

ABSTRACTS

Topic: Neurogenetics

EPNS25_557 - Neurodevelopmental Trends in SARA and mFARS among Czech Pediatric Friedreich's Ataxia and Healthy Controls: A 3-Year Cohort Analysis

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Objectives

We aimed to compare scores on the Scale for the Assessment and Rating of Ataxia (SARA) and the modified Friedreich's Ataxia Rating Scale (mFARS) between pediatric patients with Friedreich's ataxia (FA) and normally developing children, contextualizing these findings within a larger FA cohort in the Czech Republic.

Methods

We analyzed data collected since mid-2021 from a Czech registry of unique FA patients (n=45; six under 18 at first evaluation) and cross-sectional assessments of normally developing controls (n=23; 22 children). Pediatric status was defined as under 18 years.

SARA total scores (range: 0–40) were derived from eight subitems, while mFARS total scores (range: 0–93) included bulbar, upper-limb, lower-limb, and upright stability subscores. Mean SARA and mFARS values, along with age ranges, were compared between pediatric and total cohorts. Most FA participants had repeated assessments.

Results

Among pediatric normally developing controls (n=22; mean age: 6.4 years, range: 3–10), SARA scores averaged 3.6 (range: 0–9.5). Scores trended toward zero by late childhood with initially mild-to-moderate elevations in stance (primarily tandem), walking, speech, and fast alternating hand movements. mFARS scores averaged 15.2 (range: 0.5–31.8), with mild subscale elevations that gradually decreased with age—upright stability improving by age 5, speech by age 7, and upper-limb coordination by age 10—before generally reaching near-zero values. In the full normally developing control cohort (n=23, mean age: 7.6 years, range: 3–33), SARA and mFARS remained near minimal beyond age six to seven.

In contrast, pediatric FA patients (n=6, mean age: 13.7 years, range: 8–16) had a mean SARA of 16 (range: 8–31), with no approach to normally developing scores upon follow-up. mFARS also confirmed significant deficits, progressing most rapidly in upright stability, followed by lower-limb coordination, upper-limb coordination, and later bulbar symptoms. Across the full FA cohort (mean age: 35.4 years, range: 8–72), during follow-ups, SARA averaged 23 (range: 7–40, n=156), and mFARS averaged 56 (range: 23–93, n=50).

Conclusions

Mild ataxia-like features on SARA/mFARS can initially manifest in normally developing children under seven before CNS maturation. Lower-limb functions tend to normalize first, followed by upper limbs, with speech being the last to stabilize. However, pediatric FA patients never reached near-zero values, underscoring genuine pathological progression that worsens into adulthood – SARA and mFARS are therefore feasible in younger cohorts with some methodological adjustments for the youngest age groups. Emerging digital biomarkers may enhance early assessments.

ABSTRACTS

Topic: Neuromuscular Disorders

EPNS25_558 - Clinical and Molecular Perspectives in Myopathy: Next Generation Sequencing Reveals Two Candidate Genes and 17 Novel Variants

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Objectives

Myopathies are neuromuscular diseases caused by disorders affecting skeletal muscle. Hereditary myopathies, which are subdivided into congenital myopathy, muscular dystrophy, metabolic/mitochondrial myopathy, canalopathy and myotonia, have many phenotypes. Exome sequencing is frequently used to determine the genetic etiology among more than a hundred genes with known phenotype association. We aimed to determine the genetic etiology by clinical and whole exome sequencing (CES/WES) in patients with a diagnosis of myopathy.

Methods

Sixteen cases, diagnosed with myopathy or muscular dystrophy (MMD) by retrospective CES or WES, were included. In addition, prospective WES were performed on 24 cases from 22 families. The variants detected in the retrospective/prospective studies were confirmed in the cases and family segregations were performed with Sanger sequencing. In silico protein modeling for *novel* missense variants demonstrated the damaging effects.

Results

Ten patients had muscular dystrophy (*ANO5*, *CAPN3*, *CHKB*, *COL6A1*, *COL6A3*, *DMD*, *FKRP*, *GMPPB*, *HMGCR*, *SGCG*), seven had metabolic myopathy (*ACADS*, *ENO3*, *MAN2B1*, *PDHA1*, *PFKM*, *SLC22A5*, *TAFAZZIN*), six had congenital myopathy (*ACTA1*, *MYH2*, *MYH7*, *RYR1*, *TTN*) and five had variants in mitochondrial myopathy-related genes (*ACAD9*, *mt-TK*, *NDUFS4*, *NUBPL*, *OPA1*). In two different patients, homozygous pathogenic variants associated with Limb-Girdle congenital myasthenia (*GFPT1*) and Crisponi/Cold-Induced Sweating Syndrome 1 (*CRLF1*) were found to be involved in the etiology. In two cases, homozygous variants were found in *SPNS1* and *FBXO30* with unknown phenotype association in humans. In three patients, variants associated with different entities in addition to myopathy were observed with the blend phenotypes. Seventeen of the 39 different variants detected were reported as *novel*.

Conclusions

Clinical and molecular findings of MMD were presented and the contribution of CES/WES in the identification of new phenotypes/candidate genes and in the understanding of etiopathogenesis was reported.

ABSTRACTS

Topic: Cerebrovascular Disorders

EPNS25_559 - Expanding thrombectomy intervention to paediatric arterial ischemic stroke: workflow and case report of the first 2 cases in the country

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Objectives

Pediatric stroke is a rare but serious condition affecting approximately 2 per 100,000 per year with a mortality rate of 5% and long-term neurological deficits in 70% of survivors according to the American Heart Association (AHA) Scientific Statement in 2019. Paediatric acute ischemic stroke (AIS) accounts for half of all paediatric strokes. The AHA recommended endovascular therapy as a feasible option in paediatric AIS. Several cohort studies have described favourable outcomes and safety profiles in paediatric endovascular therapy as compared to the adult population. We aim to report our experience with paediatric mechanical thrombectomy, the first of its kind performed in our local population.

Methods

This is a retrospective study of 2 patients who presented with AIS. The multidisciplinary paediatric team collaborated with adult stroke specialists and neuro-interventionists within the hospital to design a paediatric-specific acute stroke workflow. The primary aim was to optimize neurological outcomes in paediatric AIS. Safety outcomes included central or peripheral access-site vascular complications.

Results

The first patient was a 14-year-old girl presenting with decreased consciousness, headache, right upper and lower limb weakness and aphasia. Computed tomography (CT) brain and angiography (CTA) showed a hyperacute left middle cerebral artery (MCA) infarct with M1 segment thrombosis. Successful thrombectomy was achieved 4 hours 57 minutes after symptom onset. Within 12 hours, she regained full consciousness and improvement in the power of the right upper and lower limbs. Her 90-day modified Rankin Scale (mRS) and 1-year mRS were both 1. There were no complications from the procedure.

The second patient was a 9-year-old boy with complex cyanotic heart disease. He presented with decreased consciousness and left upper and lower limb weakness. He sustained 2 right MCA infarcts 1 week apart, due to pre-existing intra-pulmonary shunts. He underwent 2 successful thrombectomies without complications. His 90-day modified Rankin Scale (mRS) and 1-year mRS were both 2.

Conclusions

The introduction of the paediatric stroke workflow has led to increased awareness and better recognition of paediatric AIS. The 2 patients have experienced 3 successful mechanical thrombectomy procedures in our centre. This case study adds to the small but growing pool of paediatric patients with AIS who achieved successful recanalization, including an international, multicentre registry study. Through the establishment of the workflow, we look forward to gain further insights from the present and future patients who benefit from endovascular therapy in AIS.

ABSTRACTS

Topic: Epilepsy: Diagnosis and Investigations

EPNS25_560 - Language Model Applications for Early Diagnosis of Childhood Epilepsy

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Objectives: Accurate and timely epilepsy diagnosis is crucial to reduce delayed or unnecessary treatment. While language serves as an indispensable source of information for diagnosing epilepsy, its computational analysis remains relatively unexplored. This study assessed – and compared – the diagnostic value of different language model applications in extracting information and identifying overlooked language patterns from first-visit documentation to improve the early diagnosis of childhood epilepsy.

Methods: We analyzed 1,561 patient letters from two independent first seizure clinics. The dataset was divided into training and test sets to evaluate performance and generalizability. We employed two approaches: an established Naïve Bayes model as a natural language processing technique, and a sentence-embedding model based on the Bidirectional Encoder Representations from Transformers (BERT)-architecture. Both models analyzed anamnesis data only. Within the training sets we identified predictive features, consisting of keywords indicative of ‘epilepsy’ or ‘no epilepsy’. Model outputs were compared to the clinician’s final diagnosis (gold standard) after follow-up. We computed accuracy, sensitivity, and specificity for both models.

Results: The Naïve Bayes model achieved an accuracy of 0.73 (95% CI: 0.68-0.78), with a sensitivity of 0.79 (95% CI: 0.74-0.85) and a specificity of 0.62 (95% CI: 0.52-0.72). The sentence-embedding model demonstrated comparable performance with an accuracy of 0.74 (95% CI: 0.68-0.79), sensitivity of 0.74 (95% CI: 0.68-0.80), and specificity of 0.73 (95% CI: 0.61-0.84).

Conclusions: Both models demonstrated relatively good performance in diagnosing childhood epilepsy solely based on first-visit patient anamnesis text. Notably, the more advanced sentence-embedding model showed no significant improvement over the computationally simpler Naïve Bayes model. This suggests that modeling of anamnesis data does depend on word order for this particular classification task. Further refinement and exploration of language models and computational linguistic approaches are necessary to enhance diagnostic accuracy in clinical practice.

ABSTRACTS

Topic: Neuromuscular Disorders

EPNS25_563 - Conflicts in Best Interest; Infants with severe neuromuscular disorders presenting to UK

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Objectives

Infants with severe neuromuscular disorders, presenting a birth, are often unable to move, communicate, breathe, and feed. These neuromuscular conditions are often associated with presumed normal cognition. Supporting these infants and maintaining life through medical intervention or re-orientating care to palliation is often debated, and decision-making can be extremely challenging.

Methods

We present three infants with severe neuromuscular conditions monitored in a tertiary Centre illustrating the challenges in determining best interest for these patients.

Results

The first case is an 18 months-old diagnosed with SMA type 1 before the disease modifying therapies era. His condition was quite severe and required positive ventilation via an endotracheal tube; and was fed through a gastrostomy. He remained conscious. The treatments would not change the outcome. The treating team and the experts agreed that withdrawing ventilation and re-orientating to palliative care would be in his best interest. However, the parents disagreed and made an application to court. The judge determine it was in his best interests to continue with continuous pressure ventilation and with the nursing and medical care required.

The second patient is a 10-month-old boy with a suspected diagnosis of Congenital Myasthenic Syndrome (CMS). The child was ventilator dependent since birth and had multiple failed extubating attempts. Empirical trials of medication were conducted and showed no noticeable clinical change. The medical evidence suggested that it was not in his best interest to proceed with long-term ventilation. His parents preferred the option of a tracheostomy; therefore, an application was made to the Court. In court, it was felt to be in favour of withdrawing and reorientation to palliative care.

The third child was diagnosed with severe congenital myopathic condition which resulted in significant hypotonia and muscle weakness. She was unable to move independently, communicate, swallow or cough and she was ventilatory dependent. The parents agreed with the medical diagnosis, but felt very strongly that she should continue to receive the life sustaining medical treatment in accordance with their strong religious beliefs. The judgement concluded that it was in her best interests to withdraw her care, and for a palliative care regime to be implemented.

Conclusions

Children with severe neuromuscular conditions provide the parents and medical team with enormous challenges. The medical and ethical frameworks should be considered, together with the concept of suffering by the infant due to preserved cognition, to determine what is truly in the infant's best interest.

ABSTRACTS

Topic: Neuromuscular Disorders

EPNS25_565 - Assessing the functionality and quality of life of children with spinal muscular atrophy in and out of rigid bracing

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Objectives: The landscape of spinal muscular atrophy (SMA) is changing thanks to novel treatments, but with this evolving phenotype we are encountering challenges in management for this cohort. Early management of the spine and the prevention of worsening scoliosis has become a key issue in the management of severe SMA and has been highlighted as an area of concern by both caregivers and healthcare professionals. Spinal bracing is being increasingly used to help slow the progression of scoliosis in this cohort, however there is still hesitancy in prescribing bracing for these children. One of the concerns is that rigid bracing may lead to a reduction in functionality whilst being worn. The aim of this study is to assess the impact of rigid spinal brace on functionality and assess caregivers' perceptions of quality of life both in and out of the brace.

Methods: We have undertaken a cohort study of our patients with severe SMA (Types 1 and 2) who have been prescribed spinal bracing, comparing functionality of participants in and out of their spinal brace using the age-appropriate physiotherapy assessments (eg RULM or HINE) conducted by their regular physiotherapist. We also conducted a parent questionnaire to understand how the brace affected the participants engagement in daily activities and quality of life.

Results: All patients (n=8) within this cohort showed stable physiotherapy scores, with no change observed between in and out of brace (paired T Test ($p=0.53$). 5 out of 7 parents who completed the questionnaire identified an overall improvement to their child's engagement in daily activities and quality of life scores while wearing the brace. Specifically, it identified that the children could sit for longer with decreased levels of fatiguability while wearing the brace. The children also had increased ability to play both independently and with others but there was possibly increased discomfort whilst wearing the brace.

Conclusions: This study is the first to our knowledge to illustrate that rigid spinal bracing in this cohort does not lead to a reduction in upper limb functionality. Self-reported parent /carer questionnaire showed that in a spinal brace, their children could sit for longer but with some increased discomfort. This could be addressed in future brace design to ensure better compliance and therefore achieve maximum effect of brace management in this cohort.

ABSTRACTS

Topic: Miscellaneous

EPNS25_567 - Phenotypic and molecular characteristics of a cohort of Egyptian children with neurofibromatosis type 1: A single center experience

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Phenotypic and molecular characteristics of a cohort of Egyptian children with neurofibromatosis type 1: A single-center experience

Objectives

Neurofibromatosis type 1 (NF1) has various clinical symptoms affecting several organ systems. This work aims to have more insight into the phenotypic characteristics of a cohort of Egyptian children and adolescents with neurofibromatosis type 1 to improve the care given to these children and early detection of possible complications.

Methods

A six-month cross-sectional study was conducted at The Outpatient Neurology Clinic at Alexandria University Children's Hospital and Borg El-Arab University Children's Hospital for Oncology, including patients below 18 years of age, with confirmed Diagnosis of NF1 disorder based on the revised diagnostic national institutes of health (NIH) criteria 2021.

Results

50 patients were recruited, 25 female (50%) and 25 male (50%), 24 patients (48%) had a family member affected by the same condition, and 26 patients (52%) didn't have family members with the same condition. Twenty-one patients (42.0%) had delays in the development of their developmental milestones, 7 patients (14.0%) suffered from epilepsy, seventeen patients (34.0%) suffered from headaches, and 4 patients (8.0%) were diagnosed with hydrocephalus. Thirteen patients (26%) had an intellectual disability, 9 patients (18%) had attention deficit hyperactivity disorder (ADHD) and 20 patients (40%) had a learning disability. According to the revised NIH criteria, 50 patients (100.0%) showed CALMs, while freckling in the axillary or inguinal regions was presented in 41 patients (82.0%), 5 patients (10.0%) with neurofibromas, one patient (2.0%) showed the presence of plexiform neurofibroma, 13 patients (26%) showed optic pathway gliomas, 10 patients (20%) showed the presence of lisch nodules, also regarding genetic analysis that was performed; 26 children (72.22%) showed positive results. Finally, regarding whether a parent was affected by the same condition, 18 children (36%) had a parent affected with NF1.

Conclusions

Neurofibromatosis type has no sex predilection. A considerable percentage of cases show developmental delay, learning difficulties, intellectual disabilities, and neurological disorders like, epilepsy, headache, and hydrocephalus. The most common tumor in the studied cohort is optic pathway glioma affecting 26% of cases. Behavioral disorders are common in patients with NF1, especially ADHD.

ABSTRACTS

Topic: Neurogenetics

EPNS25_568 - The utility of MitoPhen in the interpretation of POLG variants in undiagnosed paediatric patients within the 100,000 Genomes Project

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Objectives: *POLG* encodes DNA polymerase gamma which is vital for mitochondrial DNA maintenance and replication. Variants in *POLG* cause primary mitochondrial disorders with heterogenous presentations. These are often paediatric-onset with progressive neuroregression, seizures, muscle and liver involvement. Most *POLG* variants in paediatric patients are inherited in a recessive manner, however, a significant proportion are dominant. We aimed to evaluate individuals within the 100,000 Genomes Project (100kGP) carrying *POLG* variants using MitoPhen v2 – a curated reference database for mitochondrial diseases.

Methods: Phenotype and genetic data from 1071 published individuals with *POLG*-related mitochondrial disorders were manually curated using a framework established by the MitoPhen database, with Human Phenotype Ontology (HPO) terms. OntologyX and caret R packages were used for HPO analyses. We performed Receiver Operating Characteristic curve analysis to evaluate phenotype similarity score as a predictor of *POLG*-related diseases within MitoPhen v2. Phenotype similarity scoring was applied to undiagnosed individuals within 100kGP with *POLG* variants identified using a bespoke bioinformatics pipeline developed by Lifebit. Variants known to be benign/likely benign or heterozygous *POLG* variants with recessive inheritance were excluded from the dataset. Available HPO terms were supplemented with additional phenotype data gathered from Hospital Episode Statistics data.

Results: 5670 participants were identified in the 100kGP with *POLG* variants previously annotated as likely pathogenic either in MitoPhen v2 or ClinVar with at least one HPO term. 35 were participants with paediatric-onset conditions, undiagnosed through the primary analysis. The most common HPO terms in these individuals were seizures, developmental delay and intellectual disability. Monoallelic *POLG* variants were identified in 23 participants. Phenotype similarity data showed that 23 individuals had a phenotype similarity score >0.3, with two individuals diagnosed with *POLG*, two individuals diagnosed with other nuclear genes, six with biallelic variants, where one individual has likely causative variants. There were 13 individuals with heterozygous likely pathogenic variants who have phenotype similarity scores >0.3 and remain undiagnosed. We categorized variants in seven individuals as unlikely causative due to lack of phenotypic overlap.

Conclusions: We have re-analysed the 100kGP dataset for undiagnosed paediatric-onset *POLG* diseases using bioinformatics filtering and manual curation of the variants using a bespoke reference database. The phenotype similarity score corroborated two diagnoses and highlighted at least 14 individuals where the variants may be causative of the phenotype suggesting a role in focused phenotype evaluations in these challenging rare disorders.

ABSTRACTS

Topic: Epilepsy: Medical and Surgical treatment

EPNS25_570 - Diagnostic utility of source imaging methods in paediatric candidates of resective epilepsy surgery: a pilot project

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Objectives

High-density EEG (HD-EEG) enables high spatial resolution monitoring by co-registering 128 electrode positions with magnetic resonance imaging (MRI) via a 3D scanner. The aim of this study was to determine and validate the diagnostic benefit of HD-EEG in pediatric epilepsy surgery by comparing the locations of detected irritation zones and surgically defined epileptogenic zone.

Methods

This is a retrospective study on children with drug-resistant focal epilepsy examined in epilepsy surgery program who underwent HD-EEG evaluation at the Motol Epilepsy Center from 2018 to 2025. The HD-EEG workflow involved electrode co-registration with MRI, forward model calculation, detection and averaging of interictal epileptiform discharges (IED), and solving of inverse problem to localize cortical sources of IED. Postoperative outcomes were assessed 2 years after surgery. Analysis used descriptive statistics like precision and recall to determine the correlation between HD-EEG findings and resection zone in postsurgically seizure-free patients.

Results

HD-EEG was performed on 157 patients, of whom 117 subsequently underwent surgery. The most frequent reason for contraindicting epilepsy surgery was findings consistent with generalized or multifocal epilepsy (13/40). The age of the operated patients at the time of the HD-EEG was 11 (5-16) years. Postoperative outcomes were available for 96 patients, of whom 69 (72%) were completely seizure-free 2 years after surgery. A strong correlation was observed between HD-EEG-detected irritation zones and epileptogenic zone in postsurgically seizure-free patients, demonstrating the utility of HD-EEG in preoperative evaluation. Additionally, HD-EEG findings were consistent with results from other neuroimaging modalities, further supporting their diagnostic reliability.

Conclusions

Our study demonstrated the significant potential of source mapping methods in localizing the epileptogenic zone in paediatric candidates for resective epilepsy surgery. Its high spatial resolution and non-invasive nature make HD-EEG a significant auxiliary method in the localization of the epileptogenic zone, contributing to favourable postoperative outcomes of patients.

This work was supported by the Ministry of Health of the Czech Republic (AZV NU21J-08-00081)

ABSTRACTS

Topic: Epilepsy: Diagnosis and Investigations

EPNS25_571 - Paediatric Status Epilepticus: A Single Centre Retrospective Study

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Objectives

This study provides a comprehensive retrospective analysis of paediatric Status Epilepticus (SE) cases from Tawam Hospital in Alain, UAE. The study aims to examine demographics, clinical presentations, management practices and outcomes to better understand regional trends and improve treatment and care.

Methods

This single-centre retrospective study was conducted at Tawam Hospital, a large tertiary governmental hospital in Al Ain, UAE. Inclusion criteria was for paediatric patients aged from 1 month to 16 years admitted with SE between January 2015 and December 2022. Data extracted from electronic medical records included demographic information, clinical presentations, utilised treatments and measured outcomes. Statistical analyses included descriptive statistics. Frequencies and percentages were calculated for categorical variables, while means and standard deviations were used for continuous variables. Data management and analysis was done using Microsoft Excel.

Results

Of the 1,552 SE cases identified, 354 met inclusion criteria. Males accounted for 54.1% of the cohort, with the majority 54.4% aged between 5 and 16 years. Emirati nationals accounted for 59.7% of cases. Generalized seizures 59.3% were the most common presentation, followed by focal seizures 16.7%. A history of epilepsy was noted in 60.3% of patients, while febrile seizures accounted for 8.5% of cases. Benzodiazepines were the first-line treatment in most cases, followed by second-line agents. Despite protocol adherence nearly half of the patients 49.2% required extended hospitalization and mortality was recorded at 8.9%. Metabolic disorders 24.3% and genetic abnormalities 7.2% were noted comorbidities. Infectious triggers, including meningitis, sepsis and COVID-19 were identified in 37% of cases.

Conclusions

Paediatric SE in the UAE demonstrates distinct regional characteristics alongside global patterns. These findings highlight the need for continued research into region-specific aetiologies and management practices to better optimize outcomes in this population.

ABSTRACTS

Topic: Neuropsychiatric Disorders / Functional Neurological Disorders

EPNS25_572 - Pediatric Celiac Disease and Sleep: Should sleep be the part of the routine follow-up?

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Objectives

Celiac disease (CD) presents with a broad clinical spectrum, including neuropsychiatric symptoms. While studies have demonstrated a high prevalence of sleep disorders in adults with CD, data on pediatric patients remain limited. This study aimed to investigate the presence and frequency of sleep disorders in children diagnosed with CD and to identify associated subgroups using the Sleep Disturbance Scale for Children (SDSC).

Methods

A prospective, cross-sectional study. Children aged 4–18 years diagnosed with CD between December 2019 and February 2024 and a healthy control group were included. Sleep disturbances were assessed using the SDSC. Dietary adherence in the CD group was evaluated, and comparisons were made between adherent and non-adherent patients. Statistical analyses were performed using SPSS 22.0, with $p<0.05$ considered statistically significant.

Results

A total of 56 participants were included (31 CD patients, 25 healthy controls). The prevalence of sleep disturbances was 77.4% in the CD group**,** significantly higher than in the control group ($p<0.001$). When SDSC subcategories were analyzed, sleep-wake transition disorders, excessive sleepiness, and sleep hyperhidrosis were more prominent in CD patients. In the dietary adherence analysis, patients with poor adherence to a gluten-free diet had significantly higher SDSC scores ($p<0.001$).

Conclusions

Children with CD exhibit a significantly higher prevalence of sleep disturbances compared to their healthy peers. Moreover, poor adherence to a gluten-free diet is associated with worse sleep quality. Given that sleep disturbances in CD may complicate symptom management and disease control, sleep assessments should be considered as part of routine follow-up in pediatric CD patients**.**

ABSTRACTS

Topic: Infectious and Inflammatory Diseases/ Neuroimmunology

EPNS25_573 - Case Report: Area Postrema Syndrome in a Patient with Hereditary Spastic Paraplegia: Diagnostic Challenges and Multidisciplinary Management

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Objectives

- To report a case of area postrema syndrome in a 14-year-old female with Hereditary Spastic Paraplegia (HSP).
- To highlight the diagnostic challenges and the multidisciplinary management required for this condition.

Methods

- A 14-year-old girl with HSP due to a heterozygous mutation (c.1335C>A) in exon 11 of the SPAST gene presented with severe vomiting for 2-3 weeks.
- Comprehensive blood tests, endocrine tests, metabolic screens, immune screens, and CSF tests were conducted to investigate the cause of the vomiting prior to referral to neurology.
- MRI brain imaging was performed to identify any central nervous system pathology.
- The patient was treated with intravenous steroids for 3 days followed by oral steroids for 12 weeks with slow tapering.
- Further investigations included anti-aquaporin-4 antibody testing and lumbar puncture.

Results

- Blood tests, endocrine tests, metabolic screens, and immune screens were unremarkable, except for slightly raised biotinidase.
- CSF tests for anti-Hu, Ri, Yo, AQP4, and MOG were negative.
- MRI brain showed two punctate high T2-weighted signal foci with enhancement near the postrema, consistent with area postrema syndrome.
- Treatment with steroids led to significant improvement, with MRI scans at 4 months follow-up showing resolution of the area postrema syndrome.
- The patient experienced minimal ongoing symptoms and showed significant improvement despite some residual fatigue.
- The absence of anti-aquaporin-4 antibodies and oligoclonal bands suggested a low risk of relapse.

Conclusions

- Area postrema syndrome should be considered in patients with unexplained intractable vomiting.
- The occurrence of area postrema syndrome in HSP may be linked to neuroinflammatory processes affecting the central nervous system.
- While dysautonomia is frequently observed in individuals with HSP, the identification of characteristic MRI changes led to the diagnosis of APS.
- The absence of specific biomarkers (such as anti-aquaporin-4 antibodies and CSF oligoclonal bands) may reduce the risk of relapse, offering a positive prognosis for affected individuals.

ABSTRACTS

Topic: Neuromuscular Disorders

EPNS25_574 - Nationwide newborn screening for Spinal Muscular Atrophy

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Objectives
Spinal muscular atrophy (SMA) is a severe neuromuscular disorder caused by homozygous loss of function of the *survival motor neuron 1 (SMN1)* gene and characterized by progressive weakness. Its natural history is one of infantile death for cases with early onset (i.e. SMA type 1) and severe disability for chronic forms (type 2 and 3). Three genetic treatments have been introduced recently, i.e. nusinersen, onasemnogene abeparvovec (OA) and risdiplam. Early treatment gives the best results and newborn screening (NBS) programs for SMA are therefore implemented in a growing number of countries. Our objective is to describe our first two-and-half years' experience of NBS for SMA.

Methods
Data was collected prospectively from June 2022-January 2025 by the national SMA Center that provides SMA genetic treatment for all patients in our country (population 18 million). NBS uses multiplex qPCR as a first-tier test to detect homozygous deletion of *SMN1*. After referral, we use a second tier MLPA test to confirm first tier test results and to determine the copy number of *SMN2*, the most important predictor of expected disease severity.

Results
We identified 43 newborns with SMA (0.0096% of live births). Median referral age was 9 days (IQR 7-10), followed by visit to outpatient clinic 1 day (IQR 1-3) later. Another 3 days (IQR 2-3) later final test results were known. Two infants had 1 *SMN2* copy, 17 had 2 *SMN2* copies, 18 had 3 *SMN2* copies and 6 had 4 *SMN2* copies. Baseline motor function was determined with CHOP-INTEND (maximum score 64). Median score was 40 (IQR 31-51) in infants with 2 *SMN2* copies and 54 (IQR 52-55) in infants with 3 or 4 *SMN2* copies. Median age at start of treatment was initially 25.5 days (22.5-31.5) but decreased to 10.5 days (IQR 9-15.5) from April 2024 due to a new reimbursement arrangement. Seven infants, two with 1 *SMN2* copy and five with 2 *SMN2* copies, weren't treated because of poor clinical condition. Additionally, 2 infants with 2 *SMN2* copies died despite treatment with OA and risdiplam. In total 9 out of 43 (20.1%) infants died (expected mortality based on natural history 19/43 (44.2%).

Conclusions
A successfully implemented newborn screening program for SMA resulted in the identification of 43 infants. We succeeded in reducing treatment delays and NBS reduced early mortality. Continued follow-up is needed to learn about the long-term effects of early treatment.

ABSTRACTS

Topic: Neurogenetics

EPNS25_575 - Epigenetic variation underlies pleiotropy in MORC2-related disorders

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Objectives: Heterozygous missense mutations in *MORC2*, a chromatin remodeler, are associated with a wide range of clinical conditions, from pediatric neurodevelopmental disorders like Leigh syndrome and Cockayne syndrome to late-onset neuropathies. However, the mechanisms driving the phenotypic heterogeneity and pleiotropic effects of *MORC2* remain unclear. To address this, we utilized a multi-omics approach to dissect the phenotypic spectrum.

Methods: We analyzed DNA methylation, transcriptomes, proteomes, and phenotypes of 53 MORC2 patients. Epigenome-wide, transcriptome-wide, and proteome-wide association studies were conducted using over 400 affected individuals and more than 20 healthy controls for each omics layer. Outliers were identified using OUTRIDER, and SVM classifiers were trained to define diagnostic signatures.

Results: We identified a *MORC2*-specific DNA methylation episignature conserved across different tissues. Episignature leads to specific gene silencing, which form an RNA signature. Simultaneous downregulation of three disease-associated genes -*ERCC8*, *NDUFAF2*, and *FKTN*- at different levels explain the variable biochemical defects and clinical manifestations observed in *MORC2* patients. Silencing of *NDUFAF2* accounts for manifestationof Leigh syndrome, whereas dysmorphic features are caused by *ERCC8* silencing. Overall, our findings demonstrate that variability in methylation levels and its repressive effect on target genes contribute to pleiotropy and predict phenotypic heterogeneity in *MORC2*-related disorders.

Conclusions: Our study highlights the power of multi-omics analysis in uncovering the pleiotropic effect of *MORC2*. Furthermore, we provide the first example where molecular signatures go beyond diagnostic biomarkers to explain the underlying pathomechanism. We propose that epigenetic variation may contribute to pleiotropy in other Mendelian disorders.

ABSTRACTS

Topic: Movement Disorders/ Cerebral Palsy

EPNS25_577 - Disease Monitoring through the PKAN Disease Rating Scale (PKAN-DRS) in Pantothenate Kinase-Associated Neurodegeneration (PKAN)

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Objectives

To assess the utility of the PKAN-DRS as an outcome measure for monitoring disease progression in PKAN.

Methods

The PKAN-DRS was performed on patients with PKAN from two referral centres in the UK and Spain, during routine clinical visits from 2014 to 2023. Statistical analyses were performed using R version 4.3.2 (R Foundation for Statistical Computing, Vienna, Austria). Correlation between clinical scores was assessed using Pearson correlation coefficients calculated using package psych (2.4.6), Holm correction was used for multiple comparisons. Time-to-event analysis was performed on Kaplan-Meier cumulative incidence curves for loss of ambulation, falls, and dystonia onset using the survminer package.

Results

64 PKAN-DRS assessments were performed on 30 patients with PKAN. 11 patients had 3 or more assessments, 14 had 2 assessments and 5 had a single assessment. For the 25 patients who had longitudinal assessments, the meadian time between assessments was 2.5y (range 5.5). Age at assessment ranged from 2.6 to 59 years, with a median of 23.6 (inter-quartile range 13.4 to 31 years). PKAN-DRS total scores ranged from 3 to 104 (minimum scale value 0, maximum 135), with a median of 51, mean 51.9, and standard deviation of 28.0. Subscales focussed on disability, parkinsonism, and dystonia all correlate closely with each other and the overall score, with Pearson correlation coefficients of 0.68-0.97. Considering the mean slope of the 25 individual patients with longitudinal testing, there is a 6.1 points-per-year increase (95% confidence interval 2.8 to 9.5). This slope is steeper in classical patients (8.8 points-per-year; 95% confidence interval 0.76 to16.8) compared to atypical patients (5.1 points-per-year; 95% confidence interval 1.2 to 9.0). Using a mixed effects model with binary covariates for sex and classical disease status, the fixed effect of age at assessment is 1.53 points per year and is statistically significant ($p<0.0001$). By including the age of onset of symptoms in this model, both age at assessment (now 1.79 points per year, $p=0.0009$) and age at onset have fixed effects on the predicted DRS score. The effect of age at disease onset is negative (-2.9 points per year, $p=0.002$), meaning that the earlier age at onset of symptoms the more rapid is the progression.

Conclusions

Our study provides longitudinal validation of the PKAN-DRS, strengthening the case for its use in clinical trials. The scale also captured differences among phenotypes, with children having a classic phenotype showing a more rapid progression of symptoms.

ABSTRACTS

Topic: Neurogenetics

EPNS25_578 - Novel small molecule treatment in PUF60-related splicing disorders

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Objectives

Pre-mRNA splicing is a fundamental step in eukaryotic gene expression that removes non-coding intronic regions, which allows for several mRNA transcripts to arise from a single DNA sequence, thereby greatly increasing genetic plasticity and proteomic diversity. The Poly(U)-binding splicing factor gene (*PUF60*) encodes a core component of the spliceosomal complex. *PUF60* variants lead to Verheij syndrome, associated with coloboma, neurodevelopmental disorders and short stature. We have previously expanded the spectrum of *PUF60*-related disorders in human (Baum et al., 2024, Int J Mol Sci) and reported mTOR downregulation with *PUF60* knockdown in *Caenorhabditis elegans* and cells (Huang et al., 2022, Nature Aging).

Methods

We present clinical, molecular, neuropathological and imaging data from the largest cohort of patients with pathogenic heterozygous variants in *PUF60* yet. We conducted deep transcriptomic and proteomic assays from peripheral blood mononuclear cells (PBMCs) and metabolomic analysis from plasma from nine patients. We examined mTOR activity in patient fibroblasts with small molecular compound treatment. These data are complemented by experimental findings from transgenic animal models in *Caenorhabditis elegans*.

Results

We have collected the clinical information of over 100 patients with pathogenic *PUF60* variants, more than half of which are unpublished. The phenotypic spectrum ranges from mild neurodevelopmental features with late neurodegenerative course to classic Verheij syndrome including short stature. We also noted several novel clinical features, including immunodeficiency, behavioral abnormalities, and vitamin B12 deficiency. Transcriptomic analysis from PBMCs revealed intron retention in a direct mTORC1 substrate. Proteomics from PBMCs and Western Blots in fibroblasts confirmed downregulation of mTOR and upregulation of autophagy. Metabolomic analyses of patient plasma revealed dysregulated one-carbon metabolism pathway. Treatment of fibroblasts with vitamin B12 restored mTOR activity. Corresponding data from the model organism *C. elegans* showed a rescue in body size and developmental rate after vitamin B12 treatment. The trial treatment in one patient showed complementary findings, potentially paving the way for future therapeutic trials.

Conclusions

Our findings expand the phenotypic spectrum of pathogenic *PUF60* variants and show close clinical and molecular links to disorders of mTOR and autophagy. Our findings will be useful for future interventional studies and patient counselling.

ABSTRACTS

Topic: Neurogenetics

EPNS25_586 - The Genetic Landscape of epilepsies among children till eighteen of age presenting to a tertiary care centre

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Objectives: The primary objective was to identify the genotype and phenotype spectrum of genetic epilepsies in children. Secondary objectives included evaluating genotype-phenotype correlations, and analyzing EEG and MRI patterns.

Methods: An ambispective observational study was conducted at AIIMS Jodhpur, including 150 children (60 retrospective, 90 prospective). Genetic testing, primarily through whole-exome sequencing (WES), was performed. Data were analyzed using SPSS 26.0, employing chi-square tests, t-tests, and regression analysis

Results: Generalized seizures (69.33%) and developmental delay (66.67%) were predominant. WES identified pathogenic variants in 34%, likely pathogenic variants in 30.67% and variants of uncertain significance in 28.67% patients with autosomal dominant inheritance being most common (56.66%). EEG abnormalities were observed in 69.33% and MRI abnormalities in 58%.

Conclusions: This study highlights the critical role of genetic testing, particularly WES in diagnosing genetic epilepsies and understanding genotype-phenotype correlations.

ABSTRACTS

Topic: Neuropsychiatric Disorders / Functional Neurological Disorders

EPNS25_587 - A retrospective study of the clinical presentation, comorbidities and outcome of functional neurological disorders (FND) in children and young people (CYP) at our tertiary paediatric centre

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Objectives

Our aim was to study the clinical presentation of FND in CYP, including presenting symptoms, associated co-morbidities, management and outcome.

Methods

We analysed data of 30 patients from computerised case notes and clinic letters for a cohort of CYP who were diagnosed with FND in the last 7 years.

Results

The ages of onset of symptoms range from 5 to 15 years with a mean of 11.6 years and a median of 12 years. There was a female predominance of up to 74.3% (22). 26.6% (8) were males. The common presentations were pain, weakness, difficulty in mobility, numbness, abnormal movements, memory issues, cognitive regression, visual symptoms and bladder/bowel symptoms. The duration between onset of symptoms to diagnosis ranged from less than a month to 12 years, with a mean duration of 16.6 months. Associated factors were parental separation in 6, death of immediate family members in 3, road traffic accidents in 4, bullying at school in 3, chronic medical illnesses in family members in 7 and mental health problems in family members in 3. Multiple other comorbidities such as autism, attention deficit and hyperactivity disorder, anxiety, chronic fatigue syndrome, complex regional pain syndrome, gender dysphoria, eating disorder and Tourette syndrome were observed. Multiple subspeciality consultations were involved in patient care. 22 CYP (73.3%) received targeted therapy at least for a brief period during the illness, in the form of input from occupational therapy, psychology, chronic fatigue service, pain team and child and adolescent mental health services (CAMHS). 23 CYP (76.7%) had significant disruptions to school attendance. The latest outcome showed that 10 CYP (33.3%) reported improvement of symptoms, 16 (53.3%) reported ongoing symptoms or a waxing and waning course and 4 (13.3%) CYP reported worsening of symptoms with significant limitation of function.

Conclusions

FND presents a challenging landscape for CYP, their families, and the healthcare professionals involved. Research on FND in children is limited, and the lack of structured services further complicates the situation. The clinical presentation is highly variable and complex. Management often requires a multidisciplinary approach, which can lead to over-investigation. However, early targeted interventions have been shown to lead to better outcomes.

ABSTRACTS

Topic: Cerebrovascular Disorders

EPNS25_588 - Paediatric vertebrobasilar stroke: predominance of vertebral artery injury and high recurrence rate

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Objectives. To describe causes, evolution, and recurrence rate of pediatric arterial ischemic stroke (AIS) in the vertebrobasilar territories.

Methods. This multisource retrospective study included non-neonatal pediatric patients (<18 years of age) with acute AIS in the vertebrobasilar territories. Patients were identified from the KidClot national study addressing recanalization treatments in acute pediatric AIS (2015-2018), from the multidisciplinary case discussion sessions of the National Pediatric Stroke Center (2013-2022), and from a quaternary care hospital pediatric AIS database (2013-2022). We collected clinical and imaging data at presentation, and during an 18-month follow-up.

Results. We included 90 pediatric patients with vertebrobasilar AIS, 72 boys (80%), with a median age of 6 years old at stroke occurrence, and median NIHSS of 4. Most patients (n=62, 69%) displayed multiple vertebrobasilar AIS at first imaging procedure, suggesting embolic pathophysiology. Arteriopathy was the main cause (n=69, 77%), involving cervical vertebral artery (VA, n=54) and/or basilar artery (n=37). No isolated intracranial arteriopathy was observed. Only one patient had evidence of vessel wall hematoma. Other causes were cardio-embolic (n=7, 8%), thrombotic (n=2, 2%), or cryptogenic (n=11, 12%). All patients received antithrombotic treatment, with aspirin (n=36, 40%), UFH/LMWH (n=44, 49%), or Vitamin K-antagonist (n=7, 8%). 18 patients (20%) presented at least one stroke recurrence under antithrombotic treatment, within a median 7 days [3-52] after first identified stroke. VA aneurysm formation was observed in 6/54 patients with vertebral arteriopathy, with a median 71-day delay. One patient had endovascular VA occlusion because of multiple stroke recurrence.

Conclusions. Vertebrobasilar stroke represents a specific subgroup of pediatric AIS, with a predominance of male patients and frequent vertebral artery injury. An initial high recurrence risk is observed, even with antithrombotic treatment, but seems to resume later. The evolution towards aneurysm formation and the absence of vessel wall hematoma suggests a multifactorial pathophysiology, mixing artery dissection, inflammation, and perhaps local trauma.

ABSTRACTS

Topic: Neuromuscular Disorders

EPNS25_589 - Implementation of the Flexible Endoscopic Evaluation of Swallowing (FEES) and the standardised FEES scores in the diagnosis of dysphagia in spinal muscular atrophy - DYS-SMA trial

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Objectives

Spinal muscular atrophy (SMA) is an autosomal recessive neuromuscular disease characterised by progressive degeneration of the 2nd motor neurons of the motor anterior horn. The clinical characteristics of SMA are mainly characterised by progressive muscle weakness and atrophy. Those affected develop scoliosis, sometimes show limited head control, limited jaw closure, difficulties with coughing and the clearance of tracheal secretions. The bulbar symptoms, including dysphagia, pose a major therapeutic challenge with the frequent need for artificial feeding and a high risk of pulmonary complications.

The aim of the present DYS-SMA study (ClinTrials RegNo. NCT04773470; Investigator Initiated Trial supported by Roche Pharma AG) was to implement the Flexible Endoscopic Evaluation of Swallowing (FEES) and standardised FEES scores in the descriptive evaluation of the present swallowing pathomechanisms in patients with SMA type 1-3.

Methods

In the prospective, interventional, open, explorative and diagnostic study, 40 SMA patients were included in the study after detailed medical consultation. The study-related interventions were a clinical dysphagia screening and the FEES at two points in time (at visit 1 (T1) and 4 months after visit 1 (T2).

Results

The initial clinical assessment revealed dysphagia in 38.5% of SMA patients (n=15). After the subsequent initial FEES, the number of confirmed diagnoses of dysphagia increased to 84.6% (n=33) with a relevant recommendation for dietary restriction.

Severe dysphagia with tube-dependent feeding was initially observed with n=7 (18%) in SMA type 1, after FEES with n=8 (20.6%). In SMA type 2, we observed severe dysphagia in n=2 (5.1%) initially and n=6 (15.4%) after FEES. 30.8% of SMA type 2 patients showed undiagnosed dysphagia before FEES. In SMA type 3, no dysphagia was initially observed; after FEES, mild dysphagia was found in n=4 (10.3%).

Conclusions

In our trial most severe dysphagic symptoms are found in SMA type 1, most frequent in SMA type 2, however less severe. SMA type 3 shows only mild dysphagia.

The trial results indicate that FEES is a valid and very easy to implement imaging instrument for the diagnosis of dysphagia in SMA. Clinical assessments are insufficient to adequately diagnose dysphagia in SMA.

ABSTRACTS

Topic: Traumatic Brain Injury

EPNS25_590 - Olfactory Dysfunction in Pediatric Mild Traumatic Brain Injury: A Three-Month Trajectory

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Objectives

Each year, approximately 300,000 children and adolescents in Germany experience mild traumatic brain injury (mTBI). A substantial proportion develop post-concussion syndrome, potentially resulting in long-term impairments. Among pediatric patients, 12% of olfactory disorders are trauma-related, making it the second most common etiology. Despite its clinical relevance, literature on post-traumatic olfactory dysfunction (PTOD) is scarce. This study examines the characteristics and progression of PTOD in children and adolescents during the acute phase (<72 hours post-mTBI) and its trajectory over three months.

Methods

In this prospective longitudinal cohort study, 25 children (10 males; mean age 11±0,6 years) underwent standardized olfactory assessment utilizing the "Sniffin' Sticks" test-kit at three time points: within 72 hours (mean 30,0±2,2 hours), two weeks (mean 18,5±0,9 days), and three months (mean 116,0±3,8 days) post-mTBI. Testing evaluated olfactory threshold, identification, and discrimination. Trauma characteristics, symptom burden, quality-of-life questionnaires, as well as comprehensive neurological evaluations were performed as part of the centre's established Concussion Workup protocol.

Results

13 children (52%) exhibited impaired olfactory function in the acute setting post-mTBI, with similar proportions of affected children in the threshold and identification test domains. Initial neurological symptom burden was substantial, with 24 children (96%) reporting more than two symptoms. Symptom burden significantly decreased within two weeks ($p<0.001$) and nearly returned to individual pre-mTBI baseline scores by three months. In contrast, PTOD demonstrated a distinct trajectory, with prevalence increasing to 68% (17/25 children) at the three-month follow-up. Quality-of-life analysis is ongoing and will be presented at the conference.

Conclusions

This study reports a high frequency of PTOD among pediatric mTBI patients within the first three months, exceeding rates in prior literature. Interestingly, while symptom burden almost resolved within three months, PTOD exhibited an opposite trend over time. These observations suggest that olfactory recovery may not parallel the resolution of other neurological symptoms, highlighting the need for targeted approaches to contextualize PTOD as a distinct aspect of advanced mTBI care in pediatric populations.

ABSTRACTS

Topic: Neurogenetics

EPNS25_591 - The Broad Clinical Spectrum of Tubulinopathies: A Multicenter Retrospective Clinical Study

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Objectives: Tubulinopathies are a relatively newly defined family of neurological disorders caused by mutations in the genes encoding tubulins and microtubule-associated proteins that result in cortical developmental malformations. This group of disorders is characterized by microcephaly, developmental delay, intellectual disability and epilepsy. Epilepsy can manifest with different semiology and severity. The aim of this study was to present a large case series of tubulinopathies from a multicenter dataset and to raise awareness of this condition.

Methods: This study is designed as a multicenter retrospective case series.

Results: The study included 14 children (4 females) with a mean age of 7.3 ± 5 years (range: 1.2-16.3). The mean age at diagnosis was 4.6 ± 4.2 years (range: 0.5-12.3), with a delay in diagnosis ranging from 3 to 106 months after initial presentation. Ten pathogenic variants were identified in the following genes TUBA1A (alpha), TUBB2A/B, TUBB3, TUBB4A (beta), TUBG1 (gamma) and TUBGCP2 (microtubule-associated protein). Almost all patients had developmental delay of varying severity, and epilepsy was observed in 10 patients (71.4%). The age of epilepsy onset ranged from 3 months to 9 years, with a wide range of seizure semiologies, including focal/generalised motor and/or non-motor seizures. Response to antiseizure medication was variable, with seizure control achieved in seven patients and drug-resistant epilepsy in three. The most common neurological findings included microcephaly, axial hypotonia, appendicular spasticity and hyperactive deep tendon reflexes. In addition, four patients (28.6%) had movement disorders. Brain MRI findings commonly included corpus callosum agenesis/dysgenesis (10/12), lissencephaly (5/12), basal ganglia abnormalities (5/12), cerebellar atrophy/hypoplasia (5/12), and abnormal sulcal/gyral morphology (4/12). EEG abnormalities were observed in 10 patients, including hypsarrhythmia, sleep-activated spike-wave patterns, and generalized or multifocal epileptic anomalies.

Conclusions: Tubulinopathies are a heterogeneous group of disorders with broad clinical, radiological, and EEG findings. Refractory seizures represent a significant comorbidity in this condition. However, due to the substantial phenotypic diversity, there is no consensus on disease management. Further comprehensive studies are needed to enhance understanding and develop effective management strategies.

ABSTRACTS

Topic: Miscellaneous

EPNS25_592 - Patients perspective on their cross-border personalized treatment experience

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Objectives

Personalised medicine is often only accessible through specialized centres, which for patients with rare diseases are often established in different countries than the patient's country of residence. Attending specialists and affected families can seek effective treatment solutions including Advanced Therapy Medicinal Products (ATMPs) and cross-border options, which can be accessed through various routes (S2 in EU, individual requests, clinical studies, compassionate use etc). This phenomenon is a subgroup of medical tourism, which is not driven by convenience, but only by efficacy. We mapped the cross-border treatment from patient and family perspective.

Methods

We used a questionnaire to interview parents of minor patients who applied for cross-border treatment for specific, personalized treatments that were not available in the country of origin. A total of 5 families from Slovakia and 2 from the Czech Republic were interviewed, who planned treatment in Germany, Netherlands and Italy. Some families stayed more than 3 months abroad. We have focused on the challenges of travelling abroad for treatment.

Results

All families recommended cross-border treatment. Parents decided to pursue the cross-border treatment of their children based on its efficacy, even though three families also considered less effective treatment available in the country of residence. The health insurance (HI) coverage of treatment was an important aspect, as well as coverage for travel and stay. While speaking at least one foreign language, language limitations in communication with healthcare professionals (HCP) was one of the main concerns, followed by concerns about organization and financial aspects of treatment. The main source of information about treatment options was provided by an attending specialist, closely followed by Internet search and recommendations from families facing similar challenges. Communication with foreign HCP was evaluated as effective, but it was not perceived as effective with administrative personnel nor HI. All considered it important to accompany the child as a whole family.

Conclusions

Although the ATMP treatment option was highly recommended by all, the communication was the main concern and challenge. Attending physicians have a critical role in initiation of cross-border treatment. The Internet search, networking with families with similar experiences and learning the language are highly recommended by the respondents to facilitate treatment.

ABSTRACTS

Topic: Epilepsy: Diagnosis and Investigations

EPNS25_593 - Characteristics of children with hypsarrhythmia detected on EEG: A large pediatric cohort

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Objectives We aimed to evaluate the etiology, associated seizure types and treatment of patients with hypsarrhythmia detected by electroencephalography (EEG).

Methods This study retrospectively evaluated demographics, treatment modalities, etiologies, associated seizure types, follow-up EEG and magnetic resonance imaging (MRI) findings at the end of a minimum 12-month follow-up of 125 patients with hypsarrhythmia detected on EEG at a tertiary pediatric neurology center from January 2013 to January 2024.

Results Comprehensive clinical evaluation and neuroimaging revealed that structural causes were the most common etiology (50.4%). Other causes were as follows: idiopathic (23.2%), both genetic and structural (8%), metabolic (7.2%), genetic (5.6%), infectious (4%) and immunological (1.6%). Epileptic spasms were the most common type of seizure associated with hypsarrhythmia; tonic, myoclonic and focal seizures were also observed to accompany hypsarrhythmia, in that order. At final evaluation, it was noted that all patients received treatment. There was no significant difference in treatment response between Adrenocorticotropic hormone (ACTH) and vigabatrin when used as the first drug. However, in the group using ACTH as a second drug, the response rate was significantly higher at 57.8% compared to vigabatrin and other drugs (p=0.009). Nine patients achieved seizure control with a single medication (7.2%), while 52 patients (41.6%) were considered drug resistant due to persistent seizures despite the use of multiple antiseizure medication. Anti-seizure medication was discontinued in 25 patients (20%). While no association was found between the age of onset of hypsarrhythmia and response to treatment (p=0.160), the shorter the time between detection of hypsarrhythmia and initiation of treatment, the better the response to treatment (p=0.047). In the structural etiology group, the probability of abnormal findings on final EEG was found to be higher than the other groups.

Conclusions Patients with EEG-detected hypsarrhythmia are often associated with different types of seizures, mainly epileptic spasms, and almost always require treatment. Although ACTH, which is often the preferred treatment, increases the chances of success, a significant proportion of patients remain in the drug-resistant group. On reviewing repeated EEG recordings of patients, especially in the structural etiology group, even if the hypsarrhythmia disappears on the EEG, various levels of epileptic activity remain.

ABSTRACTS

Topic: Neurometabolic Disorders

EPNS25_595 - The clinical picture and GALC variant spectrum in a case series of Krabbe disease- a single center experience

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Objectives: Krabbe disease (KD) is a rare autosomal recessive disorder caused by mutations in the gene encoding the lysosomal enzyme galactocerebrosidase (GALC). It is characterized by progressive neurodegeneration and demyelination at the level of central and peripheral nervous systems as a consequence of the deficiency of GALC and the accumulation of psychosine.

Methods: We identified 7 cases of KD in our clinic (between September 2010 and March 2024) The clinical data, magnetic resonance imaging, enzymatic and genetic studies were retrospectively reviewed and analyzed.

Results: The most prevalent clinical picture was the infantile form (6/7) with the onset of symptoms before 1 year of age. For four out of the six infantile forms the whole exome sequencing (WES) or GALC gene analysis was performed, all of them being positive for severe variants of the GALC gene, explaining the early onset of the disease. One patient (1/7) with a late-infantile form of KD had the onset of the disease at 3 years of age and the genetic analysis showed a compound heterozygous mutation with one mild and one severe allele of GALC gene.

Between patients presenting the infantile form, we describe a novel severe homozygous variant c.1672_1691del, p.Thr558fs* and, to our knowledge, a novel association of two severe compound heterozygous variants: c.749T>C, p.Ile250Thr, and the classical 30 kb deletion encompassing exons 11-17. The enzymatic assays and clinical picture of our patients confirm the severity of these variants.

The patient presenting the late-infantile form is a carrier of a well known variant association described only in adult subjects: c.857G>A, p.Gly286Asp and the 30 kb deletion. Although the enzymatic studies showed a GALC activity of 17%, which was observed for adult patients, we report the first pediatric case carrying the above mentioned variants.

Conclusions: The present case series contributes to a better understanding of the KD phenotype and complex genotype. The four patients with infantile forms of KD were positive for severe variants of the GALC gene, confirming the genotype-phenotype correlation of the association of two severe alleles with the early onset of the disease. We identified three cases with a particular genetic background, expanding the spectrum of this disorder.

ABSTRACTS

Topic: Epilepsy: Medical and Surgical treatment

EPNS25_597 - Determinants of intellectual and developmental outcomes in a multicenter pediatric hemispherotomy cohort

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Objectives

This study aimed to identify the determinants of intellectual and developmental outcomes following pediatric hemispherotomy in a large, contemporary multicenter cohort.

Methods

We retrospectively analyzed the intellectual and developmental outcomes of 296 children who underwent hemispherotomy between 2000 and 2016 and received a standardized postsurgical evaluation of intelligence or developmental quotients (IQ/DQ). Outcomes at the last follow-up were classified into four categories: normal (IQ/DQ >85), mildly impaired (IQ/DQ 70–84), moderately impaired (IQ/DQ 55–69), or severely impaired (IQ/DQ <55). Determinants of these outcomes were identified using ordinal regression modeling with imputation for missing data.

Results

At a mean follow-up of 3.8 years (range 1-14.2), 84% of the children were seizure-free, and 60% had discontinued antiseizure medication (ASM). Intellectual and developmental functioning at the last assessment was normal in 11% of the children, mildly impaired in 16%, moderately impaired in 22%, and severely impaired in 51%. Higher functioning was less likely in children with polymicrogyria as the underlying etiology (odds ratio (OR)=0.3 [0.11-0.77], p=0.013), those with contralateral MRI abnormalities (OR=0.47 [0.22-0.99], p=0.047), and those who continued ASM after surgery (OR=0.51 [0.29-0.9], p=0.021). Conversely, children with a later age at epilepsy onset were more likely to achieve higher functioning (OR=1.16 [1.04-1.3], p=0.011).

Conclusions

Age at epilepsy onset, underlying etiology, the presence of bilateral structural brain abnormalities, and postsurgical ASM management were key determinants of intellectual and developmental outcomes following hemispherotomy. These findings underscore the importance of timely ASM discontinuation as the only modifiable factor that may optimize intellectual and developmental trajectories.

ABSTRACTS

Topic: Neuromuscular Disorders

EPNS25_600 - Spinal muscular atrophy in children identified by newborn screening: Real-world +2-year experience from a tertiary referral center in Turkey

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Objectives: Implementation of newborn screening (NBS) for spinal muscular atrophy (SMA) had a huge impact on natural course and outcome in newborns with clinically silent, prodromal and early-symptomatic presentations. In Turkey, SMA is included in the NBS program by May 2022. Our aim was to retrospectively evaluate newborns referred to our center.

Methods: Demographic, clinical, molecular data and outcome in terms of motor, respiratory, swallowing/feeding, cognitive profiles, CHOP-INTEND and functional data based on *SMN2* copy numbers, and final outcome in 14 newborns (girls: 7, boys: 7) between September 2022-2024 were analyzed.

Results: The current mean age of the patients is 15.3 months (±8 months) with a median follow-up period of 13.8 months (±9 months). Final body-weights, heights, and head circumferences were 9.99 kg (±3.6), 75.7 cm (±12.1), and 44.9 cm (±3.8), respectively. The mean age at diagnosis was 9.4 days (±5 days). The median time between screening results and hospital admission was 5 days (min: 1, max: 58 days). The *SMN2* copy number was 2 (n= 9, 64.3%), 3 (n= 2, 14.3%), and 4 (n= 3, 21,4%). Consanguinity and family history was present in 5 (35.7%), and 2 newborns (14.3%), respectively. At referral, 11 newborns (78.6%) were asymptomatic, and 3 (21.4%) were symptomatic. The average total number of nusinersen doses was 4.51 (±2.75). Two of our patients (14.3%) also received gene replacement therapy. Twelve of the 14 patients (85.7%) received the first dose of Nusinersen, and 11 patients (78.6%) completed their loading doses. Intraspinal hematoma developed in 1 patient after lumbar puncture, which was resorbed. 2 patients with 2 *SMN2* copy numbers had femur fracture (n= 1) and ankle foot orthosis (n= 2). One patient (7.1%) required respiratory support, and 2 patients (14.3%) required nutritional support. SMN2 copy number was 2 in these patients. The CHOP-INTEND score at onset and las follow-up was 34.2 (±10), and 54.6 (±8.1), respectively (p=0.129). Developmental profile was age appropriate in 7 patients in terms of gross-motor skills, 12 patients in terms of fine-motor and language domains. *SMN2* copy number was 2 in all patients with delayed milestones. At the last follow-up, 6 patients (37.5%) were clinically symptomatic. One patient deceased due to acute respiratory failure at 21 months of age.

Conclusions: These results reflect that despite NBS program and early access to diseases' modifying treatments, long-term outcome vary depending on several factors in play at a real-world setting with emerging new phenotypes.

ABSTRACTS

Topic: Neuropsychiatric Disorders / Functional Neurological Disorders

EPNS25_602 - Neuropsychological and Psychopathological Profiles in Paediatric Functional Neurological Disorder: Preliminary Data from a Cohort of Children and Adolescents

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Objectives:

The aim of this study is to assess the neuropsychological and psychopathological features of a sample of paediatric patients who have been diagnosed with functional neurological disorders (FND). The primary objective is to identify cognitive and emotional profiles associated with FND, to improve diagnostic and therapeutic approaches.

Methods:

We conducted a retrospective analysis of medical records from paediatric patients admitted to our Neurological Institute between 2022 and 2024. We included all patients diagnosed with FND who completed a comprehensive multi-method assessment, including neuropsychological measures, psychopathological self-report questionnaires, a narrative test, and clinical interviews. Data on socio-demographic background, medical history, clinical symptoms, cognitive and emotional-behavioral functioning were collected. Statistical analyses were conducted to describe the cohort's characteristics.

Results:

A total of 53 patients were included (85% female, 15% male). The most frequently observed FND phenotype was gait disorder (40%), followed by functional seizures (28%), tremor (19%), and other functional movement disorders (13%). The mean age at diagnosis was 13.9 years. The mean total IQ score was 106. Low scores in attention-related tasks were observed in 50% of the group. We found a significant difference between parental reports and self-reported psychopathological symptoms, especially in internalizing scales. The narrative test gave more insight into emotional processing, revealing that negative emotions are poorly represented, feelings of rejection are high, and outcomes are often unresolved. Notably, trauma-related scales did not yield clinically significant scores.

Conclusions:

Our research offers valuable insights into the cognitive and emotional characteristics of children and adolescents with FND, highlighting the need for an integrated approach in their management. Our data suggests that executive functioning, emotion recognition, and narrative functioning may be impaired. We propose therapeutic interventions based on these characteristics, addressing both cognitive and affective functioning. It will require further research to better characterize FND population and identify other possible neuropsychological profiles.

ABSTRACTS

Topic: Neurodevelopmental Disorders / Developmental Neuroscience

EPNS25_603 - A survey on neurodevelopmental screening across Europe

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Objectives: Without routine screening a substantial proportion of children with neurodevelopmental (ND) disabilities may not be identified until they reach school age or later. Recent recommendations set new goals to healthcare systems and to neuropediatricians as leading figures in ND diagnosis and management. **Aim**: To study the current ND screening practice in European countries.

Methods: The survey was conducted during Sept. 2022 - Oct. 2023 by answering questions on ND screening at ages 0-3 and 4-7 yrs in Google Forms sent to country representatives in the EPNS Committee of National Advisors.

Results: Data of 17 EPNS member countries were received. ND surveillance and/or screening at ages 0-3 yrs is responsibility of: pediatricians/ neuropediatricians/ developmental pediatricians in 7 countries; general practitioners (GPs) with/without health visitors/nurses in other 7 countries; pediatricians with GPs or with early childhood education and care services in 3 countries. Screening tools, either national or commonly used, are applied in only 5 countries. In 5 other countries checklists or other ND tools are used. No tools are applied in 4 countries, and no data are available for 3. All but 2 countries had fixed mandatory ages for ND examinations, but only half scheduled check-ups at 9 and/or 18 months. There were 3 countries with only one ND prophylactic exam until 3 yrs. ND surveillance/screening covered >80% of infants in 5 countries, 40-79% in 4; no data for 8 countries. Moderate satisfaction of ND screening is dominant. Concerning ND screening at 4-7 yrs, it is a responsibility of pediatricians/ neuropediatricians/ developmental pediatricians and/ or GPs in 6 countries, and of education specialists with/without physicians in 11 countries. Specific screening test are applied only in 2 countries. Various psychological tests are used in 6; no tests are applied in 7 countries; no data for 2. ND screening at 4 yrs in mandatory in 4 countries, at 5yrs - in 6, at 6yrs - in 4, at 7 yrs.- 1, with some counties having more than one age of mandatory screening. More than 80% coverage is reported in 4 countries, 40-79% - 2, <40% - in 3, no data for 8 countries. Satisfaction is predominantly moderate.

Conclusions: ND screening practice in Europe is quite variable. Less than third of the counties applied screening tools. Development of specific European recommendations on timing, tools and other methodological issues are reasonable and might lead to convergence screening practices and improved ND health.

ABSTRACTS

Topic: Epilepsy: Medical and Surgical treatment

EPNS25_605 - Single regional centre experience of presentation and treatment effectiveness in Dravet Syndrome

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Objectives

Dravet syndrome is a developmental and epileptic encephalopathy characterized by early onset epilepsy with multiple treatment resistant seizure types. SCN1A variants account for most cases, with presentation and outcome varying by variant type. This study examines demographics, clinical features, treatment methods and responses in SCN1A positive Dravet syndrome patients at a regional tertiary centre.

Methods

A retrospective review of electronic medical records over 10 years was conducted for children aged ≤18 years with a diagnosis of pathogenic SCN1A variant Dravet syndrome in a regional centre.

Results

Twenty-four children were included. Median age of seizure onset was 5 months (IQR 2) and genetic diagnosis at 11 months (IQR 13). Generalised tonic-clonic seizures were the most common seizure phenotype - at onset and overall. Focal, myoclonic, absence, drop attacks, and tonic seizures were observed. One patient had respiratory compromise requiring ventilatory support with every seizure.
At presentation, 15/24 patients had a normal EEG, but all later developed abnormalities. The most common EEG abnormality was diffuse background slowing. Two patients had reproducible photosensitivity. Two patients had significant MRI abnormalities (periventricular calcifications, ventriculomegaly).
Seizure burden was high despite treatment: 5 patients had daily seizures, 13 had several weekly, and only 6 had ≤1 per month. The mean number of intensive care admissions since diagnosis was 2. However, most patients' seizure frequency improved over time
At latest follow-up, nearly all patients were on multiple medications (modal number = 4, range 2–6); only one was on monotherapy. Clobazam was the most used (19/24), followed by fenfluramine, stiripentol, valproate, cannabidiol, levetiracetam, and topiramate. One patient each was on perampanel and pyridoxine. 12/14 patients on stiripentol were concurrently on clobazam. Six patients had a vagal nerve stimulator, and two followed a ketogenic diet.
Cardiac evaluation was normal in 16 patients, while one had multiple ectopics; records were unavailable for others.
All patients were delayed in achieving developmental milestones. Most (22/24) children attended specialist educational settings. One child attended mainstream school and another is awaiting placement.
Sleep difficulties were the most frequent co-morbidity (12/24). Feeding difficulties were common with 9 patients requiring some mode of feeding support.

Conclusions

This study highlights the diverse presentations, significant seizure burden, and drug resistance in SCN1A Dravet syndrome. Vagal nerve stimulation and ketogenic diet may be beneficial adjuncts. Co-morbidities such as sleep disturbance and feeding difficulties may exist in addition to developmental and cognitive delay and should be addressed.

ABSTRACTS

Topic: Neuromuscular Disorders

EPNS25_606 - CuidAME: A global view of the Spanish longitudinal Registry of SMA patients in 2025

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Objectives

CuidAME, the Spanish national registry for Spinal Muscular Atrophy (SMA), was created in 2020 to collect real-life data after the arrival of innovative therapies: Nusinersen (Ns, available in Spain since 2018), gene therapy Onasemnogene abeparvovec (GT, 2021) and Risdiplam (Rs, 2022). It includes all genetically confirmed SMA patients, treated or not, followed up in several Spanish hospitals (target population estimated at 550 patients, followed for five years). The objective is to describe the characteristics of the SMA population in Spain.

Methods

Observational registry that collects retrospective and prospective data: epidemiology, natural history, effect of treatments and impact of the disease.

Results

533 patients (264 children, 269 adults) from 25 centers. SMA type distribution is: 22% SMA1, 39% SMA2, 36% SMA3, 1% SMA4. Twelve patients (2%) were diagnosed presymptomatically, nine of them in the context of newborn screening. 488 patients (91.5%) received a disease-modifying therapy (DMT) during the follow-up: Ns 204 (38%), Rs 92 (17%) and GT 29 (5%). Additionally, 16% received multiple treatments: 77 switch from Ns to Rs (6 SMA1, 45 SMA2, 26 SMA3) and 8 SMA1 patients received both GT and Ns. 6 presymptomatic patients were treated with GT, 4 with Ns and 2 with Rs (median age at treatment: 46 days of life, current median age: 1.3 y.o). Data on the motor, respiratory, digestive and neurocognitive status of the cohort will be presented.

Conclusions

CuidAME is currently the platform containing Spanish largest, harmonized, and standardized SMA clinical lead database. It provides crucial data, allowing a better understanding of the disease, the efficacy and the adverse effects of innovative therapies. National and international collaborations among centers and registries are promoted, expanding SMA knowledge.

ABSTRACTS

Topic: Neurogenetics

EPNS25_607 - Mitochondrial dysfunction in a patient with a CTBP1 mutation

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Objectives: The C-terminal binding protein 1 (*CTBP1*) is a transcriptional corepressor with a major role in nervous system growth and development. There are only 17 published cases with *CTBP1* mutations so far, displaying a phenotype with hypotonia, ataxia, developmental delay, and tooth enamel defect syndrome (HADDTS). Although decreased mitochondrial respiratory chain activity is reported in some of these cases, data on the metabolic phenotype assessed by various cellular respiration parameters in peripheral blood cells in real time are still missing. **Aim:** To detect mitochondrial function in a patient with neurodegenerative disorder due to a *CTBP1* mutation by a rapid and non-invasive method for measuring cellular energetics in live blood cells in real time.

Methods: A case report including phenotype description and cellular metabolic profile of peripheral blood mononuclear cells (PBMCs) isolated from a patient with a *CTBP1* mutation. Mitochondrial activity was assessed via mitochondrial respiration and changes in the electron transport chain by metabolite analyzer Seahorse XFp (Agilent).

Results: A 10-year-old Caucasian female is reported that presented at age of 17 months with failure to thrive, developmental delay, muscle hypotonia and weakness, ataxia, dysmorphic features, tooth enamel dysplasia, and cerebellar atrophy. Recent blood gas analysis was dominated by hypoxia and respiratory alkalosis or acidosis. Lactate elevation was infrequent and mild. The patient underwent surgical correction of severe kyphoscoliosis at 8 years and gastrostomy for failure to thrive at 9 years. Chronic respiratory failure and several apneic episodes led to tracheostomy and intermittent ventilatory support starting at 9 years.

WES revealed the most common *de novo* heterozygous pathogenic *CTBP1* mutation c.991CT, p.Arg331Trp, along with a *de novo* variant of unknown significance - *ATP1A3* mutation c.83A>C, p.Glu28Ala.

The Cell Mito Stress Test displayed severely impaired mitochondrial function with a significant decrease in maximal respiration and spare respiratory capacity compared to the control group of typically developing children. Additionally, glycolysis was assessed by analyzing the extracellular acidification rate (ECAR). Low levels of glucose intake were registered, indicating metabolic adaptation resulting in low cell respiration.

It may be assumed that *CTBP1* mutation is responsible for the phenotype and the mitochondrial dysfunction, not discarding speculations on the possible additional role of the *ATP1A3* mutation.

Conclusions: We report for the first time the use of noninvasive mitochondrial functional tests in real time in a patient with a *CTBP1* mutation and propose this approach as a reliable tool for further personalized and relevant therapeutic implications.

ABSTRACTS

Topic: Neurodevelopmental Disorders / Developmental Neuroscience

EPNS25_609 - Orexin Type-1 Receptor Expression in Somatosensory Cortex in Post-natal 21-day-old Rats with Absence Epilepsy

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Objectives Absence epilepsy is a generalized epilepsy syndrome characterized by sudden and transient loss of consciousness, predominantly affecting children. It is estimated that 2% to 10% of pediatric patients with absence epilepsy. The development of epilepsy is driven by a series of neurobiological processes collectively known as epileptogenesis. Recent studies suggest the role of orexinergic system in epilepsy but limited number of studies between the orexinergic system and epileptogenesis of absence epilepsy. This study examined to orexin type-1 receptor (OX1R) expression in the somatosensory cortex (SSC).

Methods Post-natal 21-day-old (PN21) Wistar and Genetic Absence Epilepsy Rats from Strasbourg (GAERS) (n=4 for each group) were decapitated under deep isoflurane anesthesia. SSC were extracted to analyze OX1R protein expression. Proteins were isolated, and their concentrations were assessed using the Bradford method. Western blotting was utilized to analyze protein expression. All data were evaluated using two-way ANOVA test.

Results OX1R protein expression in the SSC brain region was analyzed and compared between GAERS and Wistar rats. OX1R expression showed a significant increase in the SSC region of PN21 GAERS compared to PN21 Wistar rats ($p<0.05$).

Conclusion This study highlights a notable upregulation of OX1R expression in the SSC of PN21 GAERS compared to Wistar rats. These results suggest a potential involvement of the orexinergic system in the pathophysiology of absence epilepsy, particularly during early developmental stages. Further investigations are warranted to elucidate the precise role of OX1R in epileptogenesis and its potential as a therapeutic target.

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ABSTRACTS

Topic: Miscellaneous

EPNS25_610 - The impact of Blenderized diet on a small cohort of patiens with severe neurological impairment

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Objectives

Our purpose was to analyze during a long observation lasted 5 years, the effects of Blended Diets (BD) applied small cohort of children with severe neurological impairment Level V of the Gross Motor Function Classification System (GMFCS).

Methods

Eight children with gastrostomy, GMFCS-V and on exclusive BD, were followed for 5-years, measuring growth curves, nutritional balance, medical complications, and also evaluating family satisfaction with an Adapted- satisfaction Questionnaire with Gastrostomy Feeding (SAGA-10).

Results

Throughout the five-year period, all children experienced consistent weight gain. The median annual weight gain was 1.16 kg/year (IQR 0.65-1.4).

These findings suggest that BD provides sufficient calories and nutrients to support steady growth in children with SNI. The use of **pathology-adjusted growth curves** allowed for accurate monitoring of growth trajectories specific to this population, and the results indicate that BD is comparable to commercial formulas in terms of supporting growth. These findings also satisfied our initial objective of not finding any patient falling below the 10th percentile. (According to modern definitions, first level of malnutrition).

No major complications, such as tube obstruction or peritonitis, were reported in any of the children during the five years of follow-up. This finding underscores the safety profile of BD, which appears to be on par with that of commercial enteral formulas. Gastrointestinal complications, such as vomiting or diarrhea, were not highlighted as significant issues in this cohort, further supporting the tolerability of BD in children

The caregivers reported high levels of satisfaction with the use of BD. The median satisfaction score was 44/50 points (IQR 41.5-46.5),

Conclusions

The long-term use of blenderized diets in children with severe neurological impairment appears to be a viable alternative to commercial enteral formulas. The study demonstrated that BD could sustain appropriate growth, with no additional risks of medical complications such as tube obstruction or peritonitis. Caregivers also reported high levels of satisfaction with this feeding method, further supporting its use in home and clinical settings.

ABSTRACTS

Topic: Neurodevelopmental Disorders / Developmental Neuroscience

EPNS25_611 - Metabolomic biomarkers of hypoxic injury of immature blood-brain-barrier and effects of C1 Esterase Inhibitor

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Objectives: Hypoxia-Ischemia (HI) severely disrupts cerebral metabolic and maturation programs, contributing to blood brain barrier (BBB) dysfunction. It has been shown that C1 esterase inhibitor (C1INH) treatment reduced BBB damage and brain oedema in neonatal hypoxic mice. However, the underlying mechanism is not fully understood. We hypothesized that neuroprotective effects of C1INH are related to lipid and fatty acid metabolism which has major impact on vascular stability.

Methods: P7-C57BL6/N mice were exposed to hypoxia (8% FiO_2, 6 h) and treated with C1INH (7.5–30 IU/10 ml/kg, i.p.; Berinert®, CSL Behring) or NaCl 0.9% (VT). After a regeneration period of 24 h tissue samples were collected. Metabolites extracted from EDTA plasma were subjected to untargeted liquid chromatography–mass spectrometry. To obtain individual biochemical fingerprints of VT- and C1INH-treated mice, raw data were processed and statistical analysis (PCA, PLS-DA, t test) was performed prior metabolite and pathway enrichment analysis were conducted.

Results: Present analysis identified 1791 metabolites including 487 lipids (43% fatty acyls, 32% glycerophospho-, 10% sterol-, 5% sphingo-, and 4% glycerolipids). PCA scores plots revealed a distinct separation along the 1st predictive component, effectively distinguishing hypoxia and C1INH samples from the control groups. Within the hypoxia group, 40 metabolites exhibited statistically significant changes ($p < 0.05$). In particular, metabolites of the amino acid (e.g. L-Carnitine, 2-Aminobutyric acid) and lipid metabolism (e.g. glycerophospholipids and -cholines, 3,4-Dihydroxybenzoate) were among the most significantly altered metabolites. When comparing the hypoxia-exposed VT- and C1INH-treated group, 164 differentially expressed metabolites were identified. The top 20 pathways mainly involved the glycine, serine and threonine metabolism, the biosynthesis of essential amino acids, the glycerophospho- and sphingolipid as well as the linoleic acid metabolism.

Conclusions: Our data suggest that hypoxia-induced changes in lipid and amino acid metabolism are significantly attenuated by C1INH treatment and provide an important basis for understanding BBB changes during HI and identifying potential targets for novel neuroprotective treatments.

ABSTRACTS

Topic: Miscellaneous

EPNS25_612 - Searching for metabolic biomarkers of paediatric Charcot-Marie-Tooth disease

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Objectives

Charcot–Marie–Tooth (CMT) disease is the most common hereditary neuromuscular disorder with the phenotype of usually slowly progressive, chronic neuropathy affecting both the motor and the sensory nerves. Currently, there are no approved therapies or treatment responsive biomarkers for monitoring the disease. In this study, we aimed to analyse selected metabolite concentration in CMT patient plasma and compare them to healthy controls.

Methods

A cohort of 12 CMT patients and 5 healthy controls (≤ 18 years of age) were enrolled in the study. All CMT individuals underwent genetic testing. Blood sampling and storage were conducted following a strict standard operating procedure. Targeted plasma metabolic analysis was performed by ultrahigh performance liquid chromatography-mass spectrometry (UHPLC-MS) to determine plasma levels of 55 selected metabolites, from which 33 were detected in plasma samples from CMT patients and healthy controls. Statistical analysis was performed with MetaboAnalyst 6.0. The study was approved by the Central Medical Ethics Committee of Latvia (No. 3/18-03- 21).

Results

The patient group was subdivided according to the genetic findings: CMT1A (n=6), CMTX1 (n=3), HINT1 (n=1), CMT2N (n=1), CMT2A (n=1). We used univariate statistical analysis to screen for differential plasma metabolites between separate genetic CMT group with a sufficient number of cases (CMT1A (n=6) and the control group. We identified differential metabolites with the volcano plot (V-plot) and orthogonal partial least squares-discriminant (OPLS-DA) using fold change (FC) > 1.5, p-value < 0.05, variable influence on projection (VIP) > 1 as significance cut-offs. We found that L-Cystine, Taurine, Carnitine, Butyrylcarnitine, L-acetylcarnitine, L-Valine in the CMT1A group are different from the controls. Further we screened for differential metabolites in all CMT patients and controls. We identified three plasma metabolites that were significantly changed to controls without being able to separate CMT subtypes based on their metabolic profiles. The plasma ratio of Butyrylcarnitine and L-Valine was elevated and the plasma ratio of L-Cystine was decreased in the CMT compared with controls.

Conclusions

Our study provides information about plasma metabolite levels in paediatric CMT patients. We have identified that CMT patients have significantly higher levels of Butyrylcarnitine and L-Valine, and decreased L-Cystine levels compared to controls. In addition, the CMT1A subgroup has increased Carnitine, L-Acetylcarnitine levels and decreased Taurine levels compared to controls. Consequently, the metabolites mentioned above might be unspecific biomarkers of neuropathy, however, longitudinal assessment is needed to evaluate metabolite marker capabilities.

ABSTRACTS

Topic: Neuropsychiatric Disorders / Functional Neurological Disorders

EPNS25_613 - PANS/PANDAS: Clinical Experience in IVIG Treatment

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Objectives

Pediatric acute-onset neuropsychiatric syndrome (PANS) is a condition characterized by the abrupt, dramatic onset of obsessive-compulsive disorder (OCD) or eating restriction accompanied by equally abrupt and severe comorbid neuropsychiatric symptoms. PANDAS (pediatric autoimmune neuropsychiatric disorder associated with streptococcal infection) is a heterogeneous syndrome identified as post-Streptococcus pyogenes infection (hemolytic Streptococcus group A) complications regarding the central nervous system with specific involvement of neuropsychiatric and behavioral skills.

In our study, we share our experience in the treatment of a group of extreme-grade (according to CY-BOCS severity scale) symptomatic patients with intravenous immunoglobulin (IVIG), following the most recent studies regarding the dosage of the drug. Our contribution is to share our experience made on a sample of 65 patients all in the highest level of a severity grade.

This study aims to evaluate the clinical features of the patients observed from different Italian cohorts, with the attempt at evaluating clinical response to IVIG treatment in children with an extreme severity grade of PANS/PANDAS disease

Methods

A total of 65 patients with a diagnosis of PANS/PANDAS, who belonged to an extreme grade of disease were enrolled. All patients were administered with IVIG treatment at 2 g/kg per day for two consecutive days**.**

Results

What comes out from our study is a noticeable improvement (transition from extreme symptom grade to lower grade) in 56 out 65 children, and in some cases (15 out 56), a complete remission of symptoms for at least one year in observed children. A total of 13 patients (5 males and 8 females) out of the 56 responders required only one cycle of IVIG therapy (2 g/kg per day for two consecutive days), showing clear clinical improvement of symptoms with no further relapse, whereas in the remaining patients, a second cycle led to clinical well-being for at least one year as in the following months they had manifested resumption of symptoms. In a small percentage (n = 9 cases) after an initial response, symptoms reappeared requiring a third further cycle one year after the first administration, without obtaining a significant result.

Conclusions

Considering the variability of the disease, we cannot establish the correct definitive therapy; however, the encouraging data from this and other studies tell us that we are not far from a better understanding of this disease.

ABSTRACTS

Topic: Neuromuscular Disorders

EPNS25_614 - Patient Demographics ; clinical presentations and genetic mutations of Duchenne muscular dystrophy and Becker muscualar dystrophy patients in XXX

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Objectives

Objective: To describe the landscape of DMD in xxx including demographics, genetics, disease progression and severity, risk factors, co-morbidities, and outcomes in patient aged 2–20 living in xxx and compare it to world-wide data.

Methods

Detailed clinical data was gathered retrospectively from all records of DMD and BMD patients from 2018-up to this date of publication from a multidisciplinary neuro-muscular clinic in Sidra Medicine Hospital, the only tertiary pediatric center in xxx.

Results

Among DMD patients (*n* = 36), the mean age was 18 (3–22) years and for the single BMD patient included, that was in 30 years. Out of the 38 patients with confirmed DMD/BMD genetic mutations, 36 are male and 2 are female (one female out of the two is an asymptomatic carrier). 46% of the patients are full time wheelchair users on average by the age of 9.6; 37.8% were on a management plan that involved corticosteroids along with other medications used in combination for cardiomyopathy, bone weakness and/or epilepsy. As expected, Deletions were the most prominent mutation that led to DMD with it being prevalent in 69% of confirmed patients, with duplication being at ~11% and all other mutations being at ~20%.

Conclusions

The prevalence of key clinical features across patients discovered in xxx was consistent with world-wide data. Although the DMD and BMD management in xxx is consistent with international guidelines, patient life expectancy and quality of life remain lower than internationally reported numbers. The collected data will help promoting strategies to improve patient outcomes. Another contributing factor is differences in research priorities, funding availability, and collaboration networks between xxx and other countries may influence the scope and depth of studies conducted on DMD and BMD. Collaborating with other research centers provides access to resources, expertise, and advanced technologies that may not be readily available in xxx. By collaborating with leading research centers, our center can accelerate the translation of scientific discoveries into clinical practice. This may involve the development of novel therapeutics, diagnostic tools, or adopting guidelines tailored to the specific needs of DMD and BMD patients in xxx , ultimately improving the outcomes and quality of life. Additionally, collaboration with international research centers can expand funding opportunities for DMD and BMD research in xxx by participating in multinational research consortia, and engaging with philanthropic organizations and importantly ensure the mixed ethnic representation in these studies

ABSTRACTS

Topic: Neurometabolic Disorders

EPNS25_616 - Clınıcal and Neuroımagıng Characterıstıcs of Chıldren Dıagnosed wıth Metabolıc Epılepsy

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Objective:
Congenital metabolic disorders are rare conditions that should be considered in unexplained and refractory seizures during the neonatal and early infancy periods, particularly in the presence of consanguinity, a history of sibling death, and accompanying encephalopathy. Early diagnosis is crucial. This study aims to evaluate the clinical and neuroimaging characteristics of children diagnosed with metabolic epilepsy.

Methods:
In our study, the data of 14 patients diagnosed with metabolic epilepsy, who were admitted to our hospital between 2014 and 2024 with drug-resistant seizures, intellectual disability, dysmorphism, movement disorders, and involvement of different systems, were retrospectively reviewed. The post-treatment seizure outcomes of the patients were assessed clinically and via electroencephalography (EEG). Brain Magnetic Resonance Imaging (MRI) was used as the neuroimaging method.

Results:
The data of 14 patients diagnosed with metabolic epilepsy between 2014 and 2024 were retrospectively analyzed. Of the 14 cases included in the study, 9 were female and 5 were male. The mean age was 157 months (range: 56–288 months). In our study, two patients experienced seizures during the neonatal period, while eight patients presented with their first seizure. The mean age of the first seizure was 37.4 months (range: 0–120 months), and the mean age of epilepsy diagnosis was 43 months (range: 0–120 months). Five patients had generalized onset seizures, one patient had focal onset seizures, and the initial seizure data were unavailable for seven patients. One patient had an unknown seizure onset type. Generalized seizures were observed during the follow-up of all patients included in the study. Levetiracetam was identified as the most commonly used antiepileptic drug. Five patients were followed up with a diagnosis of neuronal ceroid lipofuscinosis. Following treatment, seizures ceased in six patients. A reduction in seizure frequency of less than 50% was observed in seven patients, while one patient experienced a reduction in seizure frequency of more than 50%. Initial EEG findings were consistent with epileptiform activity in seven patients. Cerebral atrophy was the most common brain MRI finding. Cognitive impairment was observed during follow-up in five patients.

Conclusion:
The recognition of congenital metabolic disorders is crucial as specific treatments exist for certain metabolic conditions. In cases with refractory seizures, particularly during the neonatal and early infancy periods, metabolic epilepsies should be considered in the differential diagnosis. Early diagnosis and treatment can positively impact long-term neurological and developmental outcomes.

ABSTRACTS

Topic: Neurodevelopmental Disorders / Developmental Neuroscience

EPNS25_618 - An Investigation of Stuttering Prevalence in Children in Tashkent, Uzbekistan

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Objectives: Stuttering is a speech disorder and more than 70 million people, are suffering from it. Reports on the epidemiology of stuttering in Uzbekistan is limited. Our primary goal was to examine the prevalence of the disorder among kindergarten-aged children. This study aimed to determine the prevalence of stuttering among kindergarten-aged children in the Olmazar district of Tashkent and to evaluate potential contributing factors.

Methods: A total of 1101 children from preschools in the age range of 3-6 years were screened in clinic to which these 5 kindergartens were belonged. Stuttering were confirmed as follows: (1) direct interviews and assessment of the children's speech by an SLP, (2) questioning based on fluency severity rating scale.

Results: The prevalence of stammering among preschool children was found to be 1.45%. A significant gender difference in stuttering prevalence was observed, with 10 out of the 16 identified children being male and 6 female, resulting in a male-to-female ratio of 5:3 ($p < 0.05$). Furthermore, children with a family history of stuttering were 62.5% more likely to stutter compared to those without such a history ($p < 0.05$). However, no significant relationship was found between the prevalence of stuttering and the family's socioeconomic status or linguistic background ($p > 0.05$). Analysis was conducted using one-way ANOVA and Tukey's HSD for post-hoc comparisons.

Conclusions: The findings suggest that the development of stuttering is influenced by factors such as gender and family history, with men more often affected, and a significant association is observed in children with a family history of stuttering. These results highlight the importance of early detection, especially for high-risk groups. These results provide new insights into the epidemiology of stuttering in Uzbekistan.

ABSTRACTS

Topic: Neurometabolic Disorders

EPNS25_619 - Long Term Neurological Outcome After Hematopoietic Stem Cell Transplant in Juvenile Krabbe Disease

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Objectives

Globoid cell leukodystrophy (GLD) is a rare neurodegenerative disease caused by galactocerebrosidase deficiency, leading to progressive demyelination. Juvenile phenotypes show onset between 3 and 16 years of age. Hematopoietic stem cell transplantation (HSCT) is the only available treatment, but few transplanted cases of juvenile GLD have been reported to date. This study aims to comprehensively evaluate the long-term neurological outcomes of HSCT in juvenile GLD.

Methods

This retrospective cohort study analyzed clinical, hematological, biochemical and instrumental data (including MRIs, evoked potentials and nerve conduction studies) from children with juvenile GLD who underwent HSCT and were followed at our Institution.

Results

We included 6 children: 4 were symptomatic, while 2 were asymptomatic. All patients were followed for up to 20 years; data was comprehensively collected pre-HSCT (T0), first visit post-HSCT (T1), and at last follow-up (Tn). All 6 patients were alive at the last follow-up. 4 achieved near-normal cognitive, motor, and functional outcomes. 2 patients with pre-HSCT extensive white matter involvement and specific clinical symptoms (epilepsy and cognitive impairment) had suboptimal outcomes. Loes scores, used to score brain MRIs, stabilized/improved in 4 patients, and GALC enzyme levels normalized in all. Electrophysiological findings stabilized over time

Conclusions

HSCT significantly alters the natural history of juvenile GLD, with mostly long-term optimal outcomes, normal quality of life and near-absent disability burden. Pre-HSCT, patients should undergo extensive assessment using standardized evaluations. We speculate on possible prognostic factors. Among them an extensive degree of white matter involvement, as assessed by the Loes score, could represent a negative prognostic indicator. Pre HSCT clinical symptoms such as intellectual disability and epilepsy or the choice of a donor with a heterozygous GALC mutation could also influence a poorer prognosis, although our data is not sufficient to reach a definite conclusion. Future studies on larger cohorts are necessary to refine prognostic markers, optimize donor selection strategies, and standardize pre-HSCT evaluation tools to maximize the benefits of HSCT for juvenile GLD.

ABSTRACTS

Topic: Neuromuscular Disorders

EPNS25_620 - Modeling disease progression in Duchenne muscular dystrophy: reduced decline in forced vital capacity with givinostat compared with standard of care

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Objectives

Givinostat, an oral histone deacetylase inhibitor, was recently approved in the US and UK for Duchenne muscular dystrophy (DMD) treatment in patients aged ≥6 years, based on findings from the phase 3 EPIDYS study. Using the validated DMD Clinical Trial Simulation tool, developed by C-Path's Duchenne Regulatory Science Consortium, updated with data from EPIDYS and the ongoing long-term safety and tolerability study, simulations were conducted to assess differences in the time course of worsening forced vital capacity (FVC) among patients receiving givinostat or standard of care (SoC).

Methods

As few givinostat-treated patients in the long-term safety and tolerability study demonstrated a decaying trend in FVC over time, a modelling approach was unable to be adequately implemented to quantify the full disease progression curve for this cohort. Thus, for this analysis, simulations of the published SoC model of FVC were applied to a virtual patient population with data beyond 15 years of age (N=64) using baseline demographics matching those from the EPIDYS and long-term safety and tolerability studies, and compared with the observed givinostat data. Simulations were conducted in NONMEM (version 7.5.1) using 500 replicates and accounting for interindividual variability.

Results

The published DMD disease progression model of FVC was validated with data from patients receiving SoC in the EPIDYS study. Results from the visual predictive check diagnostics demonstrated good agreement between the observed and simulated data, suggesting that the available model was suitable for performing comparative simulations with the DMD population from the available studies. Simulated and observed FVC profiles in patients >15 years of age were summarised, assessing the percentage of patients with FVC <1 L. Treatment with givinostat showed a lower percentage of patients aged >15 years with FVC <1 L (3.1% vs 12.5%; 95% CI, 6.2–20.3%) than simulated SoC. This corresponds to fourfold-higher odds (95% CI, 2.0–6.5) of observing FVC <1 L in patients receiving SoC than in those treated with givinostat.

Conclusions

These simulations suggest a potential benefit of givinostat in delaying respiratory decline in DMD, as evidenced by lower rates of FVC reduction among treated patients. Further research is needed to validate findings, given the limited data availability in patients aged >15 years (when a decrease in FVC function is anticipated) in the givinostat studies.

ABSTRACTS

Topic: Neurometabolic Disorders

EPNS25_621 - Outcomes of miglustat use in five children with CLN3 disease

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Objectives

To describe clinical outcomes following oral miglustat treatment, an approved therapy for related lysosomal diseases, in a small cohort of paediatric patients with *CLN3* disease.

Methods

In this retrospective case series, five patients with genetically confirmed classical CLN3 disease were prescribed oral miglustat (weight-based dose to maximum 600mg daily), commencing treatment between September 2023 and October 2024. Main outcomes were comprehensive ophthalmological assessment including visual acuity, optical coherence tomography, fundus imaging and fundus autofluorescence. Functional assessments included: Vineland-3 and Unified Batten Disease Rating Score (UBDRS), as well as observational reports from families, carers and educators.

Results

Cohort included five children with classical *CLN3* disease, aged between 8 years 10 months and 12 years 10 months (median 9.9 years) at treatment commencement. Vision improvements were reported in several patients with improved visual acuity (logMAR scale) and stabilisation of retinal atrophy. The impact of the therapy was further evidenced by the improved ability to undertake the ophthalmic assessments. Vineland-3 and UBDRS assessments demonstrated stability or improvement for all patients to date. One patient demonstrated improvement in functional/adaptive scoring, though vision has not improved. Some patients have noted a subtle tremor since starting miglustat, which does not appear to impact on function.

Subjective observations from each of the families, carers and educators were grouped by theme with positive reports pertaining to improvements in overall behaviour, decreased aggression and anxiety, improved learning (commensurate with peers for some), increased independence in play and confidence in social interactions. These improvements were often notable as early as the 3 month treatment review).

Conclusions

Miglustat therapy in a cohort of five children with early stage *CLN3* disease may have clinically meaningful disease-modifying effects and warrants further prospective studies in paediatric cohorts against known natural history controls, to assess efficacy and long-term treatment outcomes in this population.

ABSTRACTS

Topic: Epilepsy: Diagnosis and Investigations

EPNS25_622 - The Evaluation of White Matter Intensities in Patients with Pediatric Epilepsy

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Objectives

Neuroimaging is an important tool, in combination with a detailed medical history, physical examination, and electroencephalography, in the diagnosis and classification of epilepsy. White matter hyperintensities (WMHs) are bright areas of high signal intensity seen in white matter at T2-weighted MRI. Aim to evaluate whether white matter hyperintensities are more common in children with epilepsy.

Methods

Patients who underwent cranial MRI with diagnoses of epilepsy based on International League Against Epilepsy (ILAE) criteria at the Balıkesir University Medical Faculty Pediatric neurology clinic, Türkiye, between 01.08.2019 and 01.03.2024 and patients who underwent cranial MRI during the same period due to indications other than epilepsy, such as headache, syncope, and vertigo, were included in the study. Written informed consent was received from all patients.

Results

The study included 173 patients with epilepsy and 127 control patients. WMHs were detected in 28 cases (16.1%) in the epilepsy group and in five cases (4%) in the control group, the difference was significant ($p=0.02$). The mean WMH volume in the epilepsy group was significantly higher than in the control group, 127 ± 15.49 mm^3 ($p<0.05$).

Conclusions

Pediatric epileptic WMHs were also significantly different in number and volume compared to the control group. Prospective studies are needed to better understand the relationship between pediatric epilepsy patients and white matter changes.

ABSTRACTS

Topic: Movement Disorders/ Cerebral Palsy

EPNS25_623 - Assessment of transdermal clonidine patches in the management of severe dystonic disorders

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Objectives Transdermal clonidine patches (TCP) are rarely used for dystonia treatment in the UK practice. Our objective was to assess effectiveness and tolerability of TPC in therapy of paediatric patients with complex dystonic disorders referred to the tertiary paediatric neurology clinic.

Methods A retrospective study of children referred by general paediatricians to the paediatric neurology services for management of neurological conditions was conducted in April 2016-April 2022 by reviewing clinical notes, electronic records, sleep-dystonia charts, neuroradiology, and neurogenetic reports.

Results Out of 1,003 referrals, 57 were assessed for management of dystonia. 18/57 cases were identified as candidates for treatment with TCP (male: female =1:1, age range - 2-17 years (mean 9.69 ±5.62). All patients had MRI and CT brain scans: 1/18 had a normal study, 7/18- basal ganglia lesions, 14/18- white matter atrophy, and others (3/18). Causes of dystonia were established as severe hypoxic-ischaemic encephalopathy in 8, genetic mutations – 4, metabolic condition – 3, inflammation-1, and unknown - 2. All patients had co-morbidities: cerebral palsy (9/18), epilepsy (14/18), global developmental delay (16/18), and neuro-disabilities (GMFCS 3-5- 18/18). All patients were started on clonidine 9mcg/kg/day (16/18- enteral, 2/18-IV) with at least 3 other antidystonic medications (ADM) and transferred to TCP. They were discharged with established doses of 24.5 mcg/kg/day (mean 24.46±15.03) and improved seating position, pain, and tone (18/18), improved involuntary movements (10/18), and reduced number of other ADM (7/18). Side-effects were all tolerated and noted with bradycardia (13/18), hypotension (6/18), bradycardia with hypotension (5/18), contact dermatitis (1/18), and none (4/18). 7 patients remained on monotherapy with TCP. After their discharge, 12 patients continued on TCP, 4 - deceased from non-neurological causes, 1- declined further TCP, and 1 –lost to follow-up.

Conclusions Our case-series study demonstrated that therapy with TCP achieved a good control of dystonic presentations, good quality of life, and improved health economics by reduction of ADM in our complex neurological patients. We also showed good patients' tolerability of TCP side-effects. This study also highlighted importance of increasing awareness among clinicians about the use of TCPs as effective and safe therapy for dystonia especially in severe neuro-disabled paediatric patients.

ABSTRACTS

Topic: Epilepsy: Diagnosis and Investigations

EPNS25_624 - High frequency ossilations (HFO) as an electroneurophysiological marker for the Self Limited Epilepsy with Centrotemporal Spikes (SeLECT) : A Retrospective Cohort Study

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Objectives: High-frequency oscillations (HFOs) are oscillatory high-frequency signals (>80 Hz) that can be recorded by scalp EEG. They can be either physiological or pathological. HFOs have been reported as potential biomarkers for predicting seizures and identifying the seizure onset zone. The aim of this study was to explore the role of HFOs in the long-term follow-up of patients with SeLECTS, the most common self-limited epilepsy syndrome in childhood.

Methods: A total of 37 children diagnosed with SeLECTS were enrolled. Demographic data (age, gender), clinical findings (age at onset, seizure frequency, semiology, antiseizure medication [ASM] choices/responses, comorbidities like learning disability and cognitive impairments, epilepsy duration, seizure control, ASM usage), and EEG findings at diagnosis, 6–12, 12–24, and 24–36 months were analyzed using N2 sleep records. EEG recordings and feature extraction were performed using MNE and YASA libraries with custom Python scripts. Extracted features included N2 sleep duration, number/duration of sleep spindles (SS), number/duration of HFOs, number/duration of spike waves (SW), and HFOs related/unrelated to SS and SW for each EEG channel. Additional parameters included feature overlap, duration, average time, and percentages. Neural networks were used for data analysis. Neural networks hide the importance of patterns or features affecting data classification thus; Leave-One-Out Feature Selection (LOOFS) was applied to interpret each iteration, allowing an assessment of the impact of specific features on the classification performance of the model

Results: Among the participants, 20 (54%) were female. No significant impact of demographic or clinical findings on seizure control was observed. After repeated LOOFS analysis, the model achieved a mean accuracy of 91.59%, specificity of 98.03%, and sensitivity of 72.27% for seizure control prediction. The most influential features contributing to the model's classification ability were:The number of overlapping HFO/SW events, Total duration of SS, Average HFO duration, and Percentage of non-overlapping HFOs. Statistical analysis revealed that persistent epileptic activity on EEG was associated with learning disability ($p = 0.03$). In the initial EEG recordings, cases with epileptiform activity exhibited significantly longer HFO durations ($p = 0.02$). During long-term follow-up, SS-related HFOs decreased, independent of the presence of epileptic activity on EEG ($p = 0.009$).

Conclusions: In patients with SeLECTS, electro-neurophysiological parameters—particularly HFO/SW co-occurrence, HFO duration and percentage, and total duration of SS—appear to play a critical role in seizure control. These findings highlight the need for larger-scale studies to further validate these observations.

ABSTRACTS

Topic: Neurological Emergencies

EPNS25_625 - Uncovering Emergency Care Processes for Paediatric Neurologic Patients: a Process Mining study

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Objectives

This population-based study provides insights into the care pathways, resource needs, and outcomes of paediatric neurological patients at a large paediatric emergency department (PED) by utilizing large scale real-world data.

Methods

Patient data from neurological visits at a University Hospital PED between January 2021 and December 2023 were analysed using modern data analysis and process mining tools. The University PED is the only one in the area providing acute specialized care for children under the age of 16 years.

Results

A total of 4854 visits, accounting for 5.5% of all PED visits, were identified among 3553 patients. The most common chief complaint was seizure accounting for 43% of all and 69% of the urgent visits (Emergency Severity Index (ESI) acuity level 1-2), followed by headache (21%), which was linked to visits with lower acuity (ESI level 3-5). Other complaints were non-specific and heterogenous. Younger children, particularly boys, were more likely to present with seizures, while headache and other causes were more common complaints in children older than 10 years. Of the PED cases requiring immediate lifesaving intervention (ESI level 1), 19% were neurological. Seizures accounted for 77% of these, emphasizing their critical nature.

Of all neurological cases, 87% were either discharged or admitted after basic laboratory tests or no paraclinical tests. Imaging, EEG and/or cerebral spinal fluid analysis were conducted in 12% of cases. The care pathways for patients who underwent more paraclinical tests than basic laboratory tests had substantial variability with over 35 distinct processes identified, some unique to a single patient. These patients were more likely to be hospitalized, though most of them, too, were discharged. Of all neurological patients, 23% required hospitalization. Less than 1% were admitted to the paediatric intensive care unit (PICU). 81% of ESI level 1 patients required hospitalization and 15% of these were admitted to the PICU. 82% of the more stable ESI level 3-5 patients were discharged, as were 90% of all patients who presented with a headache.

Conclusions

This population-based study pioneers advanced methods to analyse patient care processes and resource utilization of neurologic patients at the PED by integrating large-scale real-world data. It highlights the critical nature of paediatric neurological emergencies and shows the substantial variability of patient pathways.

ABSTRACTS

Topic: Neuromuscular Disorders

EPNS25_626 - Biallelic variants in RYR1 and STAC3 are predominant causes of King Denborough Syndrome in an African cohort

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Objectives

King-Denborough Syndrome (KDS) is a congenital myopathy (CM) characterized by myopathy, dysmorphic features, and susceptibility to malignant hyperthermia. This study aimed to investigate genotype-phenotype correlations in Black African individuals with KDS-like phenotypes who remained undiagnosed for over 25 years.

Methods

A cohort of 67 Black African patients with CM was studied, including 44 clinically diagnosed with KDS. Whole-exome sequencing (WES) was performed as part of an international genomics initiative to identify pathogenic variants and to establish genotype-phenotype correlations.

Results

Pathogenic variants in *RYR1* and *STAC3* were identified as the predominant genetic causes of KDS in this cohort, both exhibiting autosomal recessive inheritance. While *RYR1* has been traditionally associated with autosomal dominant mutations, *STAC3*, previously linked exclusively to Native American Myopathy/Bailey-Bloch Myopathy, congenital hypotonia, and malignant hyperthermia susceptibility, is newly associated with CM-KDS in this study.

Conclusions

This study represents the first genotype-phenotype correlation for 44 Black African individuals with KDS, marking a critical advancement in understanding CM in underrepresented populations. The findings highlight the prolonged diagnostic odyssey of these patients and underscore the urgent need for improved genomic medicine accessibility in underserved regions. Expanding research and diagnostic capabilities in Africa is crucial for advancing genetic medicine and enhancing patient outcomes.

ABSTRACTS

Topic: Neurometabolic Disorders

EPNS25_627 - Oral tyrosine supplementation: a novel therapeutic approach in two children with YARS2 pathogenic variants

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Objectives: *Pathogenic YARS2* variants cause myopathy, lactic acidosis and sideroblastic anemia 2 (MLASA2), with variable phenotypic manifestations. *YARS2* encodes the mitochondrial enzyme tyrosyl-tRNA synthetase, responsible for conjugating tyrosine to its cognate mt-tRNA. No effective treatments are available; a possible therapeutic approach could be the oral supplementation of tyrosine to improve enzyme function, but to date no data is to date available.

Methods: We report the follow-up of both clinical data (using standardized scales) and laboratory data in 2 patients with pathogenic *YARS2* variants who initiated oral off-label supplementation with tyrosine.

Results: Two siblings presented in infancy with MLASA2, requiring regular blood transfusions until 14 months (pt 1) and 9 months (pt 2) of age. Pt 1 remained stable until age 11, when he became transfusion-dependent and started developing progressive proximal myopathy. By age 15, he showed generalized hypotonia, pelvis girdle weakness (requiring a wheelchair for long distances), initial hypertrophic cardiomyopathy and sleep apnea necessitating non-invasive ventilation. Pt 2 is now 11 and asymptomatic. Both siblings started oral tyrosine supplementation aged 11 and 15 respectively (320 mg/day). Clinical and laboratory follow-up after 8 months of treatment demonstrated that tyrosine was well tolerated and safe. Improvement in motor function was seen in both children and confirmed by standardized scales (6-meter-walking-test and North Star Ambulatory Assessment). Patient 1 also showed a possible improvement on hematological features of disease (reduced need for blood transfusions).

Conclusions: Clinical severity varies among *YARS2* patients; however, over half experience significant morbidity, with declining motor abilities leading to wheelchair dependence.
This is the first report on tyrosine supplementation in patients harboring YARS2 pathogenic variants. Only anecdotic reports on amino acid supplementation in other aaRS2 syntethase disorders are to date available. In our case reports, tyrosine demonstrated beneficial effects on motor outcomes and, possibly, on hematological feature of disease; it showed good tolerance and no adverse effects, leading us to believe it could be a possible therapeutic approach for MLASA2 patient.
Larger studies including patients with other aaRS2 mutations are needed to validate our results.

ABSTRACTS

Topic: Basic Science

EPNS25_629 - How robot Pepper, the technological friend, supports children's well-being in hospital

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Objectives: Interesting non-medical activities in hospitals help relieve fear and anxiety in children. Healthcare personnel should implement stimulating interventions to enhance the treatment process and support children's emotional well-being. The aim of the study was to identify an innovative approach to enhance well-being and mood in hospitalized children using social robot Pepper.

Methods: 12 hospitalized children (7 girls, 5 boys) aged 3-10 years participated in the bedside program with child-like robot Pepper. The study employed a qualitative design to assess the mood in hospitalized children before and after a 30-minute dialogue with robot Pepper (h 120 cm, w 28 kg), from both the children's and parents' perspectives. Two age-specific scenarios (for ages 3–6 and 7–12 yrs) were developed including songs, games, jokes, puzzles, and medical talks. Operator-selected responses guaranteed personalized and interactive conversations. To assess children's moods, modified visual analogue scales (VAS) were used: 0 represented the happiest mood and 10 represented the saddest. Semi-structured interview forms with modified 6-point Likert scale statements were used for parents.

Results: The most commonly reported problem by children during hospital stays was fear and discomfort associated with needle procedures. Mood reported by children and their parents improved during Pepper's visit. At the first assessment with VAS, 50% of children reported mood level as very good (0-1 point out of 10) and 16.6% as very sad up to neutral. After interacting with the robot, the number of children in a very good mood increased by 33.3%. Other children's emotions after meeting with Pepper were good (2-3/10). Parents' questionnaire revealed that they assessed their child's mood as positive during the hospital stay in 66.6% of cases and as neutral in 33.3%. After meeting with Pepper, all parents described their children's mood as very good or good. Parents' feedback indicated a high satisfaction level with child-robot interaction, and in 91.6% of cases, parents expressed desire for their child to meet Pepper again during subsequent hospital visits.

Conclusions: Children's bedside support with robot Pepper during hospital stays provided comfort, mood improvement, and education through funny and meaningful dialogue, and reduced hospital anxiety contributing to a more active treatment process.

ABSTRACTS

Topic: Neurorehabiltation

EPNS25_630 - How a social robot interacts with neurologically impaired and healthy children

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Objectives: In children with neurological impairment (NI) and brain injury, social dysfunction is present in more than 50%. Social dysfunction and a lack of empathy skills are often rated as the most debilitating sequelae, affecting many areas of a child's daily life. All children have unique developmental needs and thus, social robots, which can be adapted to the age and developmental stage of the child, provide a useful platform through which these needs and deficits could be met. The aim of the study was to investigate the characteristics of child-robot interaction (CRI), in relation to neurological impairment and typical development.

Methods: Two-arm quasi-experiment was performed, including a study group of 50 children with neurological impairment (NI) and a control group of 39 healthy children (CG) to evaluate the potential different characteristic features of CRI between two groups. Children aged 4–16 years (median age 9 years) were included. The child-like social robot Pepper (h 120 cm, w 28 kg) was used. The authors designed the interaction scenario to be as natural and friendly as possible to provide a positive social and affective experience for children. During interactions, robot Pepper was operated by a human. Each interaction was examined through therapists' observations, child's self-ratings, and a survey about Pepper based on four socio-cultural concepts. The interaction session with the humanoid lasted 8–10 minutes.

Results: The study revealed high acceptance and positive influence of Pepper to children. Statistically significant differences between children with NI and CG were observed in the perceptions of robot safety. 40% of the children with NI believed the robot was very safe, compared to 17.9% of the children in the CG (OR 3.0 [1.1–8]; p = 0.025). In assessing anthropomorphism, trends showed that children with NI rated Pepper's anthropomorphic qualities higher than CG (OR 4.1 [0.87–25]; p=0.053). The study revealed that in non-verbal interactions, children in both groups (NI and CG) maintained attention, nodded, smiled and remained in an active posture. Furthermore, children from both groups actively verbally responded to Pepper's questions, which was relevant for establishing trustful contact and creating meaningful dialogue.

Conclusions: Social robot Pepper was perceived as a peer by children with neurological impairment and healthy children with whom they all interacted emotionally and socially. Data confirmed the promising potential of robot Pepper to be used for the rehabilitation of communication and social skills in children.

ABSTRACTS

Topic: Neurometabolic Disorders

EPNS25_631 - Comprehensive Analysis of Clinical, Imaging, and Genetic Features in Pediatric Metachromatic Leukodystrophy: A 15-Year Experience at a Tertiary Pediatric Neurometabolic Center

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Objectives

Metachromatic leukodystrophy (MLD) is a rare lysosomal storage disorder inherited in an AR pattern, which results from the abnormal accumulation of sulfatides in the CNS. Sulfatides, a prominent class of sphingolipids, serve as physiological substrates for arylsulfatase A (ARSA) enzyme, and play a critical role in maintaining the structural and functional integrity of myelin. Alongside Saposin B, ARSA cleaves the sulfate group from the sulfatides, yielding galactosylceramide and thereby preserving myelin sheath homeostasis in both central and peripheral nervous system.

In MLD, mutations primarily in the ARSA gene (OMIM: 250100) and less frequently in the PSAP gene (OMIM: 249900), lead to the accumulation of sulfatides, particularly cerebroside-3-sulfate, within oligodendrocytes and Schwann cells. This accumulation causes progressive myelin damage in the CNSand PNS.

Methods

This cross-sectional observational study was conducted in the Mofid Children's Hospital and enrolled 30 pediatric patients with a definitive diagnosis of MLD referred to the Neurometabolic Clinic between March 2009 and March 2024. The diagnosis was based on clinical and/or MRI findings indicative of MLD in addition to ARSA enzyme deficiency in plasma and was confirmed through direct ARSA gene sequencing. In cases with indecisive ARSA gene sequencing, PSAP direct gene sequencing was performed.

Patient's data including ,clinical findings, paraclinical findings (Brain MRI , Electromyography and Nerve Conduction Studies (EDX) findings, ARSA enzyme activity level), genetic analysis findings and outcomes were extracted from the patient's medical records using a data collection form. In cases where EDX studies, including electromyography and nerve conduction studies, were performed, findings were extracted.

Results

In this study, 10 patients showed behavioral disorders and ADHD before MLD presentation. In 3 patients (The age before 3 years) presented as motor delay and brain MRI findings were in normal limits. Nine Patients (30.0%) passed away, with 5 (25.0%) cases of late-infantile and 4 (40.0%) cases of juvenile forms. HPSC was conducted in 7 patients. Among these, 4 patients died post-transplantation. Of the surviving 3 patients, symptoms stabilized in 2 cases, while in 1 case, where the transplant was received from a carrier brother, symptoms continued to worsen.

Conclusions

The current study provides significantly important clinical, laboratory, electromyoneurography, and genetic findings of the pediatric MLD population in a tertiary pediatric Neurometabolic center in Mofid Children's Hospital in Iran. A critical assessment of the disease characteristics enables a clearer understanding of the pathogenesis, paving the way for possible of curative therapeutic approaches.

ABSTRACTS

Topic: Movement Disorders/ Cerebral Palsy

EPNS25_634 - Language Production Recovery in Unilateral Cerebral Palsy – Data from Functional Magnetic Resonance Imaging and Tractography

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Objectives: Speech production is typically represented in the left hemisphere, and damage to these areas in adults often leads to aphasia. However, when structural damage occurs during the early stages of development, children may retain speech abilities, though at a reduced level compared to peers without brain lesions. This study aims to identify the key factors influencing speech recovery, focusing on lesion morphology, the type of functional reorganization, and the integrity of white matter pathways.

Methods: From 2017 to 2021, structural magnetic resonance imaging (MRI), functional MRI with a speech production task, and tractography were performed on 36 patients with unilateral cerebral palsy (UCP) (mean age 16.6 years, including 16 males and 20 females, with Manual Ability Classification System (MACS) levels 1-3 and Intelligence Quotient (IQ) > 50, mean IQ - 70) and 38 healthy controls (age- and sex-matched, with no neurological deficit and mean IQ 98). The impact of the lesion's morphological characteristics (volume, type, and time of occurrence) on the verbal IQ performance of the patients was evaluated. Functional MRI analysis assessed speech production reorganization, its relation to lesion morphology, and its impact on verbal functioning. Tract-Based Spatial Statistics (TBSS) analysis on tractography data compared patients with verbal IQ > 80 and verbal IQ < 80 for differences in the FA of the white matter tracts.

Results: In patients with right-sided lesions, left-sided lateralization dominated, like in healthy controls, but was less pronounced. Patients with smaller or subcortical lesions and those with earlier-onset lesions showed stronger functional MRI activation in typical language regions, such as Broca's area. Verbal IQ was not influenced by lesion morphology (size, type, or timing). Instead, it correlated with higher FA values in the associative fibers bilaterally and the corpus callosum. Greater right-sided (contralesional) speech reorganization was linked to lower verbal IQ.

Conclusions: Abnormal lateralization of speech production and reduced integrity of associative white matter pathways and the corpus callosum, are associated with poorer language performance in right-sided UCP patients.

ABSTRACTS

Topic: Neuromuscular Disorders

EPNS25_636 - Gene therapy with onasemnogene-abeparvovec (Zolgensma®) for patients with SMA: Real-world experience from Qatar

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Objectives

To present a cohort of successfully treated children with SMA with the gene therapy onasemnogene-abeparvovec.

Methods

A retrospective review of the real-world experience in Qatar from two tertiary pediatric centers in treating SMA patients with the gene therapy Onasemnogene Abeparvovec (Zolgensma), over 5 years period.
All cases were diagnosed as having genetically confirmed SMA type 1 or 2 due to homozygous deletions of the SMN1 gene and two to three copies of the SMN2 gene.

Results

A total of 40 patients were treated, 26 were SMA type 1 (65%) and 24 were type 2 (35%). 24 males (60%) and 16 females (40%).
37 children (92.5%) were treated within the 2 years eligibility criteria. The other 3 children were treated based on the weight criteria.
14 children were on “bridging therapy” with Nusinersen/Risdiplam until they received Zolgensma. All, except one, were of type 1.
11 children were on ventilation support (27.5%); 10 were on non-invasive support.
23 children (57.5%) were orally fed.
One child had positive AAV9 antibodies. The test was repeated in 2 months, and he seroconverted and received the gene therapy safely.
No serious adverse side effect was observed in all treated children.
Children were enrolled on a consolidated, intensive, 3 months post-therapy rehabilitation program. 4 of the children on ventilatory support were successfully weaned off.
8 different nationalities were treated in Qatar.

Conclusions

We run a comprehensive, multidisciplinary SMA management program in our center.
An increasing number of children, from different countries, have benefited from this service.
We pioneered the concept of bridging therapy which has helped reduce the lost time waiting for Gene therapy treatment.
Our center was the hub for the SMA patients in the region ensuring children from other countries have access to it. This review has further strengthened the clinical efficacy of gene therapy and emphasized the importance of early diagnosis of SMA through the national newborn screening program.

ABSTRACTS

Topic: Epilepsy: Medical and Surgical treatment

EPNS25_641 - Evidence of sex-related pharmacodynamic differences in individuals with photosensitive epilepsy treated with valproate

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Objectives: Gender differences in the pharmacokinetics, pharmacodynamics, and response to antiseizure medication (ASM) remain underexplored, despite significant sex-related variations in drug metabolism and adverse events. This study aims to investigate and compare the response to valproic acid (VPA) in photosensitive epilepsy between sexes, focusing on EEG parameters such as the photoparoxysmal response (PPR) and the standardized photosensitivity range (SPR).

Methods: We conducted a retrospective observational study on individuals with photosensitive epilepsy, assessed before and after treatment with VPA (non-randomized), used as the first-line ASM. Data were analyzed using the chi-square test, Wilcoxon-Mann-Whitney non-parametric tests, and univariate linear regression models. Additionally, plasma VPA concentrations and patient age were considered.

Results: Changes in PPR and SPR before and after VPA therapy were analyzed in 48 patients (27 females, 21 males). The mean reduction in SPR was significantly greater in males than in females (-7.0 ± 2.6 in males vs. -3.9 ± 3.3 in females, $p = 0.0018$). Complete PPR elimination was observed in 47.6% of males compared to 14.8% of females. Linear regression analysis revealed a greater SPR decrease in males (-3.275 points) than in females ($p = 0.001$). In females, SPR increased with age (+0.19 points/year, $p = 0.02$), a trend not observed in males.

Conclusion: Significant sex-related differences in the pharmacodynamic response to VPA were identified, with males showing a greater reduction in SPR and higher rates of PPR elimination. These findings highlight the importance of considering sex in treatment planning and suggest that intrinsic biological differences may influence the efficacy of ASM. Further research is warranted to enhance gender-specific medicine and contribute to personalized treatment approaches.

ABSTRACTS

Topic: Epilepsy: Medical and Surgical treatment

EPNS25_643 - Exploring the Use of Cannabidiol in Children with Epilepsy Syndromes in South Wales: Potential Applications Beyond Current Licensing

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Objectives

Cannabidiol, a non-psychoactive compound derived from the Cannabis sativa plant, has emerged as a promising therapeutic agent for paediatric patients with neurological disorders. Currently, cannabidiol is licensed for treatment-resistant epilepsy in children with a diagnosis of Lennox-Gastaut syndrome, Dravet syndrome and Tuberous Sclerosis. This review examines the current use of cannabidiol in children with epilepsy syndromes in South Wales, assessing its outcomes and exploring its potential for broader therapeutic use.

Our objectives were to review the caseload of paediatric patients with epilepsy in South Wales who are prescribed cannabidiol. We analysed the indications for cannabidiol use, assessed it's side effect profile and evaluated its effectiveness in this patient population. Additionally, we aimed to identify specific patient cohorts that demonstrate greater responsiveness to cannabidiol therapy, with the goal of guiding it's use in paediatric neurology.

Methods

This is a retrospective clinical evaluation of paediatric patients prescribed cannabidiol. Patients were identified through departmental databases and pharmacy records. Medical notes for each patient were reviewed to collect data on the diagnosis, age of initiation of cannabidiol treatment, prior medication (including whether they were on clobazam), changes in seizure frequency, any reported side effects, additional improvements and the reasons for discontinuation of cannabidiol, if applicable.

Results

This study included 29 paediatric patients aged 1-19 years: 3 with Tuberous Sclerosis, 12 with Lennox-Gastaut Syndrome, 5 with Dravet's Syndrome and 8 with other epilepsy diagnoses. Among the 29 patients, 24 experienced a reduction in seizure frequency, with 13 also showing additional improvements such as increased alertness and responsiveness. Prior to starting cannabidiol, patients had trialled between 2 and 5 anti-seizure medications. Notably, over 50% of patients with other neurological conditions demonstrated both a reduction in seizure frequency and improvements in alertness. Cannabidiol treatment was discontinued in 8 patients due to reasons including lack of effectiveness and liver function test (LFT) abnormalities. Side effects were reported in 13 patients, including gastrointestinal issues and sleepiness

Conclusions

Our results suggest that cannabidiol is effective in reducing seizure frequency in epilepsy syndromes for which it is already licensed. Additionally, the findings indicate that cannabidiol can also be beneficial in reducing seizures as well as improving alertness in other neurological conditions where it is not currently licensed, highlighting it's potential for broader therapeutic applications.

ABSTRACTS

Topic: Neurogenetics

EPNS25_644 - Clinical phenotype of children with genetically determined epilepsy

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Objectives: to assess the clinical phenotype of children with genetically determined epilepsy.

Methods: Between December 2019 and June 2024, 330 children diagnosed with epilepsy were tested by a geneticist at tertiary care center. The indications for genetic testing were childhood epilepsies with additional features (refractory seizures, neurodevelopmental delay, unusual age of onset for a certain epileptic syndrome, specific phenotype). A gene mutation or chromosomal anomaly was identified in 147 (44.5%) children. A prospective study was conducted, including 88 children with epilepsy, who had likely pathogenic or pathogenic variant or chromosomal abnormalities that may cause seizures and epilepsy. The clinical phenotype of these patients was analyzed, including time of onset, type of seizures, epileptic syndrome, family history, neurodevelopment, MRI findings, and response to treatment with antiseizure medications. Descriptive statistical analysis was performed using MS Office Excel 2016 and SPSS Statistics 25 programs.

Results: Seventy (79.5%) patients had single gene variant and 18 (20.4%) patients had chromosomal anomalies ($p<0.05$). The most common monogenic mutations were identified in the *SCN1A* and *PRRT2* genes, each observed in 5 patients. The most common chromosomal anomaly was deletion or duplication on chromosome 16 at position p11.2, detected in 5 (27.8%) patients. A positive family history of seizures or neurodevelopmental disorders was present in 42 (47.7%) cases. West syndrome or Lennox-Gastaut syndrome was diagnosed in 23.4%, focal epilepsy in 15.2%, absence epilepsy plus in 6.8%, Dravet syndrome in 6.8% patients, and the remaining (47.8%) patients had unspecified forms of epilepsy. Almost one half of patients (46.6%) started to experience seizures before 12 months of age. Drug-resistant epilepsy was present in 35.2% of cases. Only 5.7% of patients had normal cognitive function. Abnormal brain MRI findings of different clinical relevance were identified in 58.0% of patients.

Conclusions: Diagnostic yield in our series was very good. Genetic etiology of pediatric epilepsy seems to be highly heterogeneous. Monogenic causes of epilepsy were more prevalent than chromosomal anomalies. Onset of epilepsy in the first year of life was very common in our group. In order to find genotype-phenotype correlations further research involving a larger cohort of patients is needed.

ABSTRACTS

Topic: Epilepsy: Diagnosis and Investigations

EPNS25_645 - Beyond Seizures: Deep Phenotyping of GABAA Receptor Variants Reveals Functional Segregation and Predicts Risk of Gross Motor Dysfunction

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Objectives: his study aimed to investigate the motor, and cognitive outcomes as well as the epilepsy trajectories associated with gain-of-function (GoF) and loss-of-function (LoF) variants in the *GABRB2* and *GABRB3* genes. By employing a standardized phenotyping approach, we sought to investigate differences in cognitive and motor functions between and develop a risk prediction model for gross motor dysfunction

Methods: Clinical information was collected through patient advocacy groups, international collaborations, and literature reviews. Gross motor function was classified using the Gross Motor Function Classification System, and functional assessments of variants were performed using electrophysiological recordings. Statistical analyses included Kruskal-Wallis tests, Dunn's post-hoc tests, and logistic ordinal regression.

Results: We analyzed data from 120 individuals for which functional characterization had been performed. Forty-nine individuals carried a *GABRB2* (25 GoF 24 LoF) and 71 individuals a *GABRB3* variant (31 GoF, 40 LoF). Substantial differences in epilepsy syndromes, age of seizure onset, and severity of motor and cognitive impairments were observed between the GoF and LoF groups. GoF variants were associated with earlier seizure onset ($p = 6.2 \times 10^{-7}$, Kruskal-Wallis Test) and more severe gross motor dysfunction ($p = 4.1 \times 10^{-4}$) and cognitive impairments ($p = 2.7 \times 10^{-12}$) compared to LoF variants ($p = 4.1 \times 10^{-4}$ and 2.7×10^{-12} respectively, Kruskal-Wallis test with Dunn's post-hoc test). A strong correlation was found between the age of seizure onset and the severity of gross motor dysfunction in GoF variants, leading to the development of a risk prediction model.

Conclusions: This study highlights the distinct clinical trajectories associated with GoF and LoF variants in the *GABRB2* and *GABRB3* genes. Our findings underscore the importance of seizure onset and its relation to the risk of severe motor impairment. Lastly, the risk prediction model for gross motor dysfunction provides a valuable tool for clinicians in predicting outcomes and evaluating treatment efficacy.

ABSTRACTS

Topic: Neurogenetics

EPNS25_646 - Broadening the phenotype associated with pathogenic variants in the FGF12 gene: from developmental and epileptic encephalopathy (DEE) to drug-responsive epilepsy with favorable cognitive outcome

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Objectives
The *FGF12* gene encodes a protein interacting with voltage-gated sodium channels. Two mains variants, p.(Arg52His) and p.(Gly50Ser), have been repeatedly associated with developmental and epileptic encephalopathy-47 (DEE47, MIM #617166) with poor outcome.
NM_004113.6:c.155G>A;NP:004104.3:p.(Arg52His)
NM_004113.6:c.148G>A;NP:004104.3:p.(Gly50Ser)

We aim to refine the electroclinical phenotype and outcomes these recurrent pathogenic variants in the FGF12 gene without DEE presentation.

Methods
This national retrospective multicentric study examined patients with *FGF12* variants and early-onset epilepsy without a DEE phenotype.
Data come from neurology departments across six French cities.

Results
We report eight unrelated patients, along with two related patients, with early-onset epilepsy without DEE and pathogenic *FGF12* single nucleotide variants (Arg52His: n=4; Gly50Ser: n=6).
At the last follow-up, the median age was 7.6 years (range 2 to 38 years), and 70% were female.

Epilepsy

Seizure onset ranged from 3 days to 4 months, with earlier onset in patients with (p.(Arg52His), 3–48 days) and a later onset for patients with (p.(Gly50Ser), 3–4 months).

EEG findings
Four of ten patients had normal interictal EEGs. Seizures were recorded in five patients, with ictal EEG showing focal involvement in four. Temporal lobe seizures were recorded for three.

ABSTRACTS

Brain MRI
Two patients presented with abnormal brain MRIs without cerebellar abnormalities.

Antiseizure medication (ASM)
Seizure clusters or status epilepticus were successfully treated with phenytoïn (or fosphenytoin) for four patients. The ASM chronology is shown in Figure. The sodium channel blocker (SCB) carbamazepine was the most used ASM (6/10 patients), and oxcarbazepine for one patient, as well as phenytoïn for an other one. ASM withdrawal trials was systematically failed.
One patient with mild intellectual disability has received an early SCB. Conversely, one patient with normal neurodevelopment did not receive early SCB treatment.

Neurodevelopmental assessment and outcome
Neurodevelopmental trajectories were normal in seven patients, 2.1–38 years, median 6.8 years (Arg52His: n=2; Gly50Ser: n=5). Initial seizure remission was achieved before 6 months of age for all patients with normal neurodevelopmental outcomes. Intellectual disability was mild and was associated with uncontrolled epilepsy without prolonged remission.

Conclusions
Our series of ten cases broadens the phenotypic spectrum associated with *FGF12* pathogenic variants, highlighting cases of sporadic good neurodevelopmental outcome epilepsy in contrast to the DEE phenotype. This study aims to enhance the awareness among practitioners about the significant clinical variability of *FGF12* variants. Early therapeutic interventions with SCB such as carbamazepine, may influence this variability.

ABSTRACTS

Topic: Movement Disorders/ Cerebral Palsy

EPNS25_648 - Unveiling Dysphagia in Pediatric Dystonia: Insights from a Cross-Sectional Study

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Objectives

Swallowing functions in dystonia remain largely unexplored. Dysphagia, however, can result in severe complications, including aspiration. This study, therefore, aimed to evaluate dysphagia in children with dystonia.

Methods

Children diagnosed with dystonia as the predominant movement disorder were included. Medical histories, and Gross Motor Functional Classification Scale (GMFCS) and Functional Oral Intake Scale (FOIS) levels were recorded. Oral structure characteristics were assessed, and chewing performance was evaluated using the Mastication Observation and Evaluation (T-MOE) and the Karaduman Chewing Performance Scale (KCPS). Swallowing safety was screened with the Pediatric Eating Assessment Tool-10 (PEDI-EAT-10) and the 3-ounce Water Swallow Test. The Dysphagia Disorders Survey (DDS) was used to assess swallowing disorder severity, while the Dysphagia Management Staging Scale (DMSS) was applied to determine the severity level of dysphagia.

Results

Twenty-five children (mean age: 11.32 ± 3.95 years) participated in the study; 56% were classified as level V according to the GMFCS. Three children (12%) had a FOIS level of 4 or below (Level 1 represents “nothing by mouth,” and Level 7 represents “total oral diet with no restrictions). The 84% of children with dystonia presented with halitosis, 72% exhibited tongue thrust, 64% had decayed teeth, and 16% were identified with trismus. The mean T-MOE score was 15.62 ± 7.51 (0 indicates optimal chewing performance, while 32 represents the poorest performance), and 60% of the children could bite but were unable to chew effectively according to the KCPS. Oropharyngeal dysphagia was present in all children, with abnormal swallowing (PEDI-EAT-10 score ≥4) and increased aspiration risk (PEDI-EAT-10 score ≥13) observed in 100% and 88% of the participants, respectively. Additionally, 44% of the children failed the 3-ounce Water Swallow Test. The mean DDS raw score was 23.08 ± 7.70, and 68% of the children were classified as having severe or profound dysphagia based on the DMSS.

Conclusions

Dystonia encompasses many etiological conditions, each with unique biomechanical adaptations that influence swallowing function. Severe dysphagia and an elevated risk of aspiration were prevalent in this study, underscoring the need for early identification and continuous monitoring. Tailored, multidisciplinary management strategies targeting oral motor function and swallowing safety are crucial to prevent complications such as aspiration pneumonia and malnutrition, thereby improving the quality of life for this high-risk population.

ABSTRACTS

Topic: Neurogenetics

EPNS25_649 - A Rare Case of Spastic Paraplegia 90A Presenting with Dystonia, Hypotonia and Spasticity

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Objectives: Autosomal dominant spastic paraplegia-90A (SPG90A), identified in 2023, is a progressive disorder characterized by motor delays, walking difficulties, axial hypotonia, dystonia, spasticity in the limbs, EEG abnormalities, hearing loss, and ventriculomegaly. Some cases also show associated conditions like renal tubular acidosis, nephrolithiasis, and urinary tract infections.

Methods: A 10-year-old girl presented with hypotonia, inability to walk, and spasticity. She was the third child of non-related parents, born at 38 weeks via normal vaginal delivery, weighing 2500 grams, and her mother had hypertension at 31 years old. Her developmental milestones included head control at 3 months, sitting with support at 7 months, crawling at 1 year, and walking with a walker at 2 years. At 3 years, she could hold a spoon and draw a circle. However, by the age of 8, she started having trouble lifting her arms and walking. Upon examination, significant axial hypotonia was noted, with no head control. Upper extremity dystonia was prominent, while the lower limbs showed increased tone and spasticity. Deep tendon reflexes (DTR) were exaggerated, and Babinski signs were bilaterally positive. Dysmorphic features included a short neck and a high-arched palate. She spoke in a slow, hoarse voice and had intellectual disability, though she could answer simple questions. Her swallowing function was normal, and she passed a hearing test. She had a history of a transient EEG abnormality (right temporal low amplitude sharp waves) without clinical seizures. Gabapentin was prescribed recently for upper extremity dystonia.

Results: Echocardiography revealed an atrial septal defect. She was also followed by pediatric nephrology for nephrolithiasis, pyelonephritis, neurogenic bladder, and distal renal tubular acidosis, receiving sodium bicarbonate, prophylactic nitrofurantoin and trimethoprim-sulfamethoxazole. Additionally, nephrogenic diabetes insipidus was diagnosed and treated with indomethacin. MRIs at ages 8 and 10 showed enlarged ventricles and prominent cerebellar folia, with a smaller pituitary gland. Whole exome sequencing at age 3 was normal; repeat testing revealed a heterozygous variant in *SPTSSA* gene, confirming autosomal dominant spastic paraplegia 90A.

Conclusions: SPG90A is caused by excessive sphingolipid synthesis. It is a recently reported ultra-rare condition characterized by motor impairment, cognitive dysfunction and multisystemic issues.

ABSTRACTS

Topic: Epilepsy: Medical and Surgical treatment

EPNS25_650 - The Effectiveness of Modified Atkins Ketogenic Diet on Children with Intractable Epilepsy

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Objectives : This study aims to assess the effectiveness, tolerance, compliance, and adverse effects of MAD in children with intractable epilepsy over a six-month monitoring period. The study hypothesizes that the MAD ketogenic diet can reduce seizure frequency in children with intractable epilepsy while causing minimal adverse effects.

Methods : This experimental study involving children aged 2–18 years with intractable epilepsy at the Pediatric Neurology Clinic, the Pediatric Nutrition and Metabolic Diseases Clinic, and the Children's Nutrition Service Installation between November 2021 and June 2022, who will undergo MAD ketogenic diet. Patients were provided with a dietary guidebook containing instructions and examples of the MAD food menu that are easy to adopt, inexpensive, and have a familiar taste for Indonesian children, as well as a seizure recording book which were created for this study. Patients were monitored for seizure frequency, urine ketone levels, tolerance, compliance, and adverse effects of the MAD ketogenic diet at the first, third, and sixth months. This study used a consecutive sampling method, and data were analyzed using the Wilcoxon test.

Results : A total of 31 subjects met the inclusion criteria and underwent the MAD in the first month, followed by 13 subjects in the third month and 9 subjects in the sixth month. Reduction in the mean seizure frequency was observed in 50% ($p = 0.144$) of subjects in the first month, 62% ($p = 0.221$) in the third month, and 83.3% ($p = 0.028$) in the sixth month. The most frequent adverse effects of MAD ketogenic diet were vomiting and diarrhea. Noncompliance was observed in 18 subjects (58.1%) over the six-month monitoring period.

Conclusions : The MAD ketogenic diet may be a therapeutic option for reducing the mean seizure frequency in children with intractable epilepsy by the sixth month, with statistically significant results. A further randomized, controlled, multicenter clinical trial with a larger sample size and a longer observation period is required.

ABSTRACTS

Topic: Neurodevelopmental Disorders / Developmental Neuroscience

EPNS25_651 - Maternal prenatal stress impacts toddlers´ neurodevelopmental characteristics.

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Objectives: To assess the impact of exposure to chronic prenatal stress during the third trimester of pregnancy on children's cognitive, language and motor skills at age two.

Methods: Women attending the perinatology center of a university hospital were screened in the third trimester of pregnancy using the Cohen Perceived Stress Scale 10 (PSS-10). Candidates who agreed to participate in this prospective study were thus assigned to either control or stress group, according to their PSS-10 scores. Prenatal assessment for the whole cohort included the Pregnancy Distress Questionnaire (PDQ), a tool designed to assess worries specific to pregnancy, and recollection of pertinent information regarding socioeconomic status and health habits. Birth data were collected. At 2 years of age, 96 toddlers (mean decimal age 2.26 months, 48% girls) were tested with the Bayley Scales of Infant Development III by a specialist blinded to their status. During this visit, mothers completed a questionnaire regarding their child's attendance to daycare, health, nutrition and growth. Group differences were analyzed using independent samples t-test or Mann-Whitney U for continuous variables according to distribution, and Fisher's exact or Chi-Square for homogeneity tests for the categorical variables.

Results: Children in the stress group, irrespective of sex, had a lower mean score in the overall language outcome ($p = 0.03$), resulting in a relative difference in mean scores of 7.5% with their counterparts in control group, which deepened to 23.6% among those not attending daycare ($p < 0.01$). When taking into account only monolingual children (N=69), the receptive component of language was distinctively affected ($p = 0.04$). No significant differences in performance in the cognitive ($p = 0.13$) or motor domains ($p = 0.57$) were found, except for girls in the stress group, who obtained 11.9 % lower mean scores in the gross motor subtest ($p = 0.04$). Regarding children, no significant differences between groups were found, among others, for children's percentages of daycare attendance or bilingualism.

Conclusions: Language and gross motor development can be affected long-term by maternal chronic stress during pregnancy. Exposed children not attending daycare obtained the lowest outcome in language performance, pointing to a potential beneficial role of early childhood education.

ABSTRACTS

Topic: Movement Disorders/ Cerebral Palsy

EPNS25_652 - Energy metabolism dysregulation in Pediatric Huntington's Disease

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Objectives:recent evidence showed a dysfunctional hypometabolic state in Pediatric Huntington's Disease (PHD) brains with highly expanded CAG repeats, suggesting similarities with GLUT1 Deficiency Syndrome. The purpose of this study is to characterize glucose metabolism in PHD patients.

Methods: two patients with PHD have been assessed with metabolic investigations including cerebrospinal fluid glucose and lactate, plasma glucose and lactate, and erythrocyte glucose uptake. Furthermore, brain MRI and positron emission tomography with 18F-fluorodeoxyglucose was performed.

Results: Both patients exhibited normal limits of CSF/blood glucose ratios, lactate levels and erythrocyte glucose uptake. PET scans revealed hypometabolism in the basal ganglia, consistent with impaired glucose utilization in these regions.

Conclusions: Our data did not confirm a specific biochemical glucose dysfunction in plasma and CSF in PHD patients suggesting that the underlying mechanisms driving metabolic dysfunction in PHD may be distinct from those in GLUT1DS, and indeed do not suggest proceeding with ketogenic diet. Further research is essential to fully characterize these metabolic abnormalities and explore potential therapeutic targets for PHD.

ABSTRACTS

Topic: Movement Disorders/ Cerebral Palsy

EPNS25_654 - Evolving Patterns of Movement Disorders in Genetically Identified Developmental and Epileptic Encephalopathies: A Long Term Follow-Up Study

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Objectives The relationship between developmental and epileptic encephalopathies(DEE) and movement disorders(MD) has been recognized in recent years; however, the changing course of MD in children with genetically identified DEEs has not been previously investigated.

Methods Previously published group of 59 DEE cases with established genetic etiology showed 40.5% of coexisting MD (Turkdogan D, Int J Neurosci. 2023). This group was re-assessed for posture and MD. Of the 34 cases that remained under follow-up; 23 cases (14 female;60%) with adequate data were included in the study (follow-up period of 99.47 months;15–149). Twenty different genetic diagnoses were classified into 6 groups based on biological effects. MD were categorized as hypokinesia, hyperkinesia, stereotypies, paroxysmal abnormal eye movements (PAEM) and posture disorder.

Results During the initial evaluation, MD were identified in 52% of the cases (mean age:39.83 months and median 46.18 months). At last follow-up, the mean age of the cases was 146 months (72–263) with 66% exhibiting MD. Hypokinesia initially detected in one case (*PIGQ*) was later accompanied by dystonic posture. Dyskinesia was observed in cases with *ADSL* and *SLC25A22* variants but disappeared during follow-up, and replaced by focal dystonic postures, PAEM, and stereotypies.

Among cases without initial MD, the cases with *UNC80* and *KCNT1* variants exhibited hypokinesia with paroxysmal hyperkinetic attacks during follow-up.

Focal dystonic postures were present in four variants of *SLC16A2, KCNQ2, SCN2A-gain of function* and sodium channel gene cluster deletion at baseline and persisted at follow-up, including severe opisthotonic posture in *KCNQ2*. New focal dystonic postures emerged in *SEC24B*.

The *PIGT* case with only PAEM initially, had also dystonia later. PAEM persisted as only MD in cases with variants of *ELOVL4* and *PIGQ* .

Stereotypies emerged in cases with *SCN2A-loss of function*, *SCN8A* and *GNB5*-older sibling variants, while *GNB5*-younger sibling, *SMC1A*, *GABRB2, GAMT, DEAF*, and *TBC1D24* showed no movement disorders throughout follow-up.

Conclusions The study demonstrates the changing nature of MD in DEE. Stereotypies and dystonic posture became more frequent over time and dystonia persisted. The study highlights the dynamic progression of MD in DEE, but not posture abnormalities, emphasizing the need for ongoing observation. Larger studies may further clarify these relationships.

ABSTRACTS

Topic: Epilepsy: Diagnosis and Investigations

EPNS25_655 - EIDEE: A Single - Center Experience

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Objectives: Early-infantile developmental and epileptic encephalopathy (EIDEE) is a syndrome defined drug-resistant seizures that onset at or before 3 months of age, along with abnormal interictal EEG patterns and neurological examination findings. This study aims to retrospectively analyze the clinical, genetic, EEG, neuroimaging, and outcome data of patients who developed epilepsy within the first three months of life and were diagnosed and monitored in our clinic

Methods: We evaluated patients diagnosed with EIDEE within the first 90 days of life and followed up in the pediatric neurology department of our university hospital between 2010 and 2023. EIDEE was diagnosed based on the new ILAE epileptic syndrome classification. We recorded the patients' demographics data, neuroimaging, metabolic and genetic findings, treatment strategies and long-term outcomes

Results: A total of 58 patients (32 male and 26 female) who were diagnosed EIDEE were included in the study. The mean age at the first seizure was 49.94 days (min: 0- max: 90), with a median of 60 days. Thirteen patients died during follow-up. The average age of the surviving patients is 87.15 months, with a median of 76 months (min: 16 months - max: 216 months). The average follow-up duration of the patients was 85.2 months (min: 13- max: 213 months). Perinatal risk factors were present in 38 of the patients.The etiologies were genetic (n=23; 39.65 %), structural (n=16; 27.5%), metabolic (n = 7; 12.0 %), structural-genetic (n=2; 3.4 %) and it was unknown in 10 patients (17.24 %). Six patients received hormone therapy (ACTH), ten patients received Vigabatrin and nine patients received a combination of ACTH and Vigabatrin**.** Ten patients were seizure-free (the underlying etiologies were: genetic (40%), metabolic (10%), and structural (50%). 26 patients (44.8%) had their first seizure within 0-30 days. Seven of these patients remained seizure-free during follow-up monitoring.

Conclusions: Early developmental epileptic encephalopathy (EDEE) is a severe neurological condition that significantly impacts cognitive and motor development. Genetic factors play a crucial role in its etiology, influencing both diagnosis and treatment strategies. Early detection of genetic etiological causes, in particular, allows for the evaluation of targeted treatment options.

ABSTRACTS

Topic: Epilepsy: Diagnosis and Investigations

EPNS25_656 - Comorbid disorders in epilepsy debut in children

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Objectives

The psychic, neurologic and somatic pathology in children with epilepsy at the moment of the first seizure before prescribing anticonvulsant therapy in children of different age groups are impact on the course and treatment of epilepsy.

Methods

447 children with subsequent epilepsy after the first seizure were included in a study. Age subgroups were based on the age of the children at which the first attack occurred. Frequency of comorbid disorders at the moment of epilepsy debut was compared between age groups: up to 1 year old (n=193); 1-3 y.o. (n=105); 4-5 y.o. (n=37); 6-13 y.o. (n=94); 14-17 y.o. (n=18).

Results

Significant predominance of comorbid disorders was found in epilepsy debut at the age of up to 1 year old – 80.8% (156 cases) in comparison to frequency in elder children: in 1-3 y.o. – 61.9% (65 cases), 4-5 y.o. – 56.8% (21 cases), 6-13 y.o. – 56.4% (53 cases), 14-17 y.o. – 50.0% (9 cases). Analysis within age groups showed that at the moment of the first seizure the largest specific weight of comorbid pathology (n=304) was noted in group of children before 1 year old – 51.3% (156 cases) of number of children of the mentioned age in comparison to other age groups: in 1-3 y.o. – 21.4% (65 cases), in 4-5 y.o. – 6.9% (21 cases), in 6-13 y.o. – 17.4% (53 cases), 14-17 y.o. – 3.0% (9 cases). Comorbid neurologic disorders at the moment of disease start were noted in 26.6% (119 cases). Concomitant psychic disorders at the beginning of epilepsy progress were found in almost every third child: 30.6% (137 cases). Chronic somatic diseases were found in 61.5% (275 cases). Away from that analysis of distruibution of chronic somatic pathology at the moment of epilepsy manifestation depending on age was made, with maximum presence in the age group up to 1 year old – 74.6% (144 cases) and almost in every second elder child : 1-3 y.o. – 51.4% (54 cases), in 4-5 y.o. – 56.8% (21 cases), in 6-13 y.o. – 51.1% (48 cases), in 14-17 y.o. – 44.4% (8 cases), $p_{Fisher}<0,001$.

Conclusions

Comorbid disorders in epilepsy debut before prescribing anticonvulsant therapy predominate in children of up to 1 year old (80.8%), in comparison to age of 1-17 y.o. (58.3%), $p_{Fisher}<0,001$. Somatic disorders prevail in the structure of comorbid disorders, with predomination in children up to 1 year old, $p_{Fisher}<0,001$.

ABSTRACTS

Topic: Movement Disorders/ Cerebral Palsy

EPNS25_657 - Atypical pantothenate kinase-associated neurodegeneration: assessment of Intellectual and adaptive behaviour functioning

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Objectives: Pantothenate kinase-associated neurodegeneration (PKAN) is a rare disorder with a prevalence of 1-3 cases per 1,000,000 people and is the most common condition in the group of neurodegenerations with brain iron accumulation (NBIA). It is caused by homozygous pathogenic variants in the PANK2 gene located on chromosome 20p13, which encodes the enzyme pantothenate kinase 2. Patients with PKAN show iron accumulation in the brain, primarily in the basal ganglia, with a characteristic T2 magnetic resonance imaging (MRI) pattern. The classic phenotype is characterized by stiffness, dystonia, dysarthria, choreoathetosis, and pigmentary retinal degeneration, with symptom onset typically occurring before age 6. The atypical PKAN phenotype is distinguished by later onset, speech abnormalities, psychological disorders, and slower disease progression.

Additionally, PKAN is associated with intellectual impairment and progressive loss of cognitive abilities, particularly difficulties in executive functioning, attention, spatial and verbal learning, memory, judgment, and persistence. However, the intellectual, behavioral, and functional aspects of this condition are not extensively documented.

Methods We assessed dystonia severity using the Burke-Fahn-Marsden Dystonia Rating Scale (BFMDRS). To evaluate cognitive skills, we used the Wechsler Adult Intelligence Scale – Fourth Edition (WAIS-IV) for subjects over 16 years and the Wechsler Intelligence Scale for Children – Fourth Edition (WISC-IV) for those under 16. The Behavior Rating Inventory of Executive Function – Second Edition (BRIEF-II) and Raven's Progressive Matrices were used to assess executive functions.

For adaptive behavior, we used the Adaptive Behavior Assessment System – Second Edition (ABAS-II), Child Behavior Checklist (CBCL), and the Children's Yale-Brown Obsessive Compulsive Scale (CY-BOCS). Finally, the Pediatric Quality of Life Inventory (PedsQL) was used to provide a general overview of the patients' health-related quality of life.

Results: We present data collected through the administration of standardized scales to describe the cognitive phenotype of individuals with atypical PKAN. Six patients (3 males and 3 females), diagnosed with atypical PKAN by molecular testing, participated in the study. Their ages ranged from 10 to 20 years, with symptom onset between ages 7 and 15. The time between symptom onset and assessment ranged from 1 to 11 years. The severity of motor impairment varied, and half of the patients had undergone surgical treatment with deep brain stimulation (DBS).

Conclusion: This study aims to describe the intellectual and cognitive profile of children affected by atypical PKAN, considering different ages and varying time intervals since the onset of symptoms.

ABSTRACTS

Topic: Epilepsy: Medical and Surgical treatment

EPNS25_658 - Efficacy and tolerability of Fenfluramine with concomitant Potassium Bromide in Patients with Dravet Syndrome

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Objectives: To assess efficacy and tolerability of fenfluramine (FFA) with concomitant potassium bromide (BR) in patients with Dravet syndrome (DS).

Methods: This multicenter retrospective study, conducted within the German compassionate use program, analyzed BR doses and serum levels before and after FFA initiation, adverse events (AEs), seizure reduction, and symptoms changes using the Clinical Global Impression of Change (CGIC) scale. Timepoints were defined as T0 (baseline), T1 (FFA initiation), T2 and T3 (first and second BR level measurement after FFA initiation).

Results: Data on 22 patients (median age 8.9 years (range 2.2–26.7)) treated with BR were available. Median duration of BR-FFA combination therapy was 7 months (range 0–28). BR doses were reduced at least once in 11 patients (50%) as a precaution or because of increased serum levels. At T3, mean BR dose was significantly lower compared to T0 (1217 mg/d (SD 699) vs. 1755 (752.2); p 0.04), but BR levels showed no significant difference between T2 or T3 and baseline. In contrast, for patients with stable BR doses (n=14), mean BR level significantly increased from baseline (1376 mg/l (SD 345.7)) to T2 (1762 mg/l (SD 553.3); p 0.04). AEs were reported in 15 patients (68.2%) during the combination therapy, with the most common being somnolence (59.1%) and loss of appetite (22.7%). In 40.9% either FFA or BR were discontinued due to sedation. The responder rate for seizure reduction was 68.4% at 3 months and 76.9% at 6 months.

Conclusions: BR levels increased significantly after FFA initiation when BR doses were not reduced, contributing to adverse events—primarily somnolence—and resulting in the discontinuation of BR or FFA in some patients. Close monitoring of BR levels is crucial to minimizing the risk of adverse events.

ABSTRACTS

Topic: Neurogenetics

EPNS25_659 - Clinical and genetic heterogeneity in ethylmalonic encephalopathy in Bulgaria

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Objectives: To present the broad clinical spectrum of the first five Bulgarian patients with EE.

Methods: Five patients, with genetically verified by exome or Sanger sequencing EE, belonging to three pedigrees were included in the study. They underwent neurologic examination, brain CT/MRI, EEG, neuropsychological assessment, urine and blood metabolic screening.

Results: All of the Bulgarian patients had a later onset between 5 and 12 years of age. Episodes of impaired consciousness during infections were reported in 2/5, while recurrent vomiting and/or abdominal pain were observed in 4/4. None of the patients had recurrent petechiae. From the neurologic examination pyramidal involvement with lower spastic paraparesis was observed in 5/5, ataxia was present in 1/5, while extrapyramidal hyperkinesia was found in 1/5. Cognitive impairment was found in 4/5 varying between borderline to moderate mental retardation. They were diagnosed between 5 and 14 years after the initial clinical symptoms and the most common previous misdiagnoses were hereditary spastic paraplegia and infectious encephalitis. Brain MRI was abnormal in 3/4, with hyperintense lesions on T2 and FLAIR in the basal ganglia and cerebellum being more typical. Increased C4 carnitine levels in the serum, and increased ethylmalonic acid in the urine were found in our patients. Three of the patients were homozygous for mutations in *ETHE (*c.79C>A, p.Gln27Lys and 586G>A, p.Asp196Asn), while the other two were compound heterozygous (c586G>A (p.Asp196Asn) - exon 5; c.294-2_572+2del – del of exon 3 and 4).

Conclusions: These clinical descriptions illustrate the clinical heterogeneity of ethylmalonic encephalopathy, as recurrent petechiae, orthostatic acrocyanosis, and chronic diarrhea are not consistent findings. We emphasize that physicians should consider Ethylmalonic Encephalopathy in all patients with neurological deterioration, especially progressive spastic paraplegia. increased C4 carnitine levels in the serum, increased ethylmalonic acid in urine and MRI lesions in the basal ganglia and cerebellum.

ABSTRACTS

Topic: Fetal and Neonatal Neurology

EPNS25_660 - Structural brain alterations in patients with congenital heart disease during the neonatal-infantile period

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Objectives: The present study aims at investigating the neural correlates of congenital heart diseases (CHD) during the neonatal-infantile period, prior to heart surgery, in order to obtain early neuro-markers of neurodevelopmental outcome.

Methods: In this retrospective monocentric study, T2-weighted MRI scans of a cohort of neonates with CHD (N=20), acquired prior to reparative heart surgery, were compared to those of a group of healthy controls (N=36) from the Developing Human Connectome Project (dHCP) (Edwards et al., 2022), matched for gender and corrected age at the time of scanning (all ps>.05), using voxel-based morphometry (VBM). Exclusion criteria were age over 3 months at the time of neuroimaging assessment, known or suspected genetic syndromes, and the presence of brain injuries detected on MRI. In a sub-cohort of CHD patients (N=13), average grey matter concentration within the resulting areas of the VBM correlated with the scores at the Griffiths Mental Development Scales - II (GMDS-II), performed at a mean age of 24 months.

Results: VBM revealed significantly reduced grey matter volume in CHD patients within the bilateral supramarginal gyri, watershed areas located at the border between the anterior, middle, and posterior cerebral artery circulations, particularly vulnerable to reduced cerebral blood flow. They have been associated with different functions such as tool use and gesture production (Osiurak et al., 2021). In the CHD sub-cohort, average grey matter concentration in these areas positively correlated with locomotor scale (Scale A) scores of the GMDS-II at a mean of 24 months, suggesting a potential association with motor impairments.

Conclusions: The present findings highlight the importance of early preoperative MRI in newborns and infants with CHD and serve as proof of concept for the potential of quantitative volumetric analyses that may help in predicting neurodevelopmental outcomes and guide early, targeted rehabilitation.

References:

-Edwards, A. D., Rueckert, D., Smith, S. M., Abo Seada, S., Alansary, A., Almalbis, J., ... & Hajnal, J. V. (2022). The developing human connectome project neonatal data release. Frontiers in neuroscience, 16, 886772.

-Osiurak, F., Reynaud, E., Baumard, J., Rossetti, Y., Bartolo, A., & Lesourd, M. (2021). Pantomime of tool use: looking beyond apraxia. Brain Communications, 3(4), fcab263.

ABSTRACTS

Topic: Infectious and Inflammatory Diseases/ Neuroimmunology

EPNS25_662 - Safety and Efficacy of Rituximab Treatment in Autoimmune and Inflammatory Neurological Disorders in Children

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Objectives: Despite of, the increasing usage of rituximab in child neurology practice, the efficacy and safety remain unknown. In this study we aimed to evaluate the efficacy and safety of rituximab in autoimmune and inflammatory neurological disorders in the single center.

Methods: The patients which were treated with rituximab between September 2021 and January 2025 in the child neurology clinic were retrospectively evaluated. The data for diagnosis, pre and post treatment modified Rankin scale (mRs), changes in a frequency of seizures, side effects, recurrences and patients' demographics data was collected.

Results: Rituximab was given to patients that progressive symptoms who did not respond to first-line IVIG and high-dose steroid treatment with diagnosed with autoimmune encephalitis (n=3), myasthenia gravis (n=3), neuromyelitis optica (n=2), optic neuritis (n=1), transverse myelitis (n=1), opsoclonus myoclonus syndrome (n=1), chronic inflammatory demyelinating polyneuropathy (n=1) and two patients with progressive MS with uveitis who did not respond to disease-modifying therapies. The mean follow-up period before treatment was 19 (1-75) months and post- treatment was 12.7 (1-34) months. The definite and partial benefit was seen respectively in 7 and 5 patients. In 2 patients no significant changes were determined. Before and after the treatment the median mRs of patients with demyelinated and neuromuscular disorders were respectively 3.4 and 2.3. A significant reduction (%50) in the seizures of AE patients was observed. The 4 patients had a recurrence (n= 2 multiple sclerosis, n=2 myasthenia gravis). Adverse effects: fever, upper respiratory infection-like symptoms, bradycardia, seizure and anaphylaxis were noticed in 4 patients

Conclusions: Our study supports the efficacy and safety of rituximab especially in patients with autoimmune and demyelinated disorders. For exact results further studies are needed.

ABSTRACTS

Topic: Neurometabolic Disorders

EPNS25_663 - The use of ketogenic diet as target therapy in a cohort of italian patients affected by glut1 deficiency syndrome

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Objectives

Glucose transporter type 1 deficiency syndrome (GLUT1-DS) is a neurometabolic disorder due to pathogenic variants in the *SLC2A1* gene, which determine altered glucose entrance into the central nervous system, leading to drug-resistant epilepsy, developmental delay, acquired microcephaly, and movement disorders. Ketogenic diet (KD) is known to be the target therapy for this condition. In this study we report on a cohort of GLUT1-DS patients treated with KD.

Methods

We performed a retrospective study collecting data from a cohort of 35 patients diagnosed with Glut1 deficiency syndrome. We collected demographic, genetic, and baseline clinical data before the initiation of the ketogenic diet, followed by longitudinal assessments of neurological clinical status, neuropsychological parameters, quality of life, and electroencephalographic changes at various annual time points.

Results

Thirty-five patients were included, with a median age of 13.5 years (range: 4 months – 42 years). The median age at clinical onset was 22.5 months. All were started on KD, but six interrupted the treatment because of poor family compliance and difficulty with KD management.
Among those who underwent the KD, the median follow-up time was 4.25 years (range 1-12 years). Epilepsy was reported in 28/29 (96.5%) and 18/29 (62%) reached seizure freedom after the KD start, 4/29 (13.8%) had >50% seizure reduction.
Fourteen patients (48%) presented a movement disorder (encompassing paroxysmal exercise-induced dyskinesia, choreoathetosis, abnormal eyes movements); 4/29 (13.8%) presented ataxia. After KD treatment, 6/29 (20.7%) no more presented paroxysmal movement disorders.
Fourteen/29 (48.3%) had intellectual disability, severe (14.3%), moderate (35.7%), mild (50%), one had borderline intellectual functioning.
No severe adverse events were reported.

Conclusions

We report detailed follow-up of a cohort of GLUT1-DS patients, emphasizing its safety and effectiveness in controlling epileptic seizures and movement disorders.

ABSTRACTS

Topic: Movement Disorders/ Cerebral Palsy

EPNS25_664 - Genetic and phenotypic characterization of pediatric hyperkinetic movement disorders: A cohort study from a tertiary care center

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Objectives

Pediatric movement disorders (PMDs) are a diverse group of neurological conditions characterized by abnormal tone, posture, or involuntary movements. Hyperkinetic PMDs with a suspected genetic etiology pose significant diagnostic challenges. This study investigates the genetic etiology of hyperkinetic PMDs, characterizes associated clinical phenotypes, comorbidities, and neuroimaging findings, and explores the impact of genetic diagnosis on personalized treatment strategies.

Methods

This retrospective, observational study reviewed the medical records of pediatric patients (0–18 years) treated for hyperkinetic PMDs at the Movement Disorder Unit of Hospital Sant Joan de Déu, Barcelona, between 2020 and 2023. Inclusion criteria comprised clinical diagnoses of hyperkinetic PMDs (e.g., chorea, dystonia, myoclonus) with a suspected genetic origin. Comprehensive phenotypic characterization was performed using clinical data, neuroimaging studies, and video documentation when available. Genetic testing employed targeted next-generation sequencing (NGS) panels or whole-exome sequencing (WES), with variants interpreted following international guidelines.

Results

Among 712 patients initially reviewed, 62 met inclusion criteria (mean age ± SD: 8.6 ± 4.7 years; range: 6 months–18 years). A definitive genetic diagnosis was achieved in 40% of cases, identifying pathogenic variants in genes such as GNAO1, ATP1A3, and ADCY5. Phenotypic variability was notable, with overlapping clinical features across different genetic etiologies. Neuroimaging abnormalities, including basal ganglia changes, were present in 22% of cases. Comorbidities such as intellectual disability and epilepsy were prevalent. The implementation of NGS and WES significantly outperformed conventional methodologies, such as Array-CGH, in diagnostic yield. A genetic diagnosis resulted in therapeutic management changes in 80% of cases.

Conclusions

This study highlights the heterogeneity and evolving nature of hyperkinetic PMDs in pediatric populations, emphasizing the critical role of advanced genetic testing in achieving accurate diagnoses. A precise genetic diagnosis facilitates personalized treatment approaches and improves prognostic outcomes. Further research is needed to identify novel monogenic disorders and develop targeted molecular therapies to enhance patient care.

ABSTRACTS

Topic: Epilepsy: Medical and Surgical treatment

EPNS25_665 - Effects of ketogenic diet and immunotherapy on outcomes of paediatric fires: a systematic review

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Background: Febrile Infection-Related Epilepsy Syndrome (FIRES) is a severe epileptic disorder often leading to drug-resistant epilepsy (DRE) with cognitive/behavioural issues. Outcomes of various treatment strategies have been variable.

Methods: Individualised patient data including demographics, clinical, paraclinical (EEG and MRI) and treatment (KD, immunotherapy [IT], antiseizure medications [ASMs]) characteristics in FIRES patients <18 years were extracted from systematic review of publications up to 2024 using PubMED. Multivariable matching (on age, sex, KD and first- and second-line IT) was used to select 1:1 case pairs with minimum 6-months follow-up differing only on (1) first-line IT, (2) anakinra, or (3) KD status, to compare frequencies of good outcome (modified Rankin Scale [mRS] 0-2) and survival without DRE (seizures ongoing despite two ASMs), using McNemar's test.

Results: 423 children were included from 95 publications (62% male; mean age 8.1yrs). Prodromal illness was respiratory in 53% and gastrointestinal in 33%. EEG showed slowing (96%), ictal changes (83%), status epilepticus (68%), and shifting ictal changes (37%). MRI was abnormal in 52%, mostly in the temporal lobe.

Overall mortality was 7.2%. 72% had poor outcome (mRS >2) and 96% (168/175) had epilepsy (77% [100/130] DRE) at last follow-up.

Acute treatments were IT (74%), barbiturate coma (29%), KD (27%), ketamine infusion (26%) and therapeutic hypothermia (17%). Commonest first-line IT was intravenous immunoglobulin (IVIg, 58%) and preferred second-line IT was anakinra (21%).

In the matched case-pair analysis, children treated with KD had better functional outcomes at final follow-up compared to untreated children (48 matched case pairs [MCPs], 29% mRS ≤2 vs no KD 8.3%; odds ratio [OR] 4.53 (95% CI: 1.37-15.01); p=0.03), despite longer hospital stays (median 89 vs 48.5 days; Wilcoxon test: p=0.001). Children treated with steroid had higher rate of survival without DRE (49 MCPs, 47% vs no steroid 18%; OR 3.93 (95% CI: 1.57-9.82); p=0.007). IVIg, plasma exchange and anakinra had no significant effect on functional outcome nor survival without DRE.

Conclusion :KD was associated with improved long-term functional outcome and steroids were associated with reduced DRE in FIRES. This study serves as a primer, highlighting the complexities of evaluating a condition influenced by inflammatory and excitotoxic mechanisms and their treatments.

ABSTRACTS

Topic: Infectious and Inflammatory Diseases/ Neuroimmunology

EPNS25_666 - Etiological Distribution and Prognosis of Childhood Optic Neuritis: A Multicenter Retrospective Study

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Objectives The aim was to determine the demographic, clinical, laboratory characteristics, and prognostic factors of demyelinating autoimmune optic neuritis (ON) in pediatric patients.

Methods The medical files of patients diagnosed with ON cases diagnosed in three pediatric neurology clinics in Turkey , who underwent neuro-ophthalmological examination and OCT (Optical Coherence Tomography) tests, were retrospectively evaluated.

Results We includeded the data of 30 patients, who met the inclusion criteria were analyzed. The mean age at the time of inclusion was 13.83 ± 2.98 years (range: 7–17.7). Among the 30 children who presented with an optic neuritis attack, 24 (80%) came with visual complaints (vision loss, blurred vision) as the main symptom. The average follow-up time for these patients was 9.73 ± 9.77 months (range: 4–57). Of the patients presenting with an ON attack, 8 (26.7%) had isolated ON, 9 (30%) were diagnosed with Multiple Sclerosis (MS), 4 (13.3%) with Neuromyelitis Optica Spectrum Disorder (NMOSD), 7 (23.3%) with Myelin Oligodendrocyte Glycoprotein Associated Disease (MOGAD), and 2 (6.7%) with Chronic Recurrent Inflammatory Optic Neuropathy (CRION). On ocular examination, 8 (26.7%) had papilledema, 11 (36.7%) had painful eye movements, and 20 (66.6%) had afferent pupillary defect. At the 3rd-month visual evaluation, 14 (46.7%) had complete recovery, 10 (33.3%) had partial recovery, and 6 (20%) had vision loss. In the 6th-month eye evaluation, 18 (60%) had complete recovery, 6 (20%) had partial recovery, and 6 (20%) had vision loss. During the acute phase treatment, intravenous pulse methylprednisolone combined with oral tapering, pulse methylprednisolone, and combinations of pulse methylprednisolone, plasmapheresis, or intravenous immunoglobulin were used. In cases that required combined treatment, incomplete recovery was observed in patients who were unresponsive to pulse steroids. Particularly, the most damage and lack of complete recovery were observed in the NMOSD and CRION groups. OCT imaging was performed twice at specified intervals for the patients who had an ON attack. No statistically significant difference was found between the groups in both initial and follow-up OCT data. When looking at the Retinal Nerve Fiber Layer (RNFL) thickness, the group with the most thinning was the NMOSD group.

Conclusions This finding of the study is in line with the findings in the literature. Our results will provide an important data source for this significant pediatric condition. Long-term follow-up studies investigating etiological and diagnostic markers may be useful for further defining this group.

ABSTRACTS

Topic: Epilepsy: Diagnosis and Investigations

EPNS25_668 - Children with epilepsy who suffer from depression

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Objectives

to study the combination of epilepsy and depression in children.

Methods

The study included 156 patients with epilepsy. Research participants 156 people (aged 12-17 years) were evaluated for depressive disorders during various epileptic seizures in children at the Children's Neurological Hospital. 132 were boys and 24 were girls. During the study, 63 people were diagnosed with G40.0 Focal epilepsy, and 93 people were diagnosed with G 40.3 Generalized epilepsy. The severity of depression was studied using the Hamilton scale and ICD-10. The age of the patients ranged from 12 to 17 years.

Statistical analysis was carried out in the IBM Statistics SPSS-26 program using variation, discriminant, dispersion and correlation analysis methods.

Results

Our study proves that the comorbidity of epilepsy and depression is high in children with epilepsy aged 12-17 years. 68% of the examined patients had varying degrees of depression. Our research showed that of the 106 patients, 83 suffered from mild depression; 21 from moderate depression and 2 patients from severe depression.

The positive effect of venlafaxine, the drug of choice for the treatment of depression in children with epilepsy, was studied.

Conclusions

Children with epilepsy have a high frequency of combination of epilepsy and depression. It is necessary to detect and evaluate depression early in children diagnosed with epilepsy. The treatment of depression detected and diagnosed in time has a positive effect on the prognosis of the course of the disease, and provides an opportunity to improve the condition of epileptic patients.

ABSTRACTS

Topic: Infectious and Inflammatory Diseases/ Neuroimmunology

EPNS25_669 - Characteristics and Clinical Course of Optic Neuritis in Paediatric-Onset Multiple Sclerosis; A Single-Centre Experience

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Objectives: Pediatric Multiple sclerosis (MS) is rare with 3-10% of all MS patients starting before the age of 18 years. Optic neuritis (ON) , common initial symptom, is associated with long-term visual and neurological outcomes. This study was planned to investigate the features and prognosis of ON in pediatric-onset MS patients who had ON in childhood.

Methods: The files of 108 patients with pediatric MS diagnosed according to the 2017 Revised McDonald Criteria and followed up between 2013 and 2024 were reviewed. Among these patients 35 ON attacks of 23 patients who had been followed up after ON attack for at least 1 year regularly were included. The diagnosis of ON was made jointly with the ophthalmology clinic based on clinical examination findings, OCT, VEP and MRI data. Imaging and clinical data including EDSS scores, RNFL OCT measurements were collected during attacks and follow-up period.

Statistical analyses were performed using IBM SPSS Statistics 26. Normality was assessed using the Kolmogorov-Smirnov test. Pearson correlation was used for continuous variables, independent t-tests for group comparisons and chi-square tests for categorical variables.

Results: The ages of the patiens were 12 to 19 years and 65.2% were female. The mean ages of the first MS clinical attack and the first ON attack were 14.50±1.52 years and 14.64±1.75 years. In 82.6% of the patients, the first ON episode was considered as the first attack of MS.

When 35 ON attacks were evaluated, involvement was 77% unilateral; symptoms were blurred vision 36.6%, visual loss 40%, eye pain 23.4%. Retrobulbar neuritis was seen in 60% of ON attacks and papillitis in 40%. Recovery rate was 80% in the first month after treatment.

At the last examination, 73.9% of patients had complete vision and colour vision, 52.2% had normal fundoscopic examination, 30.4% had pale optic nerve, 17.4% had optic atrophy.

There was no significant correlation between the number of ON attacks and EDSS score ($p>0.05$) or RNFL OCT parameters ($p>0.05$). There was a significant positive correlation between age at onset of MS and RNFL OCT thickness ($p=0.019$), suggesting that early onset cases had more prominent retinal atrophy.

Conclusions: The significantly reduced retinal thickness on RNFL OCT in patients diagnosed with MS at an earlier age suggests a potentially more aggressive neurodegenerative process. These findings highlight the importance of early diagnosis-treatment initiation and OCT follow-up in paediatric MS patients to assess long-term visual prognosis and tailor individualised therapeutic approaches.

ABSTRACTS

Topic: Movement Disorders/ Cerebral Palsy

EPNS25_670 - Descriptive Study and Screening of Sleep Disorders in Patients with Tourette Syndrome

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Objective:

To describe the prevalence of sleep disorders in patients with Tourette Syndrome and the associated factors.

Materials and Methods

This descriptive study included patients under 18 years of age with Tourette Syndrome. The BEARS (Bedtime issues; Excessive daytime sleepiness; Awakening during the night; Regularity and duration of sleep; Snoring) and SDSC (Sleep Disturbance Scale for Children) questionnaires were used to screen for sleep disorders. A descriptive and bivariate analysis was conducted.

Results:

A total of 83 patients were included, with a median age of 14 years (range: 12–16). Of these, 77.1% were male (64/83). The mean score on the Yale Global Tic Severity Scale was 22.15 (range: 13.7–30.5). Psychiatric comorbidities were present in 79.5% (66/83) of the patients: attention deficit hyperactivity disorder in 58.5% (48/82) and obsessive-compulsive disorder in 41.5% (34/82). Additionally, 28.9% (24/83) had other neurological diagnoses. Pharmacological treatment for tics was administered to 53% (44/83), and 42.1% (35/83) received treatment for comorbidities. Sleep questionnaires were completed by 62 patients (74.7%), of whom 59 (95.2%) screened positive on the BEARS questionnaire, and 35 (59.3%) on the SDSC. The most common sleep disorders were hypersomnolence and initiation/maintenance insomnia (60% and 51%, respectively). Tic severity was associated with abnormalities in the SDSC ($p = 0.016$), restless leg syndrome ($p = 0.047$), and sleep arousal disorders ($p = 0.046$). The presence of attention deficit hyperactivity disorder was associated with initiation/maintenance insomnia ($p = 0.044$). Patients with Tourette Syndrome exhibited poorer sleep quality compared to a control population ($p = 0.002$).

Conclusions:

The prevalence of sleep disorders in patients with Tourette Syndrome is high, particularly among those with more severe symptoms.

ABSTRACTS

Topic: Infectious and Inflammatory Diseases/ Neuroimmunology

EPNS25_672 - Pediatric Autoimmune Associated with Anti-Glutamic Acid Decarboxylase 65 Antibody: two cases report

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Purpose: Anti-GAD encephalitis is rare. Here, we report two pediatric patients with GAD65-Ab-associated autoimmune encephalitis.

Introduction: Autoimmune encephalitis is a rare neurological inflammatory disease that is often associated with autoantibodies. It is characterized by acute and subacute onset seizures, cognitive impairment and psychiatric symptoms.

Case 1:A 14-year-old girl was admitted to the emergency department with complaints of numbness in the extremities, a left shift in the corner of the mouth and an inability to speak. The fever started two days ago. Cranial MRI (magnetic resonance imaging) was performed because of nuchal rigidity and lethargy during the physical examination. Cranial MRI revealed focal signal enhancement in the bilateral frontal horn. Ceftriaxone and acyclovir treatment was started, and the patient was referred to us with a prediagnosis of encephalitis. Glucose in the lumbar puncture of the patient: 80 mg/dl protein: 32 mg/dl. Autoimmune encephalitis panel, culture and meningitis panel were sent from CSF. EEG was normal. CSF culture, meningitis panel and autoimmune encephalitis panel were negative. Serum glutamic acid decarboxylase antibody (anti-GAD) was found to be >2000 IU/ml (0-10) positive, and MODY panel and CSF anti-GAD were sent. CSF anti-GAD was negative. The patient received 2 gr/kg IVIG. After IVIG treatment was finished, the anti-GAD value was found to be 205 IU/ml.

Case 2:A 16-year-old male patient was admitted to the emergency department with vomiting and confusion that started 1 day ago and was hospitalized in the intensive care unit with a prediagnosis of encephalitis after the Glasgow coma scale (GKS) was 12. Upper respiratory tract infection symptoms started one week ago. Cerebrospinal fluid infectious studies were taken, and the patient was started on empirical antibacterial and antiviral therapy. His seizures progressed in frequency to multiple daily episodes of staring that failed to respond to antiepileptic drug poly-therapy, including levetiracetam, phenytoin, valproic acid, carbamazepine and topiramate. The patient's EEG showed slowing in the frontal parts of the hemispheres, and no epileptiform discharge was observed. The patient was given 2 gr/kg IVIG and pulse methylprednisolone for 5 days. Craniospinal MRI was normal. Anti-GAD value >2000 IU/ml was detected. Since IVIG and pulse methylprednisolone treatment were not beneficial, plasmapheresis was performed every other day for five sessions. After plasmapheresis, the patient's GKS increased to 15. The control anti-GAD value decreased to 36 IU/ml.

Conclusion: Anti-GAD antibodies have been demonstrated in various neurological syndromes, including highly heterogeneous clinical conditions such as limbic encephalitis, cerebellar ataxia and stiff-person syndrome.

ABSTRACTS

Topic: Neuromuscular Disorders

EPNS25_675 - Evaluatıon of motor functıons ın sma type 2 and 3 patıents receıvıng nusınersen treatment: our experıence at cerrahpasa pedıatrıc neurology clınıc

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Objectives

Spinal muscular atrophy (SMA) is a rare neuromuscular disease with autosomal recessive inheritance that leads to progressive loss of motor functions. Most of the data on therapeutic efficacy from conducted studies pertains to infantile SMA Type 1. There is still a lack of sufficient evidence and long-term experience regarding disease-modifying therapies in SMA type 2 and type 3 patients. In our study, our aim is to investigate the clinical efficacy of Nusinersen, one of the disease-modifying therapies, in patients with SMA types 2 and 3.

Methods

This study included 35 out of 37 patients diagnosed with SMA Type 2-3 who received Nusinersen treatment in our clinic between 2018 and 2024 and had completed at least one year of treatment. Demographic data, age at symptom onset and treatment initiation, ambulatory status, respiratory functions, feeding methods, SMN2 gene copy numbers, motor functions, and scoliosis degrees were recorded. Motor functions were assessed during follow-up using the Hammersmith Functional Motor Scale (HFMSE).

Results

The mean age at Nusinersen treatment initiation was 50.4±37.2 months (range: 12-156) for SMA Type 2 and 121.08±64.32 months (range: 48-213) for SMA Type 3.

At the final evaluation, 10 patients (59%) with SMA Type 2 had a Cobb angle greater than 10 degrees, which was considered significant for scoliosis. In contrast, only three patients (17%) with SMA Type 3 had a Cobb angle exceeding 10 degrees. During treatment, three patients with SMA Type 2 and one patient with SMA Type 3 underwent surgery due to severe scoliosis.

At the final assessment, 15 patients (88%) with SMA Type 2 were unable to walk, one could walk with support, and one could walk independently, while all could sit without support. Among patients with SMA Type 3, four (22%) were unable to walk, one could walk with support, and one lost ambulation during follow-up.

The mean pre-treatment Hammersmith Functional Motor Scale Expanded (HFMSE) score for SMA Type 2 patients was 11.05±9.3 (range: 0-27), which increased to 22.82±14.91 (range: 2-58) after treatment. For SMA Type 3 patients, the mean pre-treatment HFMSE score was 45.94±12.73 (range: 16-62), which improved to 56.33±11.73 (range: 26-69) after treatment.

Conclusions

Motor function follow-up for at least one year using the HFMSE scale was conducted in our SMA Type 2 and Type 3 patients receiving Nusinersen treatment. Motor function improvement was observed in both SMA Type 2 and Type 3 patients.

ABSTRACTS

Topic: Neuromuscular Disorders

EPNS25_676 - Intrathecal Onasemnogene Abeparvovec for Patients with Spinal Muscular Atrophy: Phase 3, Randomized, Sham-Controlled, Double-Blind STEER Study

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Objectives: While the availability of disease-modifying therapeutic options has changed the clinical course of SMA, significant unmet need remains for a broader patient population. We examined onasemnogene abeparvovec (OA) for intrathecal administration as an adeno-associated vector-based gene therapy under development for the treatment of spinal muscular atrophy (SMA) in older patients.

Methods: STEER (NCT05089656) is a phase 3, multicenter, multinational, randomized, sham-controlled, double-blind trial to investigate the efficacy and safety of intrathecal OA over 52 weeks in treatment-naïve, sitting and never ambulatory patients with SMA aged 2 to <18 years. The primary endpoint is to compare the efficacy (OA vs. sham) by change from baseline in Hammersmith Functional Motor Scale – Expanded (HFMSE) total score over 52 weeks. Secondary endpoints include additional efficacy and safety assessments.

Results: 136 patients were randomized (3:2 ratio), with 126 patients receiving either OA (n=75) or a sham procedure (n=51). Mean (range) age at dosing was 5.88 (2.1–16.6) years. The study met its primary endpoint, demonstrating a statistically significant increase from baseline in HFMSE total score in the OA group compared with the sham control. The overall incidence of adverse events (AEs), serious AEs (SAEs), and AEs of special interest were similar between both groups. The most common AEs for both groups were upper respiratory tract infection and pyrexia. The most frequent SAEs were pneumonia and vomiting for the OA group and pneumonia and lower respiratory tract infection for the sham group. Instances of transaminase increases were infrequent; most were low-grade and transient. There were no cases of Hy's law.

Conclusions: A one-time intrathecal OA infusion resulted in statistically significant improvement in motor function compared with sham control and demonstrated a favorable safety profile for older patients with SMA.

ABSTRACTS

Topic: Miscellaneous

EPNS25_678 - Development of a follow-up program for children with acquired brain injury.

Francisco Javier Brincau-García[1], Laura Ximena Herrera-Castillo[1], Rocío Uzquiano-García[1], María Concepción Miranda-Herrero[1], Jimena Del Castillo-Peral[1], Almudena Chacón-Pascual[1], Estibaliz Barredo Valderrama[1], Ana Montiel-Rey[1], Pedro De Castro-Castro[1], María Vázquez-López[1]
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Objective

Patients admitted to pediatric intensive care units (PICU) may experience severe physical, psychosocial, and neuropsychological complications after discharge. The implementation of a multidisciplinary follow-up program for survivors enables early diagnosis.

To assess the feasibility of implementing a follow-up program based on Dutch post-PICU guidelines. The program aims to diagnose and treat early physical and neuropsychological alterations while evaluating their impact on patients' quality of life.

Methods

Patients aged 1 month to 18 years were included. Follow-up initially targeted patients who experienced cardiac arrest, required extracorporeal membrane oxygenation, or used ventricular assist devices. Subsequently, it was extended to patients with stroke, severe traumatic brain injury, hypoxic encephalopathy, and status epilepticus. A multidisciplinary team was formed, and consultations were scheduled at 3, 6, and 12 months post-event, as well as at each academic transition phase. Quality of life (assessed via the PedsQL scale) and emotional well-being of patients, families, and caregivers were evaluated.

Results

Between June 2019 and January 2024, 89 patients met the inclusion criteria. Twenty-six patients died before PICU discharge, and 3 were lost to follow-up. Fifty-four patients were evaluated once, and 41 underwent a 6-month evaluation. Fifty percent showed favorable progress, while 5 patients died during follow-up. Developmental delay (45%), motor delay (3%), and cognitive delay (2%) not previously identified were observed. Mean PedsQL scores were 69 (Q1: 58.3; Q3: 76.3) for patients and 68.8 (Q1: 60.4; Q3: 90.2) for families. Lower PedsQL scores were observed in patients with spastic tetraparesis (mean: 54.4) and chronic neurological conditions (mean: 51.6).

Conclusion

Neurocognitive impairment is common in pediatric patients with acquired brain injury, with psychomotor developmental delay being the most frequently detected issue. A systematic and multidisciplinary follow-up program has enabled early diagnosis and management of neurodevelopmental alterations, while also assessing the emotional well-being of patients and families.

ABSTRACTS

Topic: Cerebrovascular Disorders

EPNS25_680 - Stroke in Childhood: Review of Royal College of Paediatrics and Child Health (RCPCH) Stroke Guidelines

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Objectives

Stroke is a serious childhood disorder, affecting several hundred children and young people in the United Kingdom each year. Despite being relatively rare in childhood, it can lead to significant morbidity and mortality. Understanding that children with strokes present differently will serve to optimise outcomes and leverage the current Royal College of Paediatrics and Child Health Stroke in Childhood (RCPCHSC 2017) guidelines.

We investigated if the RCPCHSC guidelines are being followed in X Hospital amongst children aged 2-16 years of age presenting with clinical features of stroke.

Methods

We retrospectively identified the cohort of patients using electronic patient records; aged between 2 and 16 years at time of presentation with a diagnosis of cardiovascular event or new brain imaging in the 36 month period between 1st December 2023 and 1st December 2024. Patient demographics, symptoms, NIHSS (National Institute of Health Stroke Scale), investigations, time to brain scan, thrombolysis rates and diagnosis were analysed against the RCPCHSC guidelines.

Results

15 patient cases were identified. 47% were white caucasian, 7% were black and 20% asian ethnicity. The average age of presentation was 9.3 years. 67% were male and 33% were female. Some of the comorbidities identified include Moyamoya disease, Congenital Cardiac abnormalities, Neurofibromatosis and Autism spectrum disorders. The most common symptom presentation (67%) was ‘weakness or numbness on one side of the body’. 47% presented with ‘slurred speech or difficulty with language’ and 13% presented with ‘trouble balancing or walking’ and 13% ‘sudden lethargy or drowsiness’. Notably, 6% presented with a sole symptom of headache and 27% had an incidental infarct finding on imaging. Only 13% of patients had a documented PedNIHSS score. 47% had an MRI brain and 53% had a CTA, however the time of imaging was >120 minutes in more than 50% of the patients. 20% received thrombolysis. Other treatment modalities included blood thinners in 53% (aspirin, warfarin and clopidogrel), 13% had surgical intervention and only 40% received neurorehabilitation care with 40% not having any management.

Conclusions

Despite an increased incidence of paediatric stroke, the findings have reiterated that there is a delay in diagnosis particularly the recognition of symptoms and signs, and cases may still remain under- or misdiagnosed. The lack of uniformed assessment raises difficulties in identifying the clinical presentation. Thus, there needs to be urgent attention to improve the provision of care considering the increasing demands on neurocoginitive functions, educational and social roles.

ABSTRACTS

Topic: Neurometabolic Disorders

EPNS25_681 - Mitochondrial Diseases Presenting with Different Clinical Findings and Neurological Involvement: Single Center Experience

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Objectives

Mitochondrial diseases (MDs) are a diverse group of disorders that impact organs whose main energy supply were obtained from aerobic metabolism. The central nervous system is mainly affected and organs such as the heart, liver and kidneys, which require high energy, are also affected. Mitochondrial diseases show clinical and genetic heterogenecity. In this study, we aimed to evaluate the clinical and radiological findings of genetically diagnosed mitochondrial diseases with neurological involvement in our center.

Methods

We conducted a retrospective analysis of clinical, radiological, and genetic characteristics of 26 patients diagnosed with mitochondrial diseases between 2016 and 2024 at Mersin University Faculty of Medicine, Child Neurology Outpatient Clinic.

Results

Twenty-five patients were enrolled for the study. Among the 26 patients, 13 were girls (50%), with an age range of 16-216 months (mean: 120.4 ± 60.7 months). These patients were presented with different clinical findings including seizures, hypotonia, regression in neuromotor development, ptosis, and clubfoot. The complaints started at an average age of 47,9 months. The patients were diagnosed at an average age of 92,4 months and the mean interval between complaints and diagnosis was 44,5 months. Consanguineous marriage was present in 76,9% of the cases. When the patients with different clinical findings were evaluated with genetic tests, 4 were diagnosed as MELAS, 1 as MERRF, 4 as Leigh, 5 as mitochondrial myopathy, 4 as mitochondrial depletion syndrome (MNGIE, Alpers...), 5 as mitochondrial complex deficiency, 2 as Kearns Sayre Syndrome and 1 as mitochondrial oxidative phosphorylation deficiency. Transmission of nuclear DNA was observed in 7 patients, while mitochondrial transmission occurred in 19 patients. Five patients died on the follow-up.

Conclusions

This study highlights that mitochondrial diseases can manifest at any age with a variety of systemic findings and inheritance patterns, including both nuclear and mitochondrial transmission. Mitochondrial diseases should be considered in the differential diagnosis in patients with progressive symptoms, multiple organ involvement and in cases of loss of previously acquired abilities.

ABSTRACTS

Topic: Infectious and Inflammatory Diseases/ Neuroimmunology

EPNS25_682 - Clinical outcomes of baricitinib treatment in aicardi-goutières syndrome: a retrospective cohort study at great ormond street hospital

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Objectives

In this real-world approach study, we report our experience of the use of baricitinib in patients with Aicardi-Goutières Syndrome (AGS) in a large tertiary center. AGS is a genetic disorder that significantly diminishes quality of life due to its impact on the brain, immune system, and skin. Currently, there is no cure. Baricitinib, a Janus kinase (JAK) inhibitor, has been investigated as a potential treatment by reducing excessive interferon signaling and potentially alleviating some of the inflammatory symptoms.

Methods

This was a retrospective case series of 16 children (median age: 83 months, 6 (37.5%) female) with molecularly confirmed AGS who were offered baricitinib treatment. Clinical, demographic, laboratory, treatment, and imaging data were collected at baseline and two follow-up assessments after treatment initiation. The primary clinical outcomes included neurological function, changes in inflammatory markers, and radiological findings (MRI).

Results

Seventy-five percent (12/16) of patients presented at <2 years old, and 6% (1/16) presented in older children. Developmental delay was the most common presenting symptom, observed in 81% (13/16) of patients. Seizures were reported in 43% (7/16), and chilblains in 25% (4/16). Baricitinib was initiated in 50% (8/16) of patients at a median age of 4 years. The response to baricitinib varied, with some exhibiting improvements in irritability, seizures, and chilblains, while others showed limited or no improvement in neurodevelopmental status or irritability. Dystonia was present in 87% (14/16) of patients at baseline, with improvement noted in 12% of treated patients. Baseline CSF neurotransmitter analysis revealed abnormalities in 75% (6/8) of patients, including elevated pterins, tetrahydrobiopterin, dihydrobiopterin, and total neopterin. MRI findings at baseline showed white matter signal changes and reduced white matter volume in 56% (9/16) of patients. Among the 8 patients who received baricitinib, the later imaging findings showed stable changes in 75% (6/8) of patients. Intercurrent infections occurred in 37% (3/8) of treated patients. Interferon gene expression was assessed prospectively in 25% (4/16) of patients: IF127, IFI144L, and IFIT1 gene expression remained elevated in most patients, while SIGLEC1 gene expression normalized in all.

Conclusions

Our report indicates a benefit of baricitinib treatment on certain systemic features of AGS, but a minimal measurable effect on the associated neurological phenotype. In developing future treatment strategies for AGS, it is essential to prioritize early diagnosis and intervention, along with ensuring that therapeutic agents effectively penetrate the central nervous system. These factors are crucial for preventing irreversible brain damage in AGS patients.

ABSTRACTS

Topic: Neurodevelopmental Disorders / Developmental Neuroscience

EPNS25_683 - Possible effect of VCAM-1 and PGE2 signaling in Autism Spectrum Disorder

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Objectives

Autism spectrum disorders (ASDs) are a group of heterogenous neurodevelopmental disabilities whose core signs are impairments in social interaction and communication, restricted and stereotyped behaviour.The clinical heterogeneity of ASDs makes it difficult to identify biomarkers, etiology and treatment. The role of cytokines have been clarified in this term.Several studies indicate that ASD patients exhibit increased levels of VCAM-1 in both serum and cerebrospinal fluid, suggesting endothelial dysfunction and enhanced leukocyte infiltration into the brain which may have an adverse bearing on the establishment of synaptic plasticity, axon growth and repulsion. Similarly, elevated PGE2 levels have been observed in ASD individuals, with evidence pointing toward its acting as bioactive lipid in microglial activation, excitotoxicity. In this study were explored potential links between VCAM-1/PGE2 dysregulation in disease mechanisms and ASD-associated behavioral phenotypes.

Methods

Quantify VCAM-1 and PGE2 levels in the sera of 60 children with control and study groups by ELISA. Determine the correlation of VCAM-1 and PGE2 and the severity of autism as determined by the Diagnostic Observation Scale modules (ADOS 1,2,3).

Results

VCAM-1 and PGE2 levels were categorized based on ASD severity across different age groups and language abilities. **VCAM-1 Levels (ng/mL) [Mean ± SD]** **Module 1** (Minimal/No Speech) 250.4 ± 35.6 $p < 0.01$**, **Module 2** (Phrase Speech) Children (5–8 years) 230.8 ± 30.2 . $p < 0.05$* **Module 3** (Fluent Speech) Older children & adolescents (≥9 years) 210.1 ± 25.4 $p > 0.05$ (NS). **PGE2 Levels (pg/mL) [Mean ± SD]** **Module 1** 145.2 ± 20.1, **Module 2** 135.6 ± 18.9, **Module 3** 128.7 ± 15.3, A strong correlation was found between VCAM-1/PGE2 levels and ADOS severity scores ($r > 0.6$, $p < 0.01$).

Conclusions

VCAM-1 Levels: Significantly elevated in ASD individuals, particularly in younger children with severe language impairments (ADOS Module 1 & 2). A gradual decrease was observed in older, more verbal individuals (Module 3 & 4). **PGE2 Levels:** Higher in ASD individuals across all age groups but most significantly elevated in non-verbal and minimally verbal children (Module 1). The levels decreased progressively with improved communication abilities (Modules 3 & 4). Results suggest that VCAM-1 and PGE2 may serve as biomarkers to predict the severity of ASD at an early stage, particularly in younger children with limited verbal abilities. Further research is needed to establish causality, Understanding the interplay between VCAM-1, PGE2, and neurodevelopmental processes could pave the way for improved treatment strategies.

ABSTRACTS

Topic: Neurogenetics

EPNS25_684 - TRPM3-associated disorders

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Objectives

Monoallelic variants in the *transient receptor potential melastatin-related type 3* gene (*TRPM3*) have been associated with neurodevelopmental delay and epilepsy including epileptic encephalopathy in small case series. However, an in-depth characterization of the broad phenotype spectrum and treatment options is currently lacking.

Methods

We performed an international, multicenter, retrospective study including all patients with pathogenic or likely pathogenic *TRPM3* variants. Patients were identified through GeneMatcher and collaborations (n=21), and through a systematic literature search following the PRISMA guidelines (n=22).

Results

In this international cohort-study we report 43 individuals with variants in the *TRPM3* gene, the most frequent being the gain-of-function variant p.Val1002Met (n=24). Patients presented with developmental delay and/or intellectual disability (93%), global or axial hypotonia (77%), ocular involvement (70%), musculoskeletal anomalies (65%), and dysmorphic features (58%). We highlight the high frequency of epilepsy in 72% of patients. All these patients had a developmental and epileptic encephalopathy with or without spike wave activation in sleep (DEE or DEE-SWAS). The most effective anti-seizure medication (ASM) was the TRPM3 channel blocker primidone, with patients showing an improvement in seizure frequency, motor and speech development.

Conclusions

Here, we report the biggest cohort of individuals with *TRPM3* variants. Most patients present with developmental delay/intellectual disability and epilepsy. We recommend screening with awake and sleep electroencephalogram abnormalities to detect DEE-(SWAS) and offer early interventions. The TRPM3 channel blocker primidone has shown promising effects and should be considered in every child with a *TRPM3* gain-of-function variant.

ABSTRACTS

Topic: Neurometabolic Disorders

EPNS25_685 - The Importance of Early Diagnosis in Rare Diseases: Unlocking the Potential of Gene Therapy

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Objectives

There are over 7,000 rare disorders, yet therapies are available for only about 5% of them. Even for the disorders with available treatments, the diagnostic and treatment pathways vary by country and are often shaped by individual healthcare centers, limiting their systematic reach and responsiveness to rapidly evolving therapies. Cell and gene therapies (CGT), have been introduced for some rare diseases, but it is not uncommon for specialists to remain unaware of these emerging treatment options. Newborn screening (NBS) is not universally implemented for all rare diseases with causal treatments, and healthcare systems often lack the infrastructure for differential diagnosis. Without early diagnosis, patient access to advanced therapies remains a significant challenge. The objective of the study was to map current diagnostic practice for a disease with newly approved causal treatment.

Methods

We investigated whether Slovak doctors have access to the necessary tools for diagnosing specific rare conditions. We interviewed 26 pediatric neurologists in Slovakia, who represent over 40% of specialised outpatient clinics in the country, to understand their approach to diagnosing hereditary demyelinating diseases of the central nervous system.

Results

Our findings reveal that, over the past 24 months, only one specialist tested for the condition more than five times, five specialists tested once or twice, and 20 specialists did not conduct any tests. Doctors generally followed a diagnostic approach that prioritized more common conditions, testing for rare diseases only after more symptoms had manifested, typically to confirm a diagnosis rather than to rule it out.

Conclusions

Current diagnostic approach reflects the healthcare system's limitations, which hinder early access to and the full benefits of CGT. Diagnoses of rare diseases are often confirmed in later stages, after significant symptoms have appeared, causing missed therapeutic windows. The question remains if increasing testing for high-risk populations with less specific symptoms could help identify patients earlier, potentially making them eligible for gene therapy. Until NBS is more widely implemented for treatable rare diseases and automatic referral systems to specialized centers are established, more frequent testing for treatable conditions should be considered.

ABSTRACTS

Topic: Epilepsy: Diagnosis and Investigations

EPNS25_686 - Comparison of Oral Prednisolone and ACTH therapies in Infantile Epileptic Spasms Syndrome: Using BASED and E-Chess Scores

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Objectives

We compared the efficacy of adrenocorticotropic hormone (ACTH) and oral prednisolone therapies for children with Infantile Epileptic Spasms Syndrome (IESS) using the Burden of Amplitudes and Epileptiform Discharges (BASED) score and Early Childhood Epilepsy Severity Scale (E-Chess).

Methods

A total of 40 pediatric patients 1 months and to 6 years of age with IESS (with hypsarrhytmia or hypsarrhytmia variants on electroencephalograpy) receiving ACTH or oral prednisolone were retrospectively analyzed. Clinical characteristics of patients were collected, such as age at spasm onset, gender, presence of perinatal abnormalities, underlying casues, types of seziures, prior use of anti-seizure medications (ASMs), numbers of concomitant ASMs. EEG recordings were assessed using the BASED score before treatment and at day 28 of ACTH and oral prednisolone administration. Seizure outcome was categorized into response (≤9) and non-response (>9) group using the E-Chess score at sixth months after treatment.

Results

23 patients received ACTH therapy and 17 patients received oral prednisolone therapy. When both treatment groups were analyzed, a significant reduction in BASED scores was found at pre- and post-treatment scores ($p<0.001$). Patients receiving ACTH showed a significant reduction in BASED scores at ($p<0.001$). Patients receiving oral prednisolone also showed a significant reduction in BASED scores ($p=0.007$). However, there was no significant difference in post-treatment BASED scores and E-chess scores between the ACTH and oral prednisolone therapy groups ($p=0.05$, $p=0.3$). Seizure outcome based on E-Chess score, there was not significant difference about gender ($p=0.907$), age at spasm onset ($p=0.179$), MRI findings ($p=0.739$), and etiology ($p=0.503$) between response and non-response group. Post-treatment BASED scores ($p=0.007$), and the reduction in BASED scores ($p=0.017$) were significantly lower in response group compared to non-response group.

Conclusions

Our analysis based on quantitative evaluation of electrographic response and seizure outcome show objectively that oral prednisolone has similar efficacy as ACTH therapy.

ABSTRACTS

Topic: Epilepsy: Diagnosis and Investigations

EPNS25_687 - Heterogeneous phenotypes of patients with variants within GABAA receptor subunits: a single centre, retrospective case-note review

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Objectives The Gamma-Aminobutyric acid A ($GABA_A$) receptor is a hetero-pentameric chloride channel comprised of a varying combination of at least 16 different subunit types. It mediates inhibitory synaptic neurotransmission within the brain. Variants of genes encoding $GABA_A$ subunits are associated with a spectrum of neurodevelopmental conditions, but there remains a lack of complete understanding on how these variants link to specific epilepsy phenotypes. The aim of this study was to outline the heterogeneous phenotypes of patients with $GABA_A$ receptor subunit genetic variants, including types of seizures, developmental issues and movement disorders.

Methods Retrospective, descriptive case note review was performed for all paediatric patients under the age of 16 years with $GABA_A$ receptor subunit variants from a single tertiary epilepsy service in the UK. All patients had genetic variants identified via whole genome sequencing provided by the Genomic Medicine Service within the National Health Service.

Results This study included 7 patients with variants within the $GABA_A$ receptor subunits, affecting GABRA1 (n=2), GABRA3 (n=1), GABRA5 (n=1), GABRB1 (n=1), GABRB2 (n=1) and GABRG2 (n=1). Most patients presented with epilepsy and developmental delay at <2 years of age (n=5), with 1 patient presenting with hypotonia and abnormal movements at 7 weeks of age and a second patient presenting with nocturnal frontal seizures, commencing at 7 years of age

Patients often had varying combinations of multiple seizure types, including focal tonic-clonic seizures with impaired awareness (n =1), focal to bilateral tonic-clonic seizures (n=2), generalised tonic-clonic seizures (n=1), focal atonic seizures (n=2), focal hyperkinetic seizures with automatisms (n=1), epileptic spasms (n=1), atypical absence seizures (n=2) and eyelid mycoclonia (n=1). EEG data was available for 6 patients, with 2 patients demonstrating evidence of photosensitivity, 4 patients showing focal spike wave discharges and 2 patients having normal EEGs. 3 patients' seizures were refractory to anti-seizure medication and 2 patients achieved seizure freedom with a single anti-seizure medication.

Mild to severe developmental delay was reported in 5 patients, and 4 of them were diagnosed with autistic spectrum disorder. 3 patients suffered from ataxia, poor coordination and stereotypies, with 1 patient's predominant clinical presentation being a hyperkinetic choreo-athetoid movement disorder.

Conclusions $GABA_A$ receptor subunit variants cause a heterogeneous phenotypic spectrum, including epilepsy, neurodevelopmental issues and movement disorders. Further understanding of these diverse presentations can aid in the development of precision therapy for this cohort of patients.

ABSTRACTS

Topic: Headache / Migraine

EPNS25_688 - Cranial Vault Abnormalities in Pre-Pubertal Children with Secondary Pseudotumor Cerebri Syndrome

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Objectives: Secondary pseudotumor cerebri syndrome (PTCS) is a rare condition in children, with most cases occurring in adolescence rather than early childhood. The pathophysiology of prepubertal PTCS is not well understood and is not directly linked to an elevated body mass index (BMI). The primary objective of this study was to highlight a cohort of children with craniosynostosis who were referred for suspected PTCS with atypical features.

Methods: A retrospective multi-center analysis was conducted on children diagnosed with cranial vault abnormalities who were referred to secondary and tertiary neurology services for suspected PTCS. Baseline demographic data, presenting symptoms, ophthalmologic findings, neurosurgical interventions, complications, and outcomes were collected

Results: A total of 13 children over 5 years (2019-2024) were diagnosed with cranial vault abnormalities, with an average age of presentation between 4 and 6 years. Only two children had an elevated BMI. Headaches were reported in 5/13 (38%) cases, visual symptoms such as blurred or double vision in 2/13 (15%) and vomiting in 1/13 (7%). 5/13 (38%) children had associated learning and behavioral difficulties. One child had a background of pyknodysostosis, and another was diagnosed with Sotos syndrome.

Radiological features of PTCS, predominantly optic nerve sheath distension, were identified in 7/13 (53%) cases. Sagittal synostosis was present in 7/13 (53%) children, while the remaining cases had multi-suture synostosis. Elevated opening pressures on lumbar puncture (LP) were observed in 6/13 (46%) children. Four children (4/13) underwent intracranial pressure (ICP) bolt monitoring, with raised pressures noted in 2/4 (50%).

Eight children (8/13, 61%) underwent cranial vault release, leading to resolution of papilledema in all cases at the last follow-up. However, headaches persisted in 4/13 (30%) cases. 7 children (53%) were started on medical treatment with acetazolamide. 2 children were weaned off following surgery, while the remaining 5 (38%) continued treatment as part of conservative management, showing resolution of papilledema at their last follow-up.

Conclusions: Craniosynostosis is an important condition to consider in prepubertal children with suspected raised intracranial pressure. These children may be asymptomatic or present with atypical features, including minimal headache. A CT scan should be considered in prepubertal children if there are head shape abnormalities.

Children presenting with papilledema before the age of six and without obesity, who are referred for suspected PTCS, should be thoroughly evaluated for secondary causes, including craniosynostosis. In our cohort in addition to surgery, they also benefited from medical management with an aim to preserve vision.

ABSTRACTS

Topic: Miscellaneous

EPNS25_689 - Automatic video analysis and classification of disorders of arousal in children

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Objectives

Sleepwalking, sleep terrors, and confusional awakenings—known as disorders of arousal (DOA)—are complex, sometimes dangerous behaviors arising from NREM slow-wave sleep (SWS), typically seen in childhood. While supervised video-polysomnography (vPSG) is the gold standard for diagnosis, it is costly, time-consuming, requires highly skilled personnel, and has low sensitivity, capturing DOA episodes in only 30–60% of cases. With the rise of at-home portable solutions for prolonged recordings, the need for automated selection of suspected clinical episodes has become increasingly compelling. Such automation can assist patients and physicians in reviewing multiple recordings and identifying cases requiring further evaluation at specialized centers.

Methods

We propose a custom Temporal Convolutional Network architecture to detect DOA events from whole-night video recordings. Temporal Convolutional Networks (TCNs) represent a specialized architecture designed to process sequential data, making them particularly effective for sleep disorder detection from video streams. Our architecture processes whole-night recordings and determines the presence of DOA events by analyzing temporal correlations between visual information across consecutive frames. We trained and evaluated our model using 204 behavioral events from "deep" N3 sleep identified in vPSG recordings of 18 children with DOA. Three sleep experts independently and blindly scored the selected events. A consensus was reached for 47 DOA episodes and 113 physiological sleep-related movements, while 44 events remained unclassified due to brevity or ambiguity.

Results

We tested our trained model on 30 movement episodes comprised of 13 DOA and 17 physiological events. When classifying patient behaviors between DOA and physiological events, our model obtained an Area under the Receiver Operating Characteristic curve (AUC) of 0.87, indicating that it can correctly identify visual patterns of DOA episodes.

Conclusions

Our preliminary results demonstrate that visual information from video recordings can aid in detecting potential DOA episodes. Furthermore, the proposed pipeline allows for integrating additional modalities, such as sleep staging, which will be explored in the next phase of our research. Our deep learning model has the potential to enhance physicians' ability to efficiently identify and analyze DOA episodes, ultimately improving diagnostic accuracy and patient care.

ABSTRACTS

Topic: Movement Disorders/ Cerebral Palsy

EPNS25_690 - The Hidden Burden: How Cerebral Palsy Affects Healthy Siblings

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Objectives: The presence of a sibling with a chronic illness can affect the quality of life and psychosocial well-being of healthy siblings. Cerebral palsy (CP), a leading cause of childhood disability, is often associated with comorbidities such as intellectual impairment and epilepsy, requiring continuous care.This study aimed to explore the effects of having a sibling with CP on the quality of life, psychosocial well-being, and sleep behaviors of healthy children, while also examining the influence of various demographic and clinical factors.

Methods: A total of 110 children aged 8–16 years participated in this cross-sectional study: 55 had a sibling with CP, and 55 had only healthy siblings. The Turkish versions of the Pediatric Quality of Life Inventory (PedsQL), Strengths and Difficulties Questionnaire (SDQ), and Children's Sleep Habits Questionnaire (CSHQ) were used to assess quality of life, psychosocial well-being, and sleep behaviors.

Results: Children with a sibling with CP reported lower overall and psychosocial quality of life, greater emotional and behavioral difficulties, and more sleep disturbances than those with healthy siblings. Girls and younger siblings had lower physical quality of life. We identified frequent hospitalization, epilepsy, use of assistive devices and lack of speech skills as risk factors for poor psychosocial quality of life in the sibling with CP. Children not attending school and those with siblings using assistive devices experienced more difficulties. Conversely, children with siblings who had full speech abilities and those receiving education exhibited more prosocial behaviors. When sleep habits were assessed, girls and younger children had more sleep anxiety, while younger siblings showed more bedtime resistance and delayed sleep onset.

Conclusions: Having a sibling with CP negatively affects children's quality of life, psychosocial well-being, and sleep behaviors, with the extent of impact influenced by various demographic and clinical factors. These findings highlight the need for targeted support interventions for healthy siblings. Further multicenter, longitudinal studies with larger cohorts are required to provide a more comprehensive understanding of these effects.

ABSTRACTS

Topic: Neurometabolic Disorders

EPNS25_691 - SUCLG1 Deficiency: Analyzing Severity, Prognosis, and Nucleoside Supplementation Outcomes

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Objectives: Mitochondrial DNA maintenance defects (MDS) result in mtDNA depletion, leading to severe neuromuscular impairment. Some MDS subtypes, such as TK2, SUCLA2, SUCLG1, RRM2B, and TYMP deficiencies, stem from nucleotide metabolism defects. While nucleoside therapy has shown promise in TK2 deficiency, its efficacy in SUCLG1 deficiency remains unclear. This study presents a case of SUCLG1 deficiency treated with nucleoside supplementation, assessing its impact on metabolic and motor function.

Methods: We evaluated a four-year-old male diagnosed with SUCLG1 deficiency. He presented at six months with developmental regression, hypotonia, and reduced mobility. Neurological examination at ten months revealed pronounced axial and peripheral hypotonia with preserved reflexes.

Biochemical analysis showed lactic acidosis (8.10 mmol/L) and elevated urinary methylmalonic acid (159 mmol/mol creatinine, ref: 0.8–8.5). Brain MRI demonstrated T2/FLAIR hyperintensities in the bilateral putamen and periductal regions. MR spectroscopy identified a lactate peak (1.3 ppm).

Genetic testing identified a variant of uncertain significance in *SUCLG1*: c.901G>A (p.Gly301Arg). Further RNA analysis from fibroblast-derived cDNA revealed compound heterozygosity with a second pathogenic variant: c.901G>A(;)589+1618G>A (p.Gly301Arg(;)Ile198LeufsTer2).

At 16 months, nucleoside therapy was initiated. Clinical and metabolic parameters were monitored to evaluate response and tolerability.

Results: Nucleoside supplementation was well tolerated, with no adverse effects. Lactic acidosis improved, and neurological decline stabilized. The patient demonstrated partial motor skill acquisition, with improvements in hypotonia and mobility; however, he remained non-ambulant.

A review of 32 previously reported SUCLG1 deficiency cases suggests two clinical phenotypes:

1. Severe neonatal-onset: Lethal prognosis.

2. Later-onset (3–4 months): Survival with significant disability.

Our patient belongs to the later-onset group. Although family members noted improvements post-therapy, clinical assessment indicated only subtle gains.

Conclusions: This case supports the potential role of nucleoside therapy in SUCLG1 deficiency, particularly in stabilizing metabolic derangements and slowing neurological decline. However, functional outcomes remain limited, and clear therapeutic recommendations are challenging due to variability in disease progression and natural history. Further studies are needed to define the efficacy and long-term impact of nucleoside supplementation in this disorder.

ABSTRACTS

Topic: Epilepsy: Medical and Surgical treatment

EPNS25_692 - Cannabidiol and Cognitive-Behavioral Comorbidities in Epileptic Encephalopathies

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Objectives: Developmental epileptic encephalopathies are marked by refractory epilepsy during childhood along with neurodevelopmental comorbidities. Addressing these comorbidities presents challenges due to the lack of diagnostic tools. This study aimed to replicate the BECOME questionnaire for caregivers of pediatric patients with refractory epilepsies who have been treated with cannabidiol (CBD) for at least one month from 2022 to 2024, and to independently analyze the results in cognitive, behavioral, and quality of life areas, regardless of its anti-seizure effects.

Methods: A retrospective analysis was carried out using clinical history and telephone interviews with family members to collect data related to cognition, language and communication, emotional and behavioral aspects, physical condition, sleep, and quality of life. Results were categorized into two groups based on whether seizures had been reduced by more than 50% or if the reduction was less than 50% or nonexistent.

Results: We gathered data from 16 patients who had received CBD since 2022. In terms of etiology, 2 had Dravet syndrome, 5 had Lennox-Gastaut syndrome, 1 had tuberous sclerosis, and 8 had other refractory epilepsies. The average number of previous anti-seizure medications used was 8.5, and the average age of the patients was 9 years. Of these, 15 patients had intellectual disabilities. None achieved seizure freedom; 37.5% were responders with more than a 50% reduction in seizures, 43.7% were responders with less than a 50% reduction, and 18.7% showed no response. The average duration of CBD use was 14.6 months. Seventy-five percent reported cognitive and behavioral improvements. In the group with more than a 50% seizure reduction, 100% reported cognitive improvement while 83% noted enhancements in language, behavior, and physical condition. Fifty percent experienced improvements in sleep (with no correlation to reductions in nocturnal seizures), and 83% reported enhanced quality of life. In the group with less than 50% seizure reduction or no improvements, 85% noted cognitive improvements, 57% reported better interaction abilities, 71% stated behavioral improvements, and 42% experienced physical improvements. Sleep remained unchanged in all patients, and 57% reported improvements in their quality of life.

Conclusions It is essential to know, diagnose, and treat neurodevelopmental comorbidities in patients with refractory epilepsies through specific diagnostic tools and targeted treatments. New anti-seizure drugs like CBD might have beneficial effects on cognition and behavior. A holistic approach with effective treatments targeting not only seizures but also comorbidities is necessary to improve the quality of life of patients and their families.

ABSTRACTS

Topic: Basic Science

EPNS25_693 - Arimoclomol upregulates expression of genes belonging to the coordinated lysosomal expression and regulation (CLEAR) network

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Objectives: Niemann-Pick disease type C (NPC) is an ultra-rare, fatal neurodegenerative disease caused by mutations in the *NPC1* or *NPC2* gene leading to lysosomal dysfunction due to impaired intracellular transport of lipids. NPC is a highly heterogeneous disease with relentlessly progressive symptoms. Arimoclomol, an orally available small molecule, is the first FDA-approved treatment for NPC when used in combination with miglustat.

Methods: The effect of arimoclomol on the nuclear vs cytosolic distribution of the transcription factors EB (TFEB) and E3 (TFE3) was assessed in different cell types by immunofluorescence staining. Binding of TFE3/TFEB to the promoter regions of coordinated lysosomal expression and regulation (CLEAR) genes was assessed with chromatin immunoprecipitation and qPCR in wild-type (WT) fibroblasts treated with arimoclomol. The effect of arimoclomol on the expression levels of 7 selected CLEAR genes was examined by qPCR in WT and NPC1 fibroblasts. EndoH assays and Western blotting were conducted to assess NPC1 protein level and maturation. Filipin staining was used to evaluate cholesterol clearance from lysosomes following arimoclomol treatment.

Results: Arimoclomol prolongs activation of TFEB/TFE3 and enhances the binding of TFE3/TFEB to CLEAR motifs resulting in transcriptional upregulation of CLEAR genes including *NPC1*. Arimoclomol raised the level of a mature form of NPC1 protein and decreased unesterified cholesterol in the lysosomes of NPC fibroblasts.

Conclusions: Arimoclomol activation of TFEB/TFE3 resulted in the upregulation of CLEAR gene expression including *NPC1*. CLEAR genes encode various proteins involved in lysosomal and autophagosomal functions, suggesting that arimoclomol may provide treatment effects through NPC1-dependent and NPC1-independent processes. The downstream effects of arimoclomol treatment were increased biosynthesis of NPC1 resulting in higher levels of mature protein and in improved clearance of cholesterol from the lysosomes. The upregulation of other lysosomal genes suggests that arimoclomol may generally improve lysosomal function and autophagy flux to promote cell health.

ABSTRACTS

Topic: Cerebrovascular Disorders

EPNS25_694 - Pathway for brain attack in children

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Objectives

To characterize neurological emergencies in children with congenital heart disease and those supported on mechanical circulatory support. Those children are susceptible to an 'acute brain attack,' and recognition is important for prompt diagnosis and management. Our aim was to study the incidence and establish a standard operating procedure for an acute brain attack in children admitted to a cardiac intensive care unit (CICU).

Methods

Retrospective observational study of children referred to Neurology with an acute brain attack and specifically stroke, in a single quaternary center over a 4-year study period. We collected clinical, demographic, laboratory, treatment, and imaging data, including the timing and type of first-line imaging. Modifiable risk factors such as anemia, thrombophilia, anticoagulation status, and their management were recorded.

Results

Initial findings indicated a total of 2889 admissions to the CICU; 1.9% (n=55/2889) had a stroke, with the majority, 69% (n=38/55), presenting with an ischemic stroke. Additional stroke risk factors were present in 89% (n=49/55) of patients, with infection being the most prevalent postoperative risk factor in 41% (n=25/55), followed by hypotension in 23% (n=14/55). Seizures were the main presenting symptom in 33% (n=21/55), followed by acute behavioral changes in 21% (n=12/55), focal neurological deficits in 16% (n=10/55), and raised intracranial pressure in 14% (n=9/55). A CT scan was performed as the first-line imaging in 45% (n=25/55) of cases, while MRI or MRA was conducted in only 13% (n=7/55) of cases. Unfortunately, the Pediatric NIHSS score was recorded in only 2% of the children assessed. The first imaging choice was diagnostic in 65% (n=36/55) of patients, and imaging was completed within the first 6 hours for only 38% (21/55) of patients. Modifiable risk factors on the day of stroke included anaemia 16% (n=9/55) and subtherapeutic anticoagulation in 47% (n=26/55) of patients. On the first day of ischaemic stroke, antiplatelets were used in 20% (n=11/55) and heparin in 56% (n=31/55) of patients. Neurosurgical intervention in haemorrhagic stroke was needed in 4% (n=2/55) of patients.

Conclusions

Children admitted to the CICU are at risk of an acute brain attack, but stroke is rare. Presentation with nonspecific neurological symptoms rather than focal neurological deficits is common. Although, in an intensive care setting, assessment for acute changes in a child's neurological examination may be challenging, a high index of suspicion, early recognition, and using pediatric NIHSS scoring may help facilitate a pathway for investigations within the window for intervention where applicable

ABSTRACTS

Topic: Neurodevelopmental Disorders / Developmental Neuroscience

EPNS25_695 - A study on the association of screen based media use with language development in children aged two to five years

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Objectives

- To study the association between screen-based media use and language development in a population of children aged 2-5 years.
- To determine the relationship between screen-based media use and language development in children aged 2-5 years.
- To assess the social skills in those with increased screen based media use.
- To screen for Autism Spectrum disorder (ASD) in these children

Methods

A case-control study was carried out at the Development Clinic within the Paediatrics Department of a medical college in Kerala, India, from May 2021 to August 2022. Ninety children aged 2-5 years, with suspected speech delay (study group) and normal development (control group), were enrolled based on specific inclusion and exclusion criteria.
Caregivers completed a questionnaire on demographics, birth history, illnesses, and risk factors for speech delay. The Language Evaluation Scale Trivandrum (LEST) was administered to both groups. The ScreenQ questionnaire assessed screen time, and children with high scores were evaluated for social maturity using the Vineland Social Maturity Scale. Autism screening was conducted with MCHAT, and ASD diagnosis was confirmed using the INCLEN tool and DSM-5 criteria. Ultimately, the association between screen time, language development, social maturity, and autism was analyzed. The data were analyzed using SPSS version 23. Continuous variables were presented as mean ± SD, while categorical data were expressed as frequencies. Normality was assessed, and statistical significance was evaluated at the 5% level using t-tests, Mann-Whitney, chi-square, and logistic regression.

Results

- Screen viewing before the age of one year was found to be a critical factor leading to language delay.
- Programs watched were mainly for entertainment purposes, included fast paced programs with violent content. Moreover, mealtime use was ubiquitous.
- It was also noted that children with language delay had young parents, belonged to smaller families and had fewer siblings.
- Co-viewing was seldom observed. Though parental concern on increased screen time grew over time, they were unable to spend adequate time with their wards due to work related pressures.

Conclusions

- Screen time was found to be universally increased in both cases and controls with most of them watching screens for more than 3 hours/day.
- Increased screen time reflected by increased screen Q scores also pointed towards delayed social age. However, no significant association with autism was noted.
- ScreenQ score >17 has a sensitivity 88.89% and specificity 78.89% in assessing screen use in children.

ABSTRACTS

Topic: Neuromuscular Disorders

EPNS25_696 - Intrathecal Onasemnogene Abeparvovec for Treatment-Experienced Patients with Spinal Muscular Atrophy: Phase 3b, Open-Label STRENGTH Study

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Objectives: Intrathecal onasemnogene abeparvovec (OA) has been studied in treatment-naïve patients with SMA in the phase 1 STRONG (NCT03381729) and phase 3 STEER (NCT05089656) studies. The STRENGTH study evaluated the safety and efficacy of intrathecal OA in treatment-experienced patients with spinal muscular atrophy (SMA).

Methods: STRENGTH (NCT05386680) was a 52-week, phase 3b, single-arm, open-label, multicenter study evaluating safety and efficacy of intrathecal OA for patients with SMA aged 2 to <18 years who were able to sit but never walked independently, and who discontinued nusinersen or risdiplam. The primary endpoint was to characterize the safety and tolerability of OA. Secondary and exploratory efficacy assessments included motor function (Hammersmith Functional Motor Scale–Expanded [HFMSE], Revised Upper Limb Module [RULM]) and caregiver experience (Assessment of Caregiver Experience in Neuromuscular Disease [ACEND]). Motor milestones were assessed per World Health Organization Multicentre Growth Reference criteria.

Results: 27 patients were enrolled (mean [SD] age at OA, 7.4 [3.35] years; n=10, 2–<6 years; n=17, 6–<18 years). Mean duration of prior risdiplam and nusinersen treatment were 3.0 and 4.3 years, respectively. All patients experienced at least one treatment-emergent adverse event (TEAE). The most frequent TEAEs were nasopharyngitis, pyrexia, and vomiting. Serious TEAEs were mostly suggestive of infections. No AEs leading to death or study discontinuation were reported. HFMSE, RULM, and ACEND changes for the overall study population demonstrated stabilization over 52 weeks. The majority of patients demonstrated maintenance of motor milestones or achievement of new milestones.

Conclusions: For treatment-experienced patients with SMA who received a one-time intrathecal infusion of OA in STRENGTH, the safety of OA was favorable and consistent with the expected profile. Across motor efficacy assessments, the study population demonstrated stabilization in motor function over 52 weeks.

ABSTRACTS

Topic: Epilepsy: Diagnosis and Investigations

EPNS25_697 - Sleep-Wake Circadian Rhythm in Children and Adolescents with Epilepsy

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Objectives

Epilepsy is a neurological disorder characterized by recurrent seizures that can significantly impact cognitive, emotional, and behavioral functioning. Sleep disturbances are commonly reported in individuals with epilepsy, and the relationship between epilepsy and sleep is bidirectional: seizures and interictal epileptic discharges can disrupt sleep architecture, while poor sleep may lower the seizure threshold. Although previous studies have explored sleep quality and architecture in pediatric epilepsy, the impact of epilepsy on circadian rhythm regulation remains less understood. This study aimed to investigate sleep patterns and circadian rhythm characteristics in children and adolescents with epilepsy, comparing them to healthy controls and assessing differences between focal and generalized epilepsy.

Methods

Sixty-six children and adolescents diagnosed with epilepsy according to the 2017 ILAE classification and 51 age-matched healthy controls were included in this observational cross-sectional study. Sleep parameters and circadian rhythms were assessed using one week of actigraphic recording, complemented by validated sleep questionnaires. Statistical analyses included non-parametric tests for group comparisons and linear regression models to examine the effect of epilepsy type on sleep variables.

Results

Children with epilepsy exhibited longer sleep onset latency, later wake-up times, and greater sleep fragmentation compared to healthy controls. Circadian rhythm analysis revealed reduced stability of the sleep-wake cycle and increased variability in daily activity levels. The type of epilepsy significantly influenced sleep parameters, with children with generalized epilepsy exhibiting longer sleep onset latency, greater nocturnal movement, and more fragmented sleep, whereas those with focal epilepsy had longer total sleep time.

Conclusions

This study confirms that children and adolescents with epilepsy show significant alterations in sleep architecture and circadian regulation compared to healthy peers. These findings highlight the need to consider sleep as a key factor in the management of pediatric epilepsy, as addressing sleep disturbances may contribute to better clinical outcomes and overall well-being.

ABSTRACTS

Topic: Infectious and Inflammatory Diseases/ Neuroimmunology

EPNS25_698 - Diagnostic value of MOGAD criteria in the context of low MOG-IgG antibody titer in children

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Objectives

Diagnostic criteria for MOGAD were updated in 2023, with additional required clinical and radiological criteria in patients with low-positive MOG-IgG-antibody (ab) titer.

The objective was to investigate the diagnostic value of low positive MOG-IgG-ab titer together with MRI findings.

Methods

Children with a first acquired demyelinating syndrome of the CNS (ADS) were included in our BIOMARKER-study since 2009 from different international centers. We analyzed children from this retrospective multicenter cohort. Inclusion criteria encompassed age <18 years, MOG-IgG-ab titer at first event, data from first clinical/radiological presentation and follow-up of ≥12 months with final diagnosis.

Serum samples were analyzed by live cell-based assay and titer levels of ≥1:160 are defined as MOG-IgG-ab positive.

Results

1630 children with a first ADS included in the ongoing BIOMARKER study were tested for MOG-IgG-ab. 332 patients were tested positive for MOG-IgG-ab (range≥1:160- 81920). In 100 children a low-MOG-IgG-ab titer ranging from 1:160 to 1:320 was detected (f:m=51:49; mean age 9 years). 50 patients had a titer of 1:160 and 50 patients a titer of 1:160.

72% (n=36/100) with titer 1:160 had radiological evidence of MOGAD thus fulfilled the MOGAD criteria compared to 96% (n=48/100) with a titer of 1:320.

In 16/100 patients (16%) an alternative diagnosis was found. 13/16 patients were diagnosed with multiple sclerosis (n=11 with 1:160, n=2 with 1:320). None of them fulfilled the radiologic MOGAD criteria. One patient had an episode of acute flaccid myelitis (1:160), one patient had meningoencephalitis not fulfilling the MOGAD criteria (OIND; 1:160), and one patient had cerebral lesions due to liver problems (OND; 1:160).

Conclusions

Our findings support the clinical value of the recently proposed diagnostic criteria with MOGAD in children with low-range MOG titer. MOGAD MRI criteria are shown to have a very high diagnostic value in association with low MOG-ab titer, especially in the differentiation from MS.

ABSTRACTS

Topic: Neuromuscular Disorders

EPNS25_700 - Variants in TMEM102, FGF11 and CHRNB1 associated with myopathy in Central European Roma population

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Objectives Using exome and genome sequencing, the cohort of 15 patients (all with self-reported Roma ethnicity) with a childhood-onset neuromuscular phenotype were identified to share a common 2.5 Mb region of homozygosity. We present preliminary results of our study.
Methods Exome or whole genome sequencing was performed, multi-omics analysis are ongoing.
Results The cohort consists of 8 males and 7 females (age 2-43 years) from 6 unrelated families. Parental consanguinity was reported in three families (6 patients). Patients present with motor developmental delay with independent walking from 1.5 to 3 years of age with progressive dominantly proximal muscle weakness from 5 to 6 years of age and loss of independent walking at 9 to 20 years of age. Short stature, failure to thrive, hypotonia, hypermobility, hyporeflexia or areflexia, facial stigmatization and scoliosis are also reported. Hypomimia, ptosis, ophthalmoplegia, dysphagia and reduced lung capacity is observed in some patients, apparently also due to age variability. MRI of the lower limbs showed diffuse atrophy and signal changes suggestive of lipomatous remodelling (2 patients). Small non-specific supratentorial demyelinating lesions were seen in 2 patients. EMG findings were non-specific with normal findings in some patients and polyneuropathy in others. Muscle biopsy showed disproportion of muscle fibres (4 patients). Genomic analysis identified a 2.5 Mb common homozygous region on chromosome 17 in all affected patients with three rare homozygous variants: an intronic variant in CHRNB1 (OMIM #616314, #616313) and two variants in OMIM genes not associated with the disease - FGF11, belonging to the fibroblast growth factor family, and TMEM102, involved in the mitochondria-dependent apoptosis pathway. Pedigree analysis suggests a probable new founder disease with autosomal recessive inheritance.
Conclusions Further research analysis is required to elucidate the underlying molecular pathogenesis and to confirm the causality of identified variants.

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ABSTRACTS

Topic: Epilepsy: Diagnosis and Investigations

EPNS25_701 - Automated detection of bottom-of-sulcus dysplasia on MRI-PET in patients with drug-resistant focal epilepsy

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Objectives

Bottom-of-sulcus dysplasia (BOSD) is a diagnostically challenging subtype of focal cortical dysplasia, 60% being missed on patients' first MRI. Automated MRI-based detection methods have been developed for focal cortical dysplasia, but not BOSD specifically. Use of FDG-PET alongside MRI is not established in automated methods. We report the development and performance of an automated BOSD detector using combined MRI-PET data.

Methods

The training set comprised 54, mostly operated retrospective patients with BOSD. The test sets comprised 17 prospectively collected patients with BOSD from the same center, and 12 patients from an independently reported series. 81% patients across training and test sets had reportedly normal first MRIs and most BOSDs were <1.5cm^3 in volume.

In the training set, 12 features from T1-MRI, FLAIR-MRI and FDG-PET were evaluated using a novel "pseudo-control" normalization approach to determine which features best distinguished dysplastic from normal-appearing cortex. Using the Multi-centre Epilepsy Lesion Detection group's machine-learning detection method with the addition of FDG-PET, neural network classifiers were then trained on various feature combinations (T1-MRI-only, FLAIR-MRI-only, FDG-PET-only, T1-MRI + FLAIR-MRI, and T1-MRI + FLAIR-MRI + FDG-PET) to determine the detection rate of BOSD. Finally, the MRI-PET BOSD detector was tested on the test sets. The proportion of patients whose BOSD was overlapped i) the top output cluster and ii) the top five output clusters were assessed.

Results

Cortical and subcortical hypometabolism on FDG-PET were superior in discriminating dysplastic from normal-appearing cortex compared to MRI features. When the BOSD detector was trained on all features, 87% BOSDs were overlapped one of the top five clusters (69% top cluster) in the training set, 77% in the prospective test set (71% top cluster) and 75% in the published test set (42% top cluster). Results were similar when the detector was trained on PET-only features and lower when trained on MRI-only features.

Conclusions

Detection of BOSD is possible using established MRI-based automated detection methods, supplemented with FDG-PET features and trained on a BOSD-specific cohort. In clinical practice, an MRI-PET BOSD detector could improve clinical and economic health outcomes in seemingly MRI-negative patients being considered for epilepsy surgery.

ABSTRACTS

Topic: Movement Disorders/ Cerebral Palsy

EPNS25_702 - A study of physiological dystonic features of handwriting in healthy pediatric population (3-12 years) and its comparison to children with SGCE-Myoclonus dystonia

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Objectives

To describe physiological movements and postures during handwriting in healthy children that could mimic signs of writing dystonia. As a secondary aim, to identify specific dystonic features in children with genetic dystonia.

Methods

A cross-sectional observational study of 49 healthy children between 3 and 12 years of age (50% girls) were examined in the school using a standardized video-filming protocol. The presence of dystonic postures during writing was rated using the modified version of the Writing Cramp Rating Score scale (WCRS+S) by two pediatric neurologists with expertise in movement disorders. These scores were compared to WCRS+S scores of a cohort of patients affected with Myoclonus Dystonia associated with SGCE (SGCE-MD). Median scores of WCRS+S and its subscales were compared using Student's T test. The influence of demographic variables such as age or gender on WCRS+S scores was analyzed with multivariable regression analysis.

Results

In the healthy pediatric population, postures with dystonic features appeared during writing in more than a half (67.3%), most of them showing abnormal finger posturing (59.2%). Elbow or wrist involvement was absent in all of them. Axial dystonic-like postures were present in most of the healthy children, especially anterior flexion of the neck (83.7%). None of the healthy children complained of pain when writing. An age-related positive correlation with WCRS+S scores (Rho 0,379; p 0,006) and fingers subscale scores (Rho 0,389; p 0,005) were observed. There were significant differences of WCRS mean between sex, being higher in girls (p 0.046). The means of the WCRS+S total and subscales scores were significantly higher in pediatric patients affected by SGCE-MD.

Conclusions

Most of the healthy children showed postures with dystonic features during writing with a pattern of distal involvement of fingers and anterior flexion of neck or trunk. An age-related correlation was found between WCRS scores and healthy girls scored higher than boys. The WCRS+S scale was able to detect significant differences between severity scores in healthy and affected children (SGCE-MD) and, as a result, seems to be a useful tool to assess the severity of handwriting dystonia in children. The presence of dystonic wrist and elbow postures and/or the associated pain during handwriting are exclussive of children with genetic dystonia and are important clues for the differential diagnosis with normal neurodevelopmental handwriting postures.

ABSTRACTS

Topic: Neuromuscular Disorders

EPNS25_703 - Spinal Muscular Atrophy and SMN2: Exploring Clinical Variability Beyond Copy Number

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Objectives

Spinal muscular atrophy (SMA) is a recessive neuromuscular disorder caused by the loss or presence of point pathogenic variants in the *SMN1* gene. One of the best-known disease modifiers is a paralogous *SMN2* gene and its copy numbers. While a higher *SMN2* copy number is associated with less severe phenotypes, discrepancies between SMA type and *SMN2* copy number have been observed. Moreover, access to disease-modifying treatments (DMT) is, in several situations, based on *SNM2* copy number. The aim of this study is to describe the clinical characteristics of this outlier population.

Methods

We studied patients with SMA1 and SMA3 carrying 3 and 2 *SMN2* copies respectively, included in the national Spanish registry for SMA (CUIDAME). Age at symptom onset, type and age at DMT initiation and other important milestones (ventilation initiation, nutritional support and scoliosis surgery) were collected.

Results

As for January 2025, we identified 119SMA1 (100 with 2*SMN2* copies, 15 with 3*SMN2*, none with 4*SMN2*) and 194SMA3 (16 with 2*SMN2* copies, 103 with 3*SMN2* copies, and 69 with 4*SMN2*). Description of the 15SMA1 patients with 3*SMN2* copies: 2SMA1a, 5SMA1b and 8SMA1c, 67% males, 1SMA1a patient diagnosed through newborn screening (NBS), mean age at symptoms onset 3.6 months (m) (0-10), mean age at DMT initiation 7.3 m (1-23), 8 patients receive nusinersen (Ns), 3 risdiplam (Rs) and 4 onasemnogene abeparvovec gene therapy (GT), 1SMA1c patient requires invasive ventilation (IV) and 11 patients (73%) have an non-invasive ventilation (NIV), mean age of initiation of 2.1 m (0-7.2), 27% (4) are fed through gastrostomy and 3 had a scoliosis surgery at mean age of 9.9 years (y) (7.5-11.8). Regarding the 16SMA3 patients with 2SMN2 copies: 11SMA3a and 5SMA3b, 94% males, mean age at symptoms onset 4.6 y (11m-16y), mean age at DMT initiation 31.8 y (8-51), 12 receive Ns and 4 Rs, 3 patients (19%) require NIV at mean age of initiation of 32 y (26.4-36.9), none of them require external nutritional support and 1 patient had scoliosis surgery at 11 years old.

Conclusions

Almost half of the SMA1 patients carrying 3*SMN2* copies show symptoms before three months of life, some of them needing IV and artificial feeding, which evidences a worse-than-expected disease course based on *SMN2* copy number. In-depth studies of the variability between *SMN2* copies is needed to improve genotype-phenotype correlations, better predict the evolution of cases detected by NBS, and raise the possibility of addressing tailored therapeutics.

ABSTRACTS

Topic: Neuromuscular Disorders

EPNS25_704 - Effectiveness of ataluren (Translarna®) in Duchenne muscular dystrophy: indirect comparison of data from the French DYS and STRIDE registries

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Objectives

This study aimed to evaluate the occurrence of clinical events in patients in France with Duchenne muscular dystrophy (DMD) treated with ataluren, vs untreated patients in standard clinical practice. The primary endpoint assessed the impact of ataluren in delaying loss of ambulation. Secondary endpoints included evolution of respiratory and cardiac functions.

Methods

Individual nonsense mutation DMD (nmDMD) patient data from ataluren-treated French STRIDE patients (PTC Therapeutics), and aggregated data from ataluren-naïve DMD patients from French DYS registries (AFM-Telethon) were used. Patients born after 2000 were selected. A matched-adjusted indirect comparison, adjusted on age at first symptoms, age at corticosteroids initiation, duration of treatment with deflazacort and with other steroids was performed.

Results

Untreated patients (n=498) lost ambulation earlier, at a median age of 11.1 years, vs 12.3 years in ataluren-treated patients (n=48 and effective sample size [ESS] at 20; HR: 0.45 [95% CI: 0.27, 0.75], p=0.002). The probability of having retained ambulation before 12 years of age was 35.2% (95% CI: 30.5, 40.6) in untreated patients vs 58.9% (95% CI: 38.8, 74.4) in ataluren-treated patients. Patients with nmDMD lost ambulation at age 10.6 years in untreated patients (n=41) vs 12.3 years in ataluren-treated patients (n=48 and ESS at 22; HR: 0.47 [95% CI: 0.27, 0.83], p=0.01). A difference of 0.7 years was observed for reaching FVC <50% in patients in the DYS registry vs STRIDE (16.2 vs 16.9 years, p=0.035). The difference (1.8 years) for reaching FVC <60% for patients in the French DYS vs STRIDE did not achieve statistical significance (14.4 vs 16.2 years, p=0.12). The median age of patients at LVEF <55% was 17.0 years in the DYS registry and was not estimable in the STRIDE Registry (p=0.013).

Conclusions

The study supports ataluren's role in delaying disease progression in nmDMD. This is the first time in French cohorts that a difference in age of loss of ambulation is shown in ataluren-treated vs untreated nmDMD patients receiving the same standard of care in a real-world setting. Furthermore, FVC <50% significantly favoured ataluren. An update of this research, or new data using larger real-world cohorts of ataluren-treated vs untreated patients is recommended to validate these findings and to explore ataluren's long-term effects, particularly on respiratory and cardiac health.

ABSTRACTS

Topic: Epilepsy: Diagnosis and Investigations

EPNS25_705 - Epileptological natural history and electrographic evolution of metachromatic leukodystrophy patients: interim results from a longitudinal study

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Objectives Metachromatic leukodystrophy (MLD) is a lysosomal storage disorder caused by mutations in the *ARSA* gene, causing progressive demyelination and neurodegeneration. Limited longitudinal data are available on its epileptological natural history. Our aim is to characterize EEG patterns and epilepsy features in MLD patients.

Methods This is a single-center, retrospective, and prospective observational study on MLD patients enrolled in a natural history protocol from May 2004 to December 2023. Clinical data including history of seizures and seizure frequency, drugs and dosage, and EEG tracings were collected.

Results Fifty MLD patients, 25 late infantile (LI), 12 early juvenile (EJ), 7 late juvenile (LJ), 6 adult-onset (AD) were included. Median follow-up was 4 years (IQR: 2-8; range: 1-20), with 360 EEG tracings. Epilepsy was documented in 78 % (39/50) of patients, specificially in 80% (20/25) of LI, 100% (12/12) of EJ, 43% of LJ (3/7) and 67% of AD (4/6). Epilepsy occurred at a median time of 27 (IQR: 12-40) months after disease onset in LI, 19 (IQR: 7-42 months) months in EJ, 93 (IQR: 76-169) months in LJ and 111 (IQR: 64-156) months in AD. The main seizure types reported were focal and focal-to-bilateral tonic-clonic seizures. Generalized ictal manifestations persisted in 21% (8/39) despite therapy. Status epilepticus was reported in 30% (13/39) of patients, coinciding with epilepsy onset in 10% (4/39) patients. Disease subtypes presented distinct EEG patterns: LI group presented rapid background deterioration, frequent seizures, and bursts of low-voltage rapid activity. Divergent patterns were observed in EJ and LJ, with EJ having more similarities with the LI group and LJ displaying a slower EEG deterioration. AD presented mildly disorganized backgrounds with sporadic focal anomalies.

Conclusions These results show that epilepsy represents a significant comorbidity in MLD patients, especially LI and EJ groups, often presenting with drug-resistant seizures. Moreover, distinct MLD subtypes present with different EEG features, hence this could represent a tool to further characterize MLD subtypes

ABSTRACTS

Topic: Fetal and Neonatal Neurology

EPNS25_706 - Preoperative brain injury in children with Congenital Heart Disease

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Objectives

Children with complex Congenital Heart Disease (CHD) are at high risk of preoperative and postoperative brain lesions. Preoperative brain injury reflects fetal and perinatal brain growth and susceptibility to damage, representing an independent risk factor for neurodevelopmental outcome. Primary outcome of this study was the description of preoperative brain lesions and their correlation with clinical course and neurodevelopmental outcome in a cohort of children with complex CHD. Secondary outcome was the comparison among non-syndromic and syndromic children, since preoperative brain injury in the latter subgroup of patients has not been previously described.

Methods

A single-center cohort study recruited children with complex CHD who required cardiac surgery in the first year of life and underwent preoperative brain Magnetic Resonance Imaging (MRI) between January 2020 and October 2024. Patients were subdivided according to presence or absence of known/suspected genetic syndrome. Cardiological, neurological and neurodevelopmental evaluations were performed before and after surgery and after 6 and 18 months.

Results

54 children were enrolled: 21/54 (39%) had a known or suspected genetic syndrome. 25/54 (46%) were affected by conotruncal heart defects, 13/54 (24%) by single ventricle physiology. 24/54 (44%) children (16/33 non-syndromic and 8/21 syndromic, p=0,454) showed at least one brain lesion on preoperative brain MR. The most frequent lesion was arterial ischemic stroke (20%), followed by subdural hemorrhage (11%), cerebral sinovenous thrombosis (9%) and white matter injury (6%). No substantial difference in number, type and severity of preoperative brain lesions between non-syndromic and syndromic patients was found. Syndromic children showed a more complicated perinatality: higher percentages of IUGR, caesarean section delivery and twin pregnancy. Furthermore, compared to non-syndromic children, they showed higher rates of axial hypotonia and psychomotor delay on preoperative neurological evaluations and higher rates of language and motor delay during follow-up.

Conclusions

The key and novel finding of our study is that syndromic children with CHD do not show increased rates of preoperative brain injury compared to non-syndromic children, although they remain a population at higher neurodevelopmental risk. Further studies are needed to validate our results.

ABSTRACTS

Topic: Epilepsy: Diagnosis and Investigations

EPNS25_707 - Pediatric Epilepsy Surgery: Global Trends of Referral and Presurgical Evaluation

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Objectives

Pediatric epilepsy surgery is a well-established, evidence-based treatment that has become widely adopted. Over time, changes in candidate profiles and diagnostic methods necessitate an updated overview of current international practices.

Methods

Group-level data were collected from representative centers worldwide on children and adolescents undergoing presurgical evaluation and epilepsy surgery in 2023.

Results

A total of 55 centers from 25 countries across 6 continents contributed data on 2,274 patients. The mean age at epilepsy onset was 3.8 years, with surgery performed at a mean age of 9 years after a mean epilepsy duration of 5.2 years. At surgery, 5.9% patients were non-pharmacoresistant, with the highest rate in Europe (15.3%), while 3.3% were under 1 year old, with the highest rate in Australia (5.1%). Prior neurosurgical procedures were reported in 14.4% of patients, with the highest rate in North America (28.7%). Among these, 7.8% had undergone prior resective surgery (including 6% for epilepsy and 1.5% for tumors), with the highest overall rate in Australia (16.6%). Disconnective surgery was performed in 2.4% of cases (including 1.4% corpus callosotomy), with the highest rate in Australia and South-America (5.1%). Neuromodulatory treatments were reported in 4.5% of patients (including 4% VNS and 0.2% RNS), with the highest rate in North America (12.6%). At the time of surgery, 5.2% of patients had Infantile Spasm Syndrome, 7.9% had Lennox Gastaut Syndrome, and 1.7% had Epileptic Encephalopathy with Spike-and-Wave Activation in Sleep. Auxiliary diagnostic procedures beyond video-EEG, structural MRI and neuropsychological investigations included FDG PET (54.8%, highest in Australia at 79.7%), genetic testing (49.4%), MRI post-processing (34.3%), fMRI (15.8%), MEG (12.6%), SPECT (9.5%), high-density EEG (1.7%), and Wada test (1.3%).

Conclusions

These findings highlight a global trend toward earlier interventions in very young children and non-pharmacoresistant cases, high reoperation rates, and the growing role of genetic testing in presurgical evaluation. This survey provides valuable insights into global practices and recent advancement in pediatric epilepsy surgery.

ABSTRACTS

Topic: Movement Disorders/ Cerebral Palsy

EPNS25_708 - Long-term outcome and relapse risk in Sydenham Chorea: evidence from a large corticosteroid-treated cohort

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Objectives: Although it is commonly described as a monophasic disorder, Sydenham chorea (SC) may persist or relapse in a significant proportion of patients. Corticosteroid treatment has been associated with faster chorea resolution and a reduced risk of relapse. However, optimal treatment regimens, impact of corticosteroid on psychiatric symptoms, and factors associated with corticosteroid failure are unknown. We aim at analyze the motor and non-motor outcomes of a large cohort of corticosteroid-treated patients to define treatment regimens and clinical features associated with a less favorable course.

Methods: A retrospective analysis of SC patients diagnosed between 2009 and 2023 at two Italian centers was performed. Inclusion criteria were: SC diagnosis according to the modified Jones' criteria, age under 18 years at onset, follow-up of >6 months. Kaplan-Meier curves were used to analyze chorea resolution and relapse risk, and a logistic regression model was applied to identify clinical features associated with an increased risk of relapse

Results: Sixty-eight patients were included (mean age 9.5±2.25 years). Chorea was generalized in 55.6% and unilateral in 44.3%. Motor symptoms were classified as mild in 29%, moderate in 68%, and severe in 3%. 35% of the patients showed hyperintense white matter lesions on brain MRI. The mean time to chorea resolution was 2.4 months. Non-motor symptoms occurred in 41.2% of patients at onset, gradually decreasing to 25% at one month, 17% at six months, 16.2% at one year, and 7.35% after three years. All patients received corticosteroids, either oral prednisone alone (47%) or intravenous methylprednisolone followed by oral prednisone (53%). The mean equivalent prednisone dose was 100.8 ± 51.8 mg/kg, with a mean treatment duration of 62.27±19.92 days. 19% of the patients experienced SC relapse (77% of relapses occurred within six months from onset). Logistic regression showed that prolonged steroid therapy (>60 days, odds ratio [OR] 1.086, p=0.048), white matter hyperintensities on brain MRI (OR 11.629, p=0.042), and antidopaminergic medications (OR 33.989, p=0.035) were significantly associated with a higher risk of relapse.

Conclusions: In corticosteroid-treated patients, chorea duration is shorter compared to historical cohorts. However, white matter abnormalities on MRI are associated with a higher relapse rate, possibly reflecting more severe neuroinflammation. Antidopaminergic treatment and prolonged steroid therapy are also associated with an increased relapse risk, possibly reflecting treatment-induced long-term modifications of basal ganglia circuitry. Our data suggest that prolonged steroid regimens should be avoided, and brain MRI is a useful prognostic tool for relapse risk stratification.

ABSTRACTS

Topic: Neurodevelopmental Disorders / Developmental Neuroscience

EPNS25_709 - Efficacy and Safety From a Phase 1/2 Open-label Trial of GTX-102, an Investigational Antisense Oligonucleotide for the Treatment of Patients With Angelman Syndrome

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Objectives

Describe efficacy and safety of GTX-102, an investigational intrathecally administered antisense oligonucleotide designed to target the *UBE3A* antisense transcript in individuals with Angelman syndrome (AS), a rare neurodevelopmental disorder with no approved disease modifying treatment characterized by severe cognitive and speech impairment, sleep disorders, motor dysfunction, and hyperactivity/noncompliance.

Methods

GTX-102-001 (NCT04259281) was a Phase 1/2 open-label trial in pediatric participants with full maternal *UBE3A* gene deletion. GTX-102 was administered in 3 to 4 monthly doses followed by quarterly maintenance dosing. Outcome measures were compared with deletion-positive 4 to 17-year-old AS Natural History Study (NHS) historical controls, where available.

Results

74 participants were enrolled across all Cohorts 1-7 and A-E. In a pooled analysis with 40 Cohort 4-7 and A/B participants with available Study Day 338 (D338) Bayley-4 Cognitive Growth Scale Value (GSV) data, mean (SD) change from Baseline was 6.7 (8.6). In 27 Cohort A/B participants with available D338 Bayley-4 Receptive Communication GSV data, least-squares (LS) mean (SE) change from Baseline was 6.6 (1.5). Both Bayley-4 Cognitive and Receptive Communication GSV D338 values exceeded AS NHS observations at Day 365. In 27 Cohort A/B participants with available D338 Aberrant Behavior Checklist – (ABC-C) Hyperactivity/Noncompliance data, LS mean (SE) change from Baseline was -5.3 (1.9), nearing the response threshold (-6.0). Five participants in Cohorts 1-3 who received high-dose GTX-102 had serious adverse events (SAEs) of reversible lower extremity weakness (LEW). Mitigation measures, including lower GTX-102 doses, dexamethasone premedication, aCSF flush immediately after GTX-102 administration, and post-flush Trendelenburg positioning significantly reduced LEW incidence from 100% (5/5) in early high-dose cohorts to 4% (3/69) in subsequent lower-dose cohorts. No new LEW cases occurred since the last were reported in April 2024. There were no unexpected SAEs.

Conclusions

Treatment with GTX-102 resulted in rapid and progressive improvement in Bayley-4 Cognitive/Receptive Communication and ABC-C Hyperactivity/Noncompliance at D338. Phase 3 relevant doses and mitigation procedures resulted in a much lower incidence of LEW, and no new safety concerns were identified. Lower GTX-102 doses and administration mitigation measures were advanced into a pivotal Phase 3 GTX-102 trial.

ABSTRACTS

Topic: Neuromuscular Disorders

EPNS25_711 - Atypical Therapeutic Response in Patients with Congenital Myasthenic Syndrome Type 5 related with COLQ gene mutation, single centre experience

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Objectives

The *COLQ* (OMIM: #603034) gene is associated with autosomal recessive 'Congenital Myasthenic Syndrome (CMS) Type 5' (OMIM: #603034). CMS Type 5 is a rare disease with typical clinical findings of respiratory distress at infancy, ptosis, ophtalmoparesis, hypotonia, fatigue and muscle weakness. This study aims to reveal the variations of CMS Type 5 patients in terms of clinical presentation, treatment response and genetic background.

Method

Medical records of 11 patients followed with CMS Type 5 at Marmara University Pediatric Neurology Clinic were retrospectively evaluated. Clinical characteristics and treatment responses of the patients were compared with their genetic results.

The genetic etiology of the patients were determined by Clinical Exome Sequencing (CES) (6 patients), Whole Exome Sequencing (WES) (3 patients) and *COLQ* gene sequencing (2 patients).

Results

Initial clinical symptoms of all patients appeared in the first year of life. The most common presenting complaint was respiratory distress, followed by ptosis and hypotonia. Ophtalmoparesis and neck muscle weakness were the two common features in all patients. Eight of the patients had the same nonsense variant c.444G>A p.Trp148* in the *COLQ* gene (NM_005677). Additionally, a frameshift variant c.1082delC p.Pro361Leufs*65 was detected in the *COLQ* (NM_005677) gene of one patient. There was a suspicion of homozygous deletion in exon 13 in one case and a homozygous deletion in exons 14-15 in another patient. All patients benefited from salbutamol, ephedrine and 3,4 diaminopyridine at variable levels. Ephedrine showed to be the only drug to have positive effect on ophtalmoparesis and weakness of neck muscles. Eye movements of two patients improved and they had better head control after regular use. All the patients except two either did not benefit from pyridostigmine or clinically deteriorated. Two patients improved with pyridostigmine and their condition worsened with discontinuation of the drug after genetic results were obtained, so it had to be reinitiated. Their mutations were known to be pathogenic.

Conclusions

Benefit of pyridostigmine in selected cases and improvement in ophtalmoparesis and neck muscles with ephedrine are the striking atypical features in our study. Further studies involving synaptic cleft and physiology of the channels should be planned to establish more precise phenotype-genotype correlation.

ABSTRACTS

Topic: Neuromuscular Disorders

EPNS25_713 - Amyotrophic lateral sclerosis with juvenile onset. Case report

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Objectives: Amyotrophic lateral sclerosis (ALS) is a motor neuron disease affecting both upper and lower motor neurons and leading to progressive paralysis. Juvenile ALS appears in a rare subgroup of patients with onset before the age of 25 years old. There are few reports of ALS in children. Here, we describe a 14-year-old boy with a rapidly progressing classical ALS phenotype caused by a mutation in FUS.

Methods. A previously healthy 13.5-year-old boy developed severe weakness in both upper and lower extremities and an inability to walk following a fall from a bicycle. He had also experienced intermittent weakness and imbalance in the extremities over the past three months.

Results: Post-fall, the weakness initially began in the left upper extremity, then in 2 weeks progressively spread to the lower extremities and the right upper extremity, leading to the loss of abilities to walk, stand, and lift his arms. Neurological examination revealed generalized muscle weakness, more pronounced in the proximal muscles. The patient required assisted walking and had axial hypotonia but no tremor, sensory deficits, or urinary/fecal incontinence. Deep tendon reflexes were normoactive, head control was normal, and no tongue fasciculations were observed. There were no swallowing or respiratory complaints. Infectious, rheumatologic, and metabolic tests were non-conclusive. EMG showed severe neurogenic involvement in the right tibialis anterior, peroneal, and gastrocnemius muscles, with moderate involvement in the right deltoid, interosseous, rectus femoris, and genioglossus muscles, suggesting an anterior horn cell disorder such as SMA or ALS. Genetic testing for SMA was negative, and CD59 deficiency-related proximal neuropathy was ruled out. Cranial and spinal MRI and MR spectroscopy were normal. There was no parental consanguinity; the patient's mother had died of an undiagnosed, rapidly progressing neurodegenerative disease with bulbar involvement at age 29. Whole-exome sequencing (WES) revealed a heterozygous *FUS* gene p525L (c.1574C>T) mutation associated with an autosomal dominant ALS6 phenotype. Since the patient had no respiratory distress or dysphagia, supportive treatment with physical therapy and vitamins was initiated.

Conclusions: ALS remains a rare condition in the pediatric population, but mutation in the *FUS* gene is clearly the most frequent cause of rapidly progressive pediatric ALS. Attention should be paid to searching for *FUS* mutation in pediatric ALS.

ABSTRACTS

Topic: Miscellaneous

EPNS25_714 - Etiological Factors, Clinical Characteristics and Treatment Response in Children with Recurrent Peripheral Facial Paralysis: A Single-Center Experience

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Objectives. Facial nerve paralysis is the most common cranial nerve dysfunction in children. Although recurrent peripheral facial paralysis (RPFP) is rare, the incidence in pediatric patients 3-15%. Identifying the underlying etiology is crucial for appropriate treatment and follow-up. This study aims to investigate the clinical findings, etiological factors and prognosis of pediatric patients with RPFP who presented to pediatric neurology clinic.

Methods. The medical records of 29 patients under the age of 18 and diagnosed with RPFP from January 2020 to March 2024 were retrospectively reviewed. The grade of facial nerve dysfunction was evaluated according to the House–Brackmann Facial Nerve Grading Scale (HBS).

Results. The total number of patients who applied to our clinic with PFP between January 2020-March 2024 was 403, and 29 (7.2%) were diagnosed with RPFP. Fourteen patients were female, and 15 were male, with a mean age of 12.8 years (range: 1.7–16.5 years). Twenty-two patients experienced 2 episodes, 4 patients had 3 episodes and 3 patients had 4 episodes of peripheral facial paralysis. All episodes were unilateral and recurred within 1–7 years after the initial episode.

According to the House–Brackmann Facial Nerve Grading Scale (HBS), the severity of facial paralysis during the last episode was classified as grade 2 in 5 patients, grade 3 in 9 patients, grade 4 in 13 patients, and grade 5 in 2 patients.

Etiological investigations revealed that 14 patients (48%) had idiopathic Bell's palsy, 3 (10%) were diagnosed with Melkersson-Rosenthal syndrome, 8 (27,5%) had an infectious disease, one of who was diagnosed with Lyme disease, 1 (3%) had familial mediterranean fever (FMF), 3 (10,3%) had hypertension and one of them was an obese child with Down syndrome.

Twenty-four patients received corticosteroids along with treatment targeting the underlying etiology. Vitamin B12 deficiency was detected in 5 patients, and folic acid deficiency was identified in 1 patient, all of whom received supplementation therapy. After treatment, 25 children (86%) achieved complete recovery within 1–6 months. Partial improvement was observed in three patients with hypertension, bilateral mastoiditis, and Melkersson-Rosenthal syndrome.

Conclusions. Our study concluded that the course of recurrent idiopathic peripheral facial paralysis is generally favorable, consistent with the literature. However, underlying etiological factors significantly impact prognosis. A detailed history, physical examination, laboratory tests should be utilized in the evaluation of children presenting with RPFP. Given the potential for recurrence in the following years, long-term follow-up is recommended.

ABSTRACTS

Topic: Epilepsy: Diagnosis and Investigations

EPNS25_715 - Evaluation of Photosensitive Epilepsies in Childhood

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Objectives

Photosensitivity is defined as an abnormal clinical or electroencephalographic (EEG) response triggered by intermittent photic stimulation (IFS) or visual stimuli. Photosensitive epilepsy is not an epilepsy syndrome itself; it contains epilepsies characterised by photic/pattern-induced seizures and has a prevalence of approximately 10% in childhood. Since exposure to triggering agents is increasing in our age, photosensitivity is a concern. The aim of this study was to analyse patients retrospectively with photosensitive epilepsy in childhood in detail.

Methods

Age, gender, age at onset of seizure and photosensitive seizure, mental status evaluation, neurological examination findings, seizure semiology, seizure frequency, seizure triggers, medications, imaging results, EEG characteristics, photoparoxysmal response types in EEG, epileptic syndrome classification, family history of epilepsy and photosensitive epilepsy were documented.

Results

The age at onset of seizure was 9.2 (±4.6), the age at onset of photosensitive seizure was 12.3 (±3.5), and the age at first IFS findings on EEG was 12.1 (±3.5) in a total of 82 patients, fifty-five of whom were girls (59%). Epilepsy was present in 56% and photosensitive epilepsy in 12.5% of the families. Juvenile myoclonic epilepsy in 30 patients, idiopathic photosensitive occipital lobe epilepsy in 15 patients, juvenile absence epilepsy in 11 patients, epilepsy with eyelid myoclonia in 7 patients, childhood absence epilepsy in 4 patients, myoclonic atonic epilepsy in 3 patients, genetic epilepsy febrile seizure + in 1 patient, benign myoclonic epilepsy of infancy in 1 patient, myoclonic absence epilepsy in 1 patient, neurodegenerative disease in 2 patients, epileptic encephalopathy and metabolic disease in 7 patients were defined. Seizure triggers were television (n: 23, 41%), computer (n: 17, 30%), light (n: 10, 18%), mobile phone (n: 5, 9%), video games (n: 5, 9%), sun (n: 4, 7%), pattern sensitivity (n: 4, 7%), insomnia (n: 3, 5%), fatigue (n: 3, 5%), hunger (n: 3, 5%), hyperventilation (n: 1), music (n: 1), excitement (n: 1).

Conclusions

Photosensitive epilepsies are clinical conditions that are generally associated with genetic generalised epilepsies and have a high familial predisposition to epilepsy, except for epilepsies such as idiopathic photosensitive occipital lobe epilepsy with focal origin at the beginning of adolescence.

ABSTRACTS

Topic: Epilepsy: Diagnosis and Investigations

EPNS25_717 - Continuous EEG Monitoring at Pediatric Intensive Care Unit: Implications to Patient Management

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Objectives

Continuous EEG (cEEG) in critically ill patients involves the simultaneous, long term recording of EEG and videotaped clinical behavior to detect secondary brain injury and neurological deterioration. This study investigated the impact of cEEG monitoring on the **clinical care** of critically ill children.

Methods

This is a retrospective study of pediatric patients followed up in a tertiary pediatric intensive care unit (PICU) and underwent cEEG monitoring (>1 hour) between 2023 and 2024. The clinical and demographic data of the patients were obtained from medical records, cEEG recordings were evaluated according to the 2021 American Clinical Neurophysiology Society guidelines. Modified Rankin Scale (mRS) was used to evaluate neurological outcome at the time of discharge from the PICU or the last outpatient visit.

Results

We analyzed a total of 85 cEEG recordings from 69 patients with a median age of 7 years (range 0.10-17.8 years) at the time of recording. Indications of cEEG monitoring were extracorporeal membrane oxygenation (n:23, 27.1%), hypoxic-ischemic brain injury following cardiac arrest (n:10 ,11.8%), central nervous system infection (n:8, 9.4%), developmental and epileptic encephalopathies (n:8, 9.4%), first unprovoked seizure(n:7, 8.2%), intracranial hemorrhage (n:6, 7.1%), acute metabolic disorders (n:5, 5.9%), status epilepticus (n:5, 5.9%), hepatic encephalopathy (n:4, 4.7%), encephalopathy due to other causes (n:4, 4.7%), head trauma (n:3, 3.5%), arterial ischemic stroke (n:2, 2.4%). Background EEG features showed a wide spectrum from normal for age to diffuse extreme voltage suppression. Electrographic seizures were identified in 3 (3.5%) recordings of 3 patients, electroclinical seizures were observed in 7 (8.2%) recordings of 6 patients. In 5.8% of the cases, video-EEG monitoring revealed that episodes clinically suspected as seizures were not associated with ictal EEG findings, thus excluding a diagnosis of epileptic seizure. Following cEEG analysis, 11.7% of recordings of 9 patients resulted in diagnostic revisions, 28.4% from 18 patients prompted modifications in therapeutic strategies. At the final evaluation, 29 patients (34.1%) had a diagnosis of epilepsy. At final examination mRS was 1 in 16 patients, 2 in 6 patients, 3 in 3 patients, 4 in 11 patients, 5 in 18 patients, and the remaining 15 patients resulted in death with mRS 6.

Conclusions

Continuous EEG monitoring aims to identify electrographic seizures and subclinical changes in cerebral function, enabling prompt diagnosis and management of neurological abnormalities. Continous EEG monitoring showed diagnostic and therapeutic implications in our cohort of pediatric ICU patients emphasizing the significance of cEEG on patient management at PICU.

ABSTRACTS

Topic: Epilepsy: Diagnosis and Investigations

EPNS25_718 - Pregnancy is always possible: sodium valproate and contraception use in post-menarchal adolescents in Melbourne, Australia

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Objectives

Sodium valproate (VPA) is an effective anti-seizure medication used for childhood-onset epilepsies. The risk of teratogenicity is well-established and avoidance of sodium valproate in females of childbearing potential is recommended. We describe the characteristics of post-menarchal adolescents treated with VPA at The Royal Children's Hospital (RCH), Melbourne.

Methods

Females aged 13-18 years who were prescribed VPA at last clinical review over a two-year period at the RCH were identified via a medical record search. Demographic and clinical features were recorded and whether discussion regarding contraception and/or teratogenicity had occurred.

Results

Between 2022-2024 VPA was prescribed for 245 females, with a median age of 16 (IQR: 14-17) years. The median daily dose prescribed was 600 (IQR: 400-800) mg. The reason for prescription was epilepsy (n=221, 90%), headache (n=4, 2%), mood disorder (n=17, 7%), and pain (n=3, 1%). Of the patients with epilepsy, 97 (44%) had drug-resistant epilepsy defined as having ongoing seizures following adequate trials of two antiseizure medications. 164 (67%) had a neurodevelopmental disorder encompassing intellectual disability, autism or a specific learning disorder. Of these patients, 33% were non-verbal and 11% were non-ambulant. In only 32 patients (13%) a discussion regarding the teratogenicity of VPA was documented in the clinical notes, with this less likely in those with a neurodevelopmental disorder (chi-square: 5.5 p=0.02). Contraception was discussed or prescribed in 69 patients (28%), this being more likely in those with a neurodevelopmental disorder (chi-square: 7.9 p=0.003). One patient became pregnant whilst on sodium valproate.

Conclusions

Despite wide dissemination of its teratogenicity risk, VPA continues to be prescribed frequently to adolescents at the RCH, Melbourne, Australia. Informed discussions regarding teratogenicity and/or contraception were infrequent. Contraceptive use was relatively higher amongst those with a neurodevelopmental disorder.

ABSTRACTS

Topic: Epilepsy: Diagnosis and Investigations

EPNS25_720 - Unusual EEG abnormalities in childhood epilepsy syndromes: A retrospective case-series

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Objectives-*:* To identify unusual EEG patterns for the diagnosis of a particular electro-clinical syndrome.

Methods- A retrospective analysis of 225 EEG records was done to identify unusual EEG patterns

Results- *Results:* A total of 225 EEG records were analyzed, of which 56% were males. The final diagnoses of an epilepsy syndrome was established in 36 (16%) children. Six EEG records (16.6%%) had EEG features that were unusual or less commonly associated with a particular epilepsy syndrome.

Case1 and Case2 -Developmentally normal adolescents with Primary generalised epilepsy sleep EEG record showed marked generalization of discharges during sleep, in contrast to the fragmentation of discharges typically observed in Idiopathic Generalized Epilepsy (IGE).

Case-3: A13-year-old developmentally normal boy presented case of GTCA alone showed the awake EEG record showed normal background activity with 3-4 Hz GSWD and frequent runs of GPFA lasting for 10-15 seconds . However, GPFA is an unusual finding in IGE and generally seen in malignant epilepsy syndromes like Lennox-Gastaut Syndrome (LGS).

Case-4**:** A developmentally normal nine-year-old boy presented with electroclinical features of occipital epilepsy and showed Occipital discharges along with GPFA .However child later had a drug-refractory course and required multiple ASMs for the control of seizures. Next-generation sequencing revealed a likely pathogenic variant (c.3803G>A) in exon-37 of DEPDC5 gene. Similar to the third case, the appearance of GPFA is unusual in this case of drug-refractory epilepsy

Case-5: A 9-year-old cognitively normal girl with seizure semiology consistent with self-limiting epilepsy with autonomic seizures (SeLAS), and the sleep EEG revealed occipital spike-wave discharges. Additionally, synchronous frontopolar spike-wave discharges were observed with the occipital discharges, suggestive of Fp-O spikes . Presence of Fp-O spikes seen in this case is a less commonly encountered EEG pattern in SeLAS.

Case-6: A 14-year-old girl presented with childhood occipital visual epilepsy (COVE). .An EEG was done for tapering ASMs which showed bilateral occipital discharges along with time locked frontal intermittent rhythmic delta activity (FIRDA) . COVE is generally associated with occipital lobe discharges and additionally frontal, centro-temporal or generalized discharges maybe found.[8] However, the presence of time-locked FIRDA was an unusual EEG finding in this case.

Conclusions- *Conclusions:* Unusual patterns on EEG in common childhood epilepsy syndromes is common. Familiarization with such patterns is essential to avoid diagnostic dilemma and exploration of alternate diagnosis.

ABSTRACTS

Topic: Neurodevelopmental Disorders / Developmental Neuroscience

EPNS25_721 - Developmental Trajectories of Children from Nursery and NICU: Insights over Time

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Objectives

Objective of the study is to identify, the early interventions of the children's neurodevelopmental outcomes from the neonatal period to childhood. By assessing progress over time, study highlights the critical role of early intervention in mitigating impairments and promoting overall growth and development of children.

Methods

This facility-based retrospective study was conducted from April 2019 to November 2021, with follow-up continuing until December 2024. The study included all neonates born at the hospital, aged 15 to 28 days. A total of 2,928 neonates were enrolled and assessed by both a doctor and a developmental therapists using “Neonatal Rapid Neurodevelopmental Assessment (n-RNDA)” tool to identify any neurodevelopmental impairments. Follow-up assessments were conducted using both the n-RNDA tool and the Bayley Scales of Infant and Toddler Development (III), administered by a certified child psychologist.

Results

A total of **2,928** newborns were enrolled, with neurodevelopmental impairments identified in **237 (8.1%)**. Among them, most common impairment was in **gross motor skills 235(99.2%),** which decreased to **45 (19.1%)** after intervention, while **21** were lost to follow-up. Fine motor impairments were initially present in 3(1.3%), but were resolved after interventions, although one neonate developed speech and communication issues. Speech impairments affected 9(3.8%), with 6 showing improvement, 1 continuing with speech issues, and 2 developing both speech and motor impairments. Vision impairments were present in 6(2.5%), 2 continued with vision impairment, one had both vision and mild motor delay, and 3 were lost to follow-up. Hearing impairments were identified in 6 (2.5%), 4 continued with hearing issues combined with speech impairment, and 2 had hearing, speech, and motor impairments. Cognitive impairment affected 5(2.1%), with 3 showing normal development after interventions and 2 exhibiting both cognitive and mild motor delay. Overall, early intervention proved highly effective in improving motor skills. However, challenges persisted in addressing vision, hearing, and speech impairments.

Conclusions

This study showed significant improvement in neurodevelopmental impairments among children. Early detection and immediate interventions reduced significantly motor impairments, but managing vision, hearing, and speech deficits remained challenging.

ABSTRACTS

Topic: Epilepsy: Diagnosis and Investigations

EPNS25_722 - Clinical and Genetic Analysis of CHD2-related disease in Pediatric Patients

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Objectives

Chromodomain helicase DNA-binding (CHD) protein family, which consists of nine members distinguished by structural differences, is known as chromatic remodeler, regulating the structure of chromatin and ultimately affecting gene expression. CHD2 is a member of CHD protein family, and the pathogenic variants in CHD2 gene have been reported to be associated with brain-restricted phenotypes in human, particularly, developmental epileptic encephalopathy.

Methods

Among the patients who performed customized gene panel study, which contains 172 genes related to developmental and epileptic disease, in a single tertiary medical institution in Korea, 22 patients with pathogenic/likely pathogenic variants in CHD2 gene were identified. Excluding two patients with insufficient clinical data, 19 patients were included in this study. Retrospective review of medical records was conducted, including demographic, clinical, radiological, and electroencephalographic characteristics.

Results

Eighteen pathogenic/likely pathogenic variants, including 12 novel variants, were identified in 19 individuals. They included 9 nonsense variants (50%), 5 splicing sites variants (27.8%), and 2 missense variants (11.1%). Two were large deletion, skipping one or more exons. All patients manifested epilepsy with a median age of 2 years (range 0.42 – 6.75 years) at onset. Accompanying clinical presentations other than epilepsy were observed in 18 patients, including intellectual disability (13/19, 68.4%), global development delay (14/19, 73.7%), and psychiatric disorder (8/19, 42.1%). The history of febrile convulsions was found in 11 patients (57.9%). Sixteen (84.2%) patients presented a generalized seizure, 1 (5.2%) presented focal seizure, and 2 (10.5%) patients showed both generalized and focal seizure. Regarding response treatment, 13 patients (68.4%) achieved seizure-free status more than 1 year with anti-seizure medication, 4 of them had recurrence of seizures after drug discontinuation. Two patients who carried identical variant showed distinctive clinical features, including onset age, seizure semiology, and electroencephalography findings. Additionally, in a patient who carried a deletion of Exon 5, paternal inheritance was revealed through trio test. However, her father was asymptomatic.

Conclusions

Epilepsy was the most common clinical manifestation in CHD2-related disease, with various accompanying neurological deficits. The discrepancy between the genotype and clinical characteristics was observed in this study. Further research on phenotype-genotype correlation is warranted.

ABSTRACTS

Topic: Neurodevelopmental Disorders / Developmental Neuroscience

EPNS25_723 - Recent Neurodevelopmental Outcomes of Extremely and Very Preterm Birth

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Objectives

Technology and advances in medical knowledge increased the survival of children born preterm. Preterm children have a high risk for neurodevelopmental delay. This study aims to evaluate recent neurologic outcomes in around 1.5 and 3 years with prematurity.

Methods

This study was a prospective longitudinal cohort study from 2013 to 2024 in two tertiary hospitals. Preterm children with gestational age less than 32 weeks or birth weight less than 1500g are followed up and evaluated Magnetic Resonance Imaging and neurodevelopment and behavior with Sequenced language Scale for Infants (SELSI), Bayley Scales of Infants and Toddler Development third edition, Childhood Autism Rating Scale second edition (CARS2) and Social Maturity Scale (SMS) in their corrected 18 months age.

Results

In total 222, 60 extremely preterm (EP), 133 very preterm (VP) children and another 29 less than 1500g were assessed. Earlier preterm needed respiratory and nutritional support(P<0.001), and showed more neonatal seizure (P=0.001) and more than 3 intraventricular hemorrhage grade (P=0.03), but not correlated with periventricular leukomalacia (PVL) in MRI. Significant delays under 2 standard deviation (SD) in any developmental domain were 31.7% in EP, and 14.5% in VP at 18 months age. Mild delays under 1 SD were 30% in EP, and 40.5% in VP at 18 months age. Significant delays were 39% in EP, and 25.7% in VP and mild delays under 1 SD were 17% in EP, and 35.1% in VP at 36 months age. All Neurodevelopmental scores were correlated with all other inter-sections. Motor is correlated with language, cognition, adaption and PVL (P<0.05). The group born between 2018-2023 showed significantly better outcome in cognitive(P=0.003),, language(P=0.004),, and motor (P=0.027) domain than the group born between 201-2017 at 18 months age.

Conclusions

We analyzed neurodevelopmental outcomes in preterm children with advanced neonatal care. In corrected age 18months, children with severe developmental delays were 8.3%, Neurodevelopmental categories are closely related and influence to each other. The recently cared group in NICU showed significantly better neurodevelopmental outcome.

ABSTRACTS

Topic: Neurometabolic Disorders

EPNS25_724 - Auditory and visual neurophysiological changes in patients with adrenoleukodystrophy (ALD) with or without hematopoietic stem cell transplantation (HSCT)

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Objectives

This study aimed to evaluate changes in cognitive function following hematopoietic stem cell transplantation (HSCT) for adrenoleukodystrophy (ALD) using neuropsychological and neurophysiological assessments and to discuss the significance of HSCT as a treatment modality.

Methods

The subjects were 21 patients with ALD who visited our outpatient clinic. Among them, 13 patients had undergone HSCT (Treatment Group, TG; 4 to 18 years), while 8 patients had not (Non-Treatment Group, non-TG; aged 6 to 21 years). all patients and their guardians provided informed consent after receiving an explanation of the examinations for the procedures of examinations by their physicians in charge.

Neuropsychological assessment included intelligence tests (WISC or WAIS based on their age), as well as visual and auditory function evaluations. Neurophysiological tests consisted of Auditory Brainstem Response (ABR) and flash-visual evoked potential (F-VEP) tests.

Results

In the TG, IQ scores showed a sharp decline immediately after HSCT, but the rate of cognitive decline showed rather slowly after 2 to 3 years. In contrast, some non-TG patients exhibited rapid cognitive deterioration within months to a few years after disease onset, rendering impossible to evaluating their intelligence by the standard tests.

Regarding ABR findings, inter-peak latency (IPL) remained relatively stable in non-TG patients initially but exhibited prolongation after 2-3 years. In contrast, in TG patients, IPL values of ABR remained unchanged even 7 years after HSCT. Configuration of ABR declined in non-TG but was kept in TG.

As to VEP, there was a patient whose wave IV of VEP disappeared as early as 7 months after the disease onset. Whereas TG patients exhibited long term preservation of wave IV latency, with effective HSCT.

Conclusions

HSCT appears to play an important role in slowing cognitive and neurophysiological decline in ALD patients. Though a transient decline in IQ was observed soon after HSCT, long term preservation of ABR and VEP components along with a reduced rate of cognitive deterioration, suggests that HSCT contributes to maintaining neurological function. These findings show the clinical importance of early treatment in ALD patients.

ABSTRACTS

Topic: Neurodevelopmental Disorders / Developmental Neuroscience

EPNS25_725 - Non-verbal social communication and expressive language in Williams syndrome and Angelman syndromes

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Objectives

In typically developing children, the development of non-verbal social communication skills (nVSC) is a prerequisite for the emergence of expressive language. The development of nVSC and expressive language was compared in Williams syndrome and Angelman syndrome, both of which are known to have characteristics in language expression.

Methods

The following data from three WS, two AS and eight preschool children with no apparent neurodevelopmental disorder (PC) were retrospectively reviewed.

- nVSC was assessed using the ESCS modified version (ESCS_m), a Japanese translation of Mundy et al.'s (1987) chart. The ESCS_m consists of three levels for six domains: (social interaction (respond, initiate), joint attention (JA) (respond, initiate), behavior regulation (respond, initiate)).
- Presence or absence of expressive words (EW) (for WS and AS, using the pilot version of the Japanese MacAther Communicative Development Inventory; for PC, as reported by parents)
- Developmental age (days) as measured by the Kyoto Scale of Psychological Development.
- Presence or absence of symbolic acts in WS and AS, as reported by parents.

Results

PC: The two PC without EW were at level 1 or 2 in most domains of the ESCS_m and their developmental age was less than 1 year. The six PC with EW were at level 3 in three or more domains.

WS: On the ESCS_m, those who were at level 3 in 5 or more domains had EW. There was one case in which the developmental changes were observed over time on the ESCS_m. His EW was observed when JA reached level 3. Of the WS with EW, only one showed symbolic acts.

AS: None had EW, but one was at level 3 in all domains of ESCS_m and showed symbolic acts. Her developmental age was as high as PC with EW.

Conclusions

WS patients are considered to be relatively good at expressive language, but in this study, the emergence of EW was not early relative to developmental days. nVSC influenced the emergence of EW as much as PC.

AS patients have very little expressive language and more receptive language. The AS in this study also did not have EW. However, one of the AS showed symbolic acts and had the same or higher level of nVSC and developmental days compared to PC or WS who had EW. This finding suggests the involvement of factors other than nVSC, symbolic acts and developmental age in the emergence of expressive language in AS.

ABSTRACTS

Topic: Miscellaneous

EPNS25_726 - Clinical Characteristics and Genetic Analysis of Children with Corpus Callosum Abnormalities

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Objectives

Abnormalities of the corpus callosum (ACC) are common in pediatric populations. Classification by its morphology did not correlate well with the clinical characteristics of the patients. We aim to analyze the clinical and genetic characteristics of ACC, with categorizing them based on whether they are congenital lesions or secondary changes to to other brain lesions.

Methods

This retrospective study analyzed the clinical, demographic, and genetic characteristics of 35 children and adolescents whose brain magnetic resonance imaging revealed ACC at our institution between August 2016 and July 2022.

Results

Patients were categorized into primary ACC without an underlying cause and secondary ACC resulting from lesions, such as periventricular leukomalacia or a surrounding cystic mass. Eighteen patients exhibited primary ACC, while seventeen patients exhibited secondary ACC; eleven patients (64.7%) were associated with preterm brain injuries. The age at diagnosis for primary ACC was earlier than that for secondary ACC (0.32 ± 0.48 vs. 6.73 ± 4.95, $p < 0.001$). Patients with secondary ACC experienced more seizures than those with primary ACC (70.6% vs. 33.3%, $p = 0.028$). Minor anomalies were significantly more common in patients with primary ACC than in those with secondary ACC (38.9% vs. 5.9%, $p = 0.041$). Genetic tests, including karyotype, chromosomal microarray, and whole exome sequencing, were performed in 21 patients; 15 with primary ACC and 6 with secondary ACC. Genetic diagnosis was confirmed in 13 out of 35 patients, with no significant difference in diagnostic rates between the two groups (60.0% vs. 50.0%, $p = 1.00$).

Conclusions

Appropriate use of genetic studies is required in patients with both primary and secondary ACC. Sei zures were more common in secondary ACC patients, and minor anomalies and facial dysmorphism were more prevalent in primary ACC patients. Both groups had high rates of developmental delay or intellectual disability.

ABSTRACTS

Topic: Infectious and Inflammatory Diseases/ Neuroimmunology

EPNS25_727 - fingolimod therapy in paediatric-onset multiple sclerosis: a single centre experience

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Objectives

Pediatric multiple sclerosis (MS) is associated with rarer but higher disease activity than in adults. First-line drugs using in treatment are not always effective. Therapeutic studies mostly involve the adult period. As a matter of fact, there are a limited number of studies examining the use of fingolimod in childhood. In this study, we aimed to evaluate the clinical and radiological features and treatment outcomes of our pediatric MS patients treated with fingolimod.

Methods

Among 132 patients with pediatric MS who were followed up in our clinic between January 2016 and January 2025, 25 MS patients who received fingolimod treatment were included in the study. Clinical, laboratory and radiologic characteristics, number of attacks, annual relapse rate, Expanded Disability Status Scale (EDSS) scores and side effects, if any, before and after fingolimod treatment were recorded. The results were discussed in terms of the place of fingolimod treatment in the treatment of pediatric MS.

Results

In a total of 25 patients (M/F: 16/9), the age at first diagnosis was 13.8±2.1 years and the age at initiation of fingolimod treatment was 15.3±1.4 (12-17) years. Fingolimod was initiated after first-line treatment in 20 patients (80%) and as the first choice in five patients (20%). The reason for switching to fingolimod was lack of response to the first drug (85%), side effects (15%) or both (5%). During the follow-up period (6-48 months), fingolimod was discontinued in 7 patients. The reason was new attacks and/or radiologic worsening in 5 (20%) and side effects in 2. The distribution of clinical findings by localization during the first attack and before fingolimod treatment showed a significant increase (posterior fossa: 60%/80%; spinal: 60%/76%; hemispheric: 20%/60%; optic neuritis: 32%/72%, respectively). After fingolimod, new clinical attacks were observed in only 4 patients. In the MRI findings of the patients before fingolimod, lesion distribution was dense with periventricular: 100%, juxtacortical: 96%, posterior fossa: 92%, spinal: 76%. After treatment, 11 patients showed new lesions, mostly in the periventricular region. However, the drug was changed in 1 patient due to isolated radiologic deterioration. The mean annual recurrence rate before and after treatment was 1.5/0.3 ($p < 0.05$) and EDSS 1.5/0.8 ($p<0.05$), respectively.

Conclusions

With appropriate patient selection, fingolimod therapy can be considered as an effective and safe treatment option in the treatment of pediatric MS.

ABSTRACTS

Topic: Neurodevelopmental Disorders / Developmental Neuroscience

EPNS25_728 - Evaluation of the efficacy of oral probiotics supplementation in children with Autism Spectrum disorders (ASDs): a randomized double blind, placebo controlled trial

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Objectives

Probiotics are believed to help reduce inflammation and influence gastrointestinal (GI) and behavioral symptoms in Autism Spectrum Disorder (ASD) through the gut-brain axis. This study evaluated whether adding oral probiotics to standard treatment could improve core ASD symptoms, measured by the Childhood Autism Rating Scale-2 (CARS-2), in children aged 2-18 years. Additionally, it assessed the effects of probiotics on behavioral comorbidities, cognitive function, sleep disturbances, GI dysfunction, and sensory processing. A subset of participants underwent functional MRI (fMRI) brain connectivity and stool microbiota analysis.

Methods

This randomized, double-blind, placebo-controlled trial (NCT04939974) included children aged 2-18 years diagnosed with ASD based on DSM-V criteria and receiving standard treatment for at least 12 weeks. Those with chronic systemic illnesses, allergies, or on alternative therapies were excluded. Participants were divided into two groups: one received a probiotic supplement containing **Lactobacillus rhamnosus** ATCC 21052, **Lactobacillus plantarum** ATCC 8014, and **Bifidobacterium longum** subspecies infantis ATCC 15707 (total **3×10⁹ CFU/g**), while the other received a placebo alongside standard care. Outcome measures included CARS-2, the Applied Behavior Checklist (ABC), the Child Behavior Checklist (CBCL), the Children's Sleep Habits Questionnaire (CSHQ), the Development Quotient (DQ), and the Sensory Profile-2, assessed at baseline and 24 weeks. Additionally, fMRI scans and stool microbiota analysis were conducted on 10 randomly selected participants at baseline and 24 weeks to evaluate functional connectivity changes and microbial composition.

Results

A total of **103 children** were enrolled (52- probiotic group, 51-placebo group), with **13.5%-female** and **56.4%-DQ ≤50%**. At 24 weeks, there was no significant difference in mean scores for CARS-2 (0.01, p=0.99), ABC (-5.16, p=0.1), and CSHQ (1.3, p=0.5) between groups. Improvements in sensory issues, GI dysfunction, and behavioral comorbidities were comparable between groups ($p \geq 0.05$). fMRI analysis showed a significant (p=0.01) increase in connectivity between the right supramarginal gyrus (SMG) and the right sensorimotor cortex (SMC), while decreased connectivity was noted between the right and left precentral and postcentral gyri. Microbiota analysis indicated an increase in **Lactobacilli** ($p \geq 0.05$) in the probiotic group, but no significant changes in **Bifidobacteria**. Pathogenic bacteria such as **Clostridium, Escherichia,** and **Shigella** decreased in both groups.

Conclusions

The study found no significant benefit of probiotic supplementation in improving core ASD symptoms or related conditions.

ABSTRACTS

Topic: Epilepsy: Medical and Surgical treatment

EPNS25_729 - Efficacy of ACTH Therapy in Epileptic Encephalopathies: Single-Center Study

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Objectives: The objective of this study is to evaluate the effectiveness of Adrenocorticotropic hormone (ACTH) therapy in controlling seizures in children with various types of epileptic encephalopathies.

Methods: We retrospectively reviewed patients diagnosed with epileptic encephalopathy who received ACTH treatment at a single center. Early seizure response was defined as a reduction in seizures by more than 50% within the first 3 months of ACTH therapy. After 3 months of therapy, seizure response was classified as "late seizure response".

Results: Thirty-five children were included in the study, and 23 of them were girls. The median age was 11 months (range 0-96 months, IQR 14 months). The median duration of follow-up after ACTH therapy was 27 months (range 3-92 months). The epileptic syndrome classification of the cohort was as follows: Infantile Epileptic Spasm Syndrome (IESS) 63%, Lennox-Gastaut Syndrome (LGS) 17.1%, Myoclonic Atonic Epilepsy (MAE) 8.6%, Spike Wave Activation During Sleep (SWAS) 5.7%, and Developmental and Epileptic Encephalopathy (DEE) 5.7%. According to etiologic classification, 31% had a genetic cause, 21.4% had a structural cause, and 31% had an unknown etiology. Four patients had focal epilepsy, 16 had generalized epilepsy, and 15 had both focal and generalized epilepsy. There was no correlation between etiology and ACTH response. ACTH early and late responses according to epileptic syndrome were as follows: IESS, 20/22 early response, 11/21 late response; MAE, 2/3 early response, 2/3 late response; LGS, 4/6 early response, 2/6 late response. There was no response in 2 patients with DEE and 2 with SWAS. Although patients with isolated focal epilepsy were rare in our cohort, generalized epilepsy syndromes (either isolated or combined with focal epilepsy) were more likely to respond to ACTH therapy (p=0.268). Among 13 patients with a genetic etiology, four patients (one with PIGT - MAE, SIK1 - IESS, TSC1, and Trisomy 21) showed both early and late responses to ACTH.

Conclusions: ACTH therapy significantly improves seizure control in IESS and MAE. The etiology of the epileptic encephalopathy, whether genetic or structural, did not significantly correlate with the ACTH response, though patients with specific genetic variants (e.g., PIGT, SIK1, TSC1) showed a good response in both early and late stages of treatment.

ABSTRACTS

Topic: Epilepsy: Medical and Surgical treatment

EPNS25_731 - Clinical and Etiological Profile of Developmental and Epileptic Encephalopathy with Burst Suppression at a Tertiary center in Oman

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Objectives: This study aims to describe the clinical characteristics of Omani patients with Developmental and Epileptic Encephalopathy with Burst Suppression (DEE-BS) and compare the underlying etiologies.

Methods: A retrospective chart review was conducted on patients diagnosed with DEE-BS at Sultan Qaboos University Hospital (SQUH) in Oman over a 14-year period (2008–2022).

Results: A total of 92 patients were included, with an equal male-to-female ratio (1:1). The underlying etiologies were classified as genetic disorders (19/92, 20.7%), metabolic disorders (13/92, 14.1%), structural abnormalities (16/92, 17.4%), and unknown causes (44/92, 47.8%). The onset of symptoms occurred in infancy in 56.5% of cases. Generalized tonic-clonic and myoclonic seizures were the most common seizure types, with intractable seizures observed in 64% of patients. Global developmental delay was noted in 74%, while speech delay was present in 93%. High consanguinity rates were observed among patients with genetic and metabolic etiologies. Brain MRI findings were abnormal in 57.6% of cases, with brain atrophy and corpus callosum abnormalities reported in 37%. Genetic testing was performed in 58.7% of patients, yielding conclusive results in 34.8%. Identified genetic variants were associated with various DEE phenotypes, including mutations in *STXBP1, SCN1A, SCN1B, KCNT1, KCNQ2, CYFIP2, SCN8A, UGP2, EEF1A2, CHD2,* and *SV2A*. The most common metabolic disorders included glycine encephalopathy (4/13) and congenital disorders of glycosylation (3/13).

Conclusions: Nearly half of the patients with DEE-BS had an undetermined etiology. Genetic and metabolic aetiology are the main causes in our cohort due to high consanguinity in the community. Comprehensive evaluation using brain MRI and genetic testing is crucial for identifying underlying etiologies and optimizing management strategies.

ABSTRACTS

Topic: Neurogenetics

EPNS25_732 - Phenotypic variability in PPP2R5D- related Mental Retardation 35

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Objectives

PPP2R5D- related Mental Retardation 35 syndrome is a rare genetic disorder, characterized by a complex phenotype which includes global developmental delay (GDD) or intellectual disability (ID), epilepsy, macrocephaly, hypotonia, and autism. 190 patients sharing 35 variants of the *PPP2R5D* gene were reported by now. In this paper we report on two new cases with different phenotypes.

Methods

Case 1 is a 32 month-old female with drug-resistant epilepsy, severe GDD, macrocephaly, and hypotonia.
Case 2 is a 5 year-old boy with autism spectrum disorder, severe speech delay, gross and fine motor inability, and moderate ID.
Whole genome sequencing was performed in both children.

Results

In both cases a missense pathogenic variant of *PPP2R5D* gene was identified, but in different positions: c.592G>A (p.Glu198Lys) in case 1, and c.598G>A (p.Glu200Lys) in case 2. Both variants are highly recurrent, with 79 and 34, respectively previously reported cases. c.592G>A variant is associated with the most severe phenotype, with a high percentage for epilepsy, severe GDD and macrocephaly, In contrast, patients with c.598G>A variant have a milder phenotype, with moderate ID, speech delay and autism as main clinical features. These aspects are explained by an impaired PP2A A/C-subunit binding or a decreased short linear interaction motif-dependent substrate binding, c.592G>A showing the highest C-binding defect.

Conclusions

The clinical features associated with *PPP2R5D* gene are variable, correlated with the gene variant. GDD or ID are common in all variants, while epilepsy and macrocephaly are more common in c.592G>A variant, and autism in c.598G>A.

ABSTRACTS

Topic: Neuro-Oncology

EPNS25_734 - Café-Au-Lait Macules In Neurofibromatosis Type 1: Birthmark Or Biomarker?

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Objectives: Neurofibromatosis type 1 (NF1) is a rare multisystem disorder characterized by variable expressivity and increased tumor risk. Café-au-lait macules (CALMs) are a hallmark of the disease, often representing one of the earliest clinical manifestations and allowing a clinical NF1 diagnosis if equal or more than six. In this study, we aimed at investigating the prognostic value of CALMs at birth in NF1 patients.

Methods: We conducted a retrospective study in patients aged ≥4 years presenting with CALMs at our Institution between 2020 and 2021, with a minimum follow-up of four years. We retrospectively collected data on CALMs at birth and other clinical manifestations associated with NF1.

Results: Among 208 patients evaluated, including 147 with a confirmed diagnosis of NF1, 110 did not show CALMs at birth and 98 had at least one. The absence of CALMs at birth did not correlate with a lower likelihood of NF1. In contrast, CALMs number at birth directly correlated with likelihood of NF1, up to 95% in patients with ≥5 macules. Additionally, a higher number of CALMs correlated with a greater prevalence of plexiform neurofibromas ($p < 0.001$).

Conclusions: Our findings suggest that a higher number of CALMs may indicate a more severe form of NF1, with an increased risk of plexiform neurofibromas. These results emphasize the importance of a comprehensive evaluation of patients with CALMs, especially in case of multiple lesions, aiming at implementing early NF1 diagnosis, follow-up strategies, and overall patient management.

ABSTRACTS

Topic: Movement Disorders/ Cerebral Palsy

EPNS25_736 - Using zebrafish model to investigate complex hereditary spastic paraplegia caused by ept1 variants

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Objectives

Hereditary Spastic Paraplegia (HSP) comprises a broad and heterogeneous group of inherited neurodegenerative and neurodevelopmental disorders. Among the identified spastic paraplegia genes (SPGs), 19 are involved in membrane phospholipid metabolism. The Kennedy pathway is a major biosynthetic route for phosphatidylethanolamine (PE), in which *EPT1* encodes ethanolaminephosphotransferase catalyzing the conversion of CDP-ethanolamine to PE. Biallelic loss-of-function mutations in *EPT1* have been associated with SPG81. Therefore, the objectives of this project are:

1. To generate disease-representative zebrafish models using CRISPR-Cas9 technique.
2. To characterise the zebrafish models by performing phenotypic characterization, neurobiological experiments, lipidomic and RNASeq studies
3. To test targeted therapies for the Kennedy-pathway-related disorders using the characterised zebrafish models.

Methods

CRISPR-Cas9 technique was used to create ept1 ex5 knock-out mutants and crispants. A series of phenotypic characterization, RNA sequencing and lipidomic profiling on these zebrafish models were conducted in the zebrafish model.

Results

The *ept1* ex5 knock-out mutants harbored an 8-bp deletion in the catalytic domain and were viable, exhibiting a 60% reduction in *ept1* mRNA levels. Compared to wild-type controls, homozygous knockouts displayed significant impairments in locomotion, as well as reduced body length and head width. Transcriptomic analysis revealed downregulation of genes involved in light response, synaptic activity, and lipid metabolism, whereas genes associated with immune signaling and neuroinflammation were upregulated. Lipidomic profiling showed a reduction in total PE and phosphatidylcholine (PC) levels in knockouts, with plasmenyl-PE being most severely affected. Through crispant analysis, we found that both *ept1* ex5 and *cept1b* ex4 crispants exhibited significantly impaired locomotion; however, only *ept1* ex5 crispants displayed reductions in body length and head width.

Conclusions

The *ept1* knock-out mutants and crispants recapitulate the movement disorder and developmental delay observed in SPG81 patients, making them valuable models for disease research. Moreover, our findings suggest that neuroinflammation may play a crucial role in HSP pathogenesis and could serve as a potential therapeutic target.

ABSTRACTS

Topic: Basic Science

EPNS25_737 - Behavioral and Neuroanatomical Alterations in epsilon-sarcoglycan deficient mice

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Objective

Mutations in ε-sarcoglycan (*SGCE*) cause myoclonus-dystonia (MD), a rare childhood-onset movement disorder. The pathogenic mechanism of SGCE is unclear, although evidence points to a synaptic disruption. The aim of the study was to characterize SGCE synaptic localization, and explore its impact in the phenotype and neuronal morphology.

Methods

Studies were performed in wild-type (WT) and *Sgce*-knockout (KO) mice, and in control human brain samples. Expression was analyzed in cerebellum, hippocampus, cortex and striatum by western blot. Expression in mice was also studied in different synaptic fractions and at various postnatal stages (n=9 per stage) to investigate the role of Sgce on neurodevelopment. Golgi staining was performed to examine neuronal morphology in WT and KO mice (n=4 per group) with the hypothesis that Sgce deficiency could alter dendrite morphology. Finally, we studied mice behavior in the Open field (OF) and treadmill to investigate phenotypic changes. Statistical analyses included one-way ANOVA and t-test.

Results

SGCE was widely expressed in all the brain regions studied. Developmental analysis showed elevated expression in newborn mice, followed by a progressive decline until day 21, at which point expression increased again in hippocampus, striatum and cerebellum. Western blot confirmed the presence of SGCE in the synapse of both WT mice and human brain. Brain-specific isoforms were predominant in the presynaptic fraction, while ubiquitous isoforms were enriched in the post-synaptic density of mice, suggesting distinct roles. Morphological analyses revealed that KO mice had a higher number of primary dendrites and reduced spine density compared to WT in the somatosensory cortex. Finally, KO mice exhibited behavioral differences compared to WT in the OF, including reduced overall movement, increased grooming, shorter distances travelled, and decreased exploration of the center area, indicative of anxious and compulsive behaviors.

Conclusions

SGCE isoforms exhibit differential localization and distribution in the synapse, potentially reflecting a functional specialization. Its high expression during early postnatal stages suggests a structural role in neuronal development. Finally, the absence of Sgce in the mouse brain results in significant alterations in neuronal morphology and animal behavior. These findings highlight the critical role of SGCE in brain development and function, providing insights into MD-pathophysiology.

ABSTRACTS

Topic: Epilepsy: Diagnosis and Investigations

EPNS25_738 - "Optimizing Early Pediatric Epilepsy Diagnosis Through Nurse-Led Consultations"

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Objectives : Epilepsy and other paroxysmal clinical events are common reasons for consultation in pediatric neurology. Nurses are increasingly adopting advanced practices, playing an essential role in the initial detection, evaluation and management of these conditions.

Methods : A retrospective descriptive analysis was conducted on a cohort of 405 caregivers and children aged 0 to 18 years who, over three years, attended first seizure managed by a specialized pediatric neurology nurse. Data were collected on diagnostic clinical hypotheses, use of electroencephalogram (EEGs), and the concordance between nurse's initial assessments and final medical diagnoses

Results Clinical diagnostic hypotheses included: Non-Epileptic Paroxysmal Disorder (NEPD) in 154 cases (38%), syncope in 65 cases (16%), and epilepsy in 186 cases (45.9%). Of the 196 EEGs initially requested (48.4%), 128 were pathological (65.4%). Among the 212 children without an initial EEG, the medical consultation led to the request for EEG in 36 cases (17%), with only one showing pathological findings (2.8%). In children with epilepsy, the agreement between the initial suspicion and the final diagnosis was 100%. In children with a final diagnosis of NEPD, EEG was not requested in 79.7% of cases.

Conclusions : Advanced practice nurses specializing in pediatric epilepsy enhance diagnostic accuracy, optimize resource use, and improve early detection, highlighting their essential role in multidisciplinary clinical teams.

ABSTRACTS

Topic: Neuromuscular Disorders

EPNS25_739 - Short- and Long-Term Efficacy and Safety of Nusinersen Treatment in SMA Type 2 and 3 Cases: A Multicenter Experience from the Marmara Region of Turkey

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Objectives

Spinal muscular atrophy (SMA) is a hereditary neuromuscular disorder characterized by progressive muscle weakness and atrophy. Nusinersen, an antisense oligonucleotide targeting the SMN2 gene, is approved for all SMA patients regardless of age and has shown significant improvements in motor function as a disease-modifying therapy. This multicenter pediatric study, conducted across three centers in the Marmara Region of Turkey, aimed to evaluate the efficacy and safety of nusinersen treatment in SMA type 2 and 3 patients.

Methods

This study included 98 SMA patients who received at least five doses of nusinersen (four loading doses and at least one maintenance dose) between 2018 and 2023. Clinical data, including age, sex, symptom onset, physical examination findings, and SMN2 copy number, were analyzed. Patients were grouped by age at treatment initiation (0–<2, 2–5, 5–10, and ≥10 years). The Hammersmith Functional Motor Scale Expanded (HFMSE) was used to assess motor function in patients older than two years. Changes in motor function, nutritional status, respiratory support, and orthopedic outcomes were evaluated at baseline and the last nusinersen dose. The correlations between these clinical outcomes and age at SMA diagnosis, age at nusinersen treatment initiation, and SMN2 copy number were analyzed.

Results

A total of 98 patients (62 males) with a median age of 11.75 years were included in the study. The median time to SMA diagnosis was 30 months (range: 8 days to 207 months). The median age at the first application of nusinersen was 65.5 months (from 37 days to 216 months). The distribution of SMN2 copy numbers was as follows: 10 patients had 2 copies (10.2%), 66 patients had 3 copies (67.3%), and 22 patients had 4 copies (22.4%). The median number of nusinersen dosages was 11, with a range of 5 to 21 dosages. Eighteen patients (18.3%) started treatment before the age 2 , while 33 patients (33.6%) began after the age 10. Regardless of SMN2 copy number, patients under 10 years showed better neuromotor development (81.8% vs. 92.3%). No significant treatment-related adverse effects were observed.

Conclusions

This multicenter study demonstrated the short- and long-term efficacy and safety of nusinersen treatment in pediatric patients with SMA types 2 and 3. The findings highlight the significance of early diagnosis and timely initiation of nusinersen treatment for achieving better functional outcomes.

ABSTRACTS

Topic: Neurogenetics

EPNS25_744 - Expanding the clinical spectrum of CACNA2D2: Two cases of severe intellectual disability and complex movement disorder

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Objective:
The *CACNA2D2* gene encodes the α2δ2 subunit of voltage-gated calcium channels, crucial for synaptic transmission and neuronal excitability. Mutations in *CACNA2D2* are linked to early-infantile epileptic encephalopathy, cerebellar atrophy, and global developmental delay. This study aims to describe two new clinical cases of *CACNA2D2* mutations, focusing on their inheritance patterns and therapeutic implications in patients with complex movement disorders but without epilepsy.

Methods:
Two unrelated patients with severe intellectual disability and complex movement disorders, but without epilepsy, were analyzed. Diagnosis was made using whole-exome sequencing (WES), and clinical data were reviewed descriptively. A systematic review of *CACNA2D2* variants was conducted, focusing on phenotype-genotype correlation, inheritance patterns, and functional impacts.

Results:
We report two siblings, aged 12 and 18 years, with a similar phenotype of encephalopathy, severe intellectual disability, spastic tetraparesis, and stereotypies (hand-flapping, body rocking). The older sibling also showed action tremor in the upper extremities. Both achieved stable sitting but never developed independent ambulation or functional language, with severe receptive impairment, absent social interaction, and no spontaneous smiling. Neurological exam revealed microcephaly, limb hypertonia, axial hypotonia, hand-flapping, head-turning stereotypies, failure to thrive, difficulty maintaining eye fixation, and absence of autonomous walking. Coordination showed stable sitting with continuous rocking. Both could grasp objects but had intentional tremor. Spinal exam revealed moderate scoliosis.

Brain MRI showed cerebellar atrophy with T2-FLAIR hyperintensities. Video-EEG showed slowed background activity, and metabolic tests were unremarkable. Notably, these patients never developed epilepsy, which distinguishes these cases from typical *CACNA2D2*-related disorders.

WES identified a homozygous *CACNA2D2* variant (3:50431598, NM_001174051.3, c.407G>C/p.Arg136Thr) in both siblings, inherited from both parents. The older sibling was treated with risperidone, resulting in reduced irritability and stereotypies.

Conclusions:
This case expands the clinical spectrum of *CACNA2D2*-related disorders, describing a non-epileptic phenotype with persistent stereotypies. It highlights the importance of genetic diagnosis in unclassified neurodevelopmental disorders and the need for targeted therapies to improve patient outcomes.

ABSTRACTS

Topic: Infectious and Inflammatory Diseases/ Neuroimmunology

EPNS25_745 - Seizures in Omicron Variant of COVID-19 Infections: Patterns, Profiles, and Implications

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Objectives

The coronavirus disease 2019 (COVID-19) pandemic, caused by the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), has led to significant morbidity and mortality worldwide. Omicron variant has generated a new wave, evidenced by high infection rates worldwide and is very high compared to the waves of the variants such as the Alpha and Beta. This study aims to investigate the relationship between COVID-19 and seizures by analyzing the clinic-demographic profiles of affected patients.

Methods

This retrospective, cross-sectional, record-based study was conducted at Department of Pediatrics, Malankara Orthodox Syrian Church Medical College, Kerala, India, to assess the risk of seizures in children with SARS-CoV-2 infection during the third wave (Omicron variant) of the COVID-19 pandemic. The study included pediatric patients aged from 2 months to 18 years admitted in the Department of Pediatrics between December 28, 2021, and March 15, 2022. Data on demographics, clinical features, seizure characteristics, laboratory findings, and imaging results were systematically extracted from hospital records and analyzed using EZR software. Statistical tests, including the Chi-square test and Mann-Whitney U test, were used to determine significant associations. Ethical approval was obtained, and patient confidentiality was maintained.

Results

A total of 276 children were admitted during the Omicron wave of COVID-19, 81 of whom presented with seizures. The study participants had a median age of 23 months (IQR: 12–51 months). Most were male (65.9%), while females made up 34.1%. Most COVID-19 cases were mild (97.6%), with only one participant (2.4%) experiencing moderate severity. Among the 49 children with confirmed COVID-19, 41 (50.62%) had seizures, compared to 8 (4.10%) without seizures, showing a statistically significant association ($p < 0.001$) with an odds ratio (OR) of 23.95 (95% CI: 10.43–54.99). Seizures were predominantly generalized (97.6%), with febrile seizures accounting for most cases (70.7% simple, 24.4% complex). Anemia was significantly associated with seizures ($p = 0.019$, OR = 4.26 [1.20, 15.04]), while other laboratory parameters, including lymphocyte count and sodium levels, were not.

Conclusions

The study results align with emerging evidence that COVID-19 can impact the central nervous system (CNS) and the need for heightened vigilance for seizure activity in patients with COVID-19, especially those with severe disease. Further research is needed to explore the pathophysiological mechanisms linking COVID-19 to seizures

ABSTRACTS

Topic: Neuromuscular Disorders

EPNS25_746 - Real-World Outcomes of Spinal Muscular Atrophy Treatment with Onasemnogene Abeparvovec in Croatia: Case Series

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Objectives

The development of novel treatment options and the implementation of newborn screening programs have significantly transformed the landscape of care for patients with spinal muscular atrophy (SMA). Onasemnogene abeparvovec-xioi, an adeno-associated viral vector-based gene therapy delivering a functional copy of the SMN1 gene, has shown significant efficacy in improving motor function and survival rates. In Croatia, this therapy has been integrated into routine clinical practice for several years, providing valuable real-world data on its long-term outcomes and effectiveness.

Methods

We describe a series of five patients, four of which initially presented with varying degrees of hypotonia and delay in motor development, while one patient was discovered through newborn screening program. All patients received genetic confirmation of SMA, underwent Children's Hospital of Philadelphia Infant Test of Neuromuscular Disorders (CHOP-INTEND) testing and received onasemnogene abeparvovec treatment.

Results

Four out of five patients achieved adequate clinical improvement as show by the increase in CHOP-INTEND score. One patient showed signs of regression and required additional care.

Conclusions

Despite the widespread use of novel treatment modalities that have drastically improved patient outcomes, there remains a paucity of real-world case reports documenting the care of SMA patients. Our study aims to address this gap, providing valuable insights and experiences that are essential for the continued enhancement of treatment approaches. We hope that our findings will contribute meaningfully to the expanding body of literature and knowledge on spinal muscular atrophy, ultimately fostering better patient care and outcomes.

ABSTRACTS

Topic: Headache / Migraine

EPNS25_747 - Temporal association of neck pain and headache – implications for the diagnostic approach to the myofascial involvement in migraine

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Objectives

Migraine is related to disability and loss of life quality. Next to central mechanisms of migraine pathophysiology, peripheral mechanisms including the myofascial involvement of neck muscles play a role. The temporal association of headache and neck pain and objectifiable imaging measures for assessing muscular involvement are not yet established. We aimed to explore the association between headache and muscular involvement of neck muscles in patients with episodic migraine and healthy controls.

Methods

We included 13 migraine patients (age: 26.92±.47 years, 12 females) and 13 matched healthy controls (age: 26.62±3.43 years). Clinical data on headache, migraine, and neck pain was collected using headache and neck pain calendars. A 12-week observational period was followed by a cross-sectional physical examination of the upper trapezius muscles (UTM) with the identification of myofascial trigger points (mTrP), algometry (pressure pain thresholds [PPT]), and B-mode sonography. Image analysis included measurement of muscle and fascia thickness, and gray scale analysis.

Results

Compared to healthy controls, migraine patients reported significantly higher neck pain frequency (8.60 vs. 4.17 days/month), intensity (4.31 vs. 2.82 on a 10-point NRS), and duration (13.50 vs. 2.85 h), and significantly lower PPT above the UTM ($p<0.05$). In migraine patients, mean PPT values of mTrP did not significantly differ from pooled PPT values of reference points on the same side. The odds ratio of having any headache or migraine on days with neck pain was 5.6 and 7.2 times higher than on days without neck pain, respectively. The ultrasound analysis showed only few significant differences between groups.

Conclusions

The data highlight the importance of myofascial symptoms in the UTM in migraine patients compared to healthy controls. We were able to depict that the muscular component has an important role in the UTM overall and is not limited to focal points. The complex process underlying this phenomenon is not yet completely understood but will have to be examined more closely in future research. The muscular component in its different manifestations is a relevant, but underrecognized factor in diagnosis and treatment. Further investigation of ultrasound as measure of point-of-care imaging to detect alterations in tissue composition fitting myofascial symptoms in the clinical examination are needed.

ABSTRACTS

Topic: Movement Disorders/ Cerebral Palsy

EPNS25_748 - Multiparametric investigation of network-reorganization promoted by repetitive neuromuscular magnetic stimulation applied to the anterior tibial muscle

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Objectives

Upper motor neuron syndrome due to congenital or acquired brain injury represents a major health issue with a high need for novel treatment approaches to address motor impairment. Here, neurostimulation based on electromagnetic induction, conceptualized as repetitive neuromuscular magnetic stimulation (rNMS), is a promising option. Yet, the distinct mechanisms of action at the muscular and the central level are not yet completely understood. Here, we outline the treatment-goal adapted neuromodulation (TaNeMo) study's design, that attempts to contribute important evidence to this research field. The project is funded by the Federal Ministry of Education and Research (KMU-Innovative: medical engineering; 13GW0607C).

Methods

Healthy participants receive a one-time rNMS treatment targeting the right tibialis anterior muscle (TAM) to explore dose dependent effects on cortical excitability by neuronavigated transcranial magnetic stimulation (nTMS). Stimulation protocols with a reliable efficacy profile will be further evaluated in a longitudinal study design comprising 12 rNMS sessions within 3 weeks and a comprehensive multiparametric set of investigations at baseline, one day and one week after the intervention. Safety, practicability, and satisfaction data will be collected throughout the study.

Results

rNMS and nTMS were both found to be safe methods without any clinically relevant adverse events. There was a significant difference between the different stimulation protocols in latency after 60 min ($p=0.040$), but not for MEP amplitude ($p=0.547$). For the longitudinal intervention the stimulation protocol with the most reliable efficacy profile and the highest increase in cortical excitability (20% increase after 60 min compared to baseline) was identified: 15 Hz, 26 min, on-time 3s, off-time 6s.

Conclusions

In terms of changes in cortical excitability higher frequencies or longer duration of rNMS stimulation are likely not superior to lower frequencies and shorter duration. Findings of the study will contribute to elucidate the mechanism of action of rNMS on different biological levels. To date, there are no studies on the effects of rNMS treatment that are comparable in scope, methodological significance, and depth. The findings will contribute to further develop rNMS to make it available to young and adult patients in the best effective and resource-efficient manner.

ABSTRACTS

Topic: Neurodevelopmental Disorders / Developmental Neuroscience

EPNS25_749 - A Prospective Study of Sensory Processing Patterns in (17) children with STXBP1-deficiency

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Objectives

STXBP1-related disorders (STXBP1-RD) encompass a broad phenotypic spectrum characterized by developmental delay, intellectual disability, epilepsy, movement disorders, and behavioral disorders. Understanding sensory processing in individuals with STXBP1-RD is crucial due to its impact on daily functioning and its role in evaluating previously difficult-to-assess aspects of the condition.

This study aims to identify the sensory processing patterns in pediatric patients with STXBP1-RD and to examine potential correlations between these patterns and various clinical variables.

Methods

This prospective study included pediatric patients with a genetic diagnosis of STXBP1-RD. The Sensory Profile 2 (SP2), a standardized tool which assesses sensory processing patterns, and the Children's Sleep Habits Questionnaire (CSHQ) were administered through the secure REDCap online platform. Statistical analysis included descriptive statistics and the Mann-Whitney test, with a significance level set at $p < 0.05$.

Results

Seventeen participants (9 female, 8 male), aged between 2-18 years were included in the study. All had intellectual disability (17/17), followed by epilepsy (13/17), behavioral problems (7/16), and autism spectrum disorder (ASD) (3/16). The most frequently elevated SP2 sensory and behavioral domains (scoring >2 SD above the mean) were attentional responses (7/17), movement (6/17), body position (5/17), and tactile processing (5/17). The predominant sensory profile was a high threshold for activation (11/17), with the Registration/Bystander pattern being the most common (7/11). ASD correlated with low-threshold sensory profiles (Sensitivity $p = 0.028$, Avoidance $p = 0.010$). Behavioral difficulties correlated with higher registration ($p=0.008$), sensitivity ($p=0.021$), avoidance ($p=0.013$), and conduct scores ($p=0.014$). No significant correlations were found between CSHQ and SP2.

Conclusions

This study highlights the sensory processing patterns of children with STXBP1-RD, revealing a predominance of high-threshold profiles. These findings suggest that children with STXBP1-RD may actively seek sensory input yet have difficulty registering stimuli, providing valuable insights for guiding the development of targeted, sensory-based interventions.

ABSTRACTS

Topic: Epilepsy: Medical and Surgical treatment

EPNS25_751 - Treatment of children with superrefractory status epilepticus

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Objectives The causes of epileptic status can be different forms of epilepsy, most often is genetic forms. Despite the most intensive methods of treatment of epileptic status, not all of them are successful.

Methods In the Neurology Department from 2019 to 2024, six patients with super-refractory status epilepsy (SRSE) were treated. The patient's age ranged from the neonatal period to 11 years. All patients in SRSE were on the background of taking polytherapy of basic anticonvulsants (AEDs). At the beginning of SRSE, treatment was started in our department, intravenously, with the following drugs: Diazepam, Valproic acid, Levotiratsetam in appropriate doses. All these patients did not respond to the administration of emergency anticonvulsants in the department. In this regard, the patients were transferred to the intensive care unit for the administration of Propofol/Dexmedetomidine.

Results Patients with SRSE were examined for genetic analysis, the following gene mutations were identified: The first patient had a mutation in the POLG gene (8 months of age), the outcome was fatal. The second patient - a mutation in the PIGA gene (1.5 years of age) - the improvement was short-term, the status recurred in a week. The third patient had a mutation in the KCNQ2 gene (9 days of life), the improvement was noted on carbamazepine. The fourth patient had a mutation in the SCN1A gene (8 years old), the improvement was on polytherapy with cannabidiol. The fifth patient did not have a genetic analysis, but the cause of SRSE was always associated with infectious diseases, he was diagnosed with FIRES syndrome, he improved on clonazepam. The sixth patient (5-6 days of life) - without genetic analysis, but the cause of SRSE was associated with a deficiency of vitamin Pyridoxal-5-phosphate, the improvement was on the introduction of vitamin P5P

Conclusions The most severe status epilepticus was observed in patients with certain genetic disorders and metabolic disorders.

ABSTRACTS

Topic: Neuromuscular Disorders

EPNS25_752 - The Spectrum of Laminopathies: Experience from a Reference Center

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Objectives

Laminopathies are rare and progressive genetic disorders characterized by muscular dystrophy with early-onset tendon contractures, proximal muscle weakness, and cardiac involvement. The clinical phenotype and prognosis are highly variable. The objective of this study is to characterize the case series of all children diagnosed with laminopathies followed at a tertiary hospital.

Methods

Retrospective descriptive study based on the review of medical records of patients with Lamin A/C mutations followed at the neuromuscular disease outpatient clinic of a tertiary hospital in Portugal. Data analysis included demographic and clinical characteristics, complementary diagnostic tests, and treatments performed.

Results

We included seven patients, predominantly male, with two half-siblings among them. Two patients were lost to follow-up due to relocation to another country.

All patients exhibited clinical manifestations in early childhood. We identified two distinct phenotypic groups: one with an early-onset severe phenotype, including neonatal axial hypotonia, head drop within the first months of life, and loss of ambulation in early childhood; the other with gait disturbances due to tendon contractures disproportionate to muscle weakness and rigid spine, presenting the classical phenotype of Emery-Dreifuss muscular dystrophy.

Four patients developed respiratory failure requiring non-invasive ventilation (NIV). Cardiac manifestations were mostly identified during adolescence in both groups: six patients had severe cardiac arrhythmias, one developed complete atrioventricular block, and two presented with dilated cardiomyopathy and heart failure with severe left ventricular dysfunction. Three of the five patients with continued follow-up experienced cardioembolic ischemic stroke, coinciding with worsening cardiac disease.

Genetic confirmation of laminopathy was obtained in six patients, while one patient remained without a genetic diagnosis. Older patients underwent muscle biopsy, which was inconclusive.

Regarding disease progression, six patients lost independent ambulation, three died due to cardiac complications, and survival status remains unknown for two patients.

Conclusions

Our case series reflects the phenotypic variability described in the literature. Cardiac muscle involvement followed skeletal muscle manifestations, significantly impacting morbidity and mortality. This study highlights the importance of early cardiac screening and intervention to prevent potentially fatal complications.

ABSTRACTS

Topic: Neurodevelopmental Disorders / Developmental Neuroscience

EPNS25_753 - Genotype-phenotype correlations in a large cohort of patients with Nicolaides-Baraitser syndrome (NCBRS)

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Objectives
Nicolaides-Baraitser syndrome (NCBRS, OMIM:601358) is a rare autosomal dominant genetic disorder predominantly caused by variations in the SMARCA2 gene, which encodes the core catalytic subunits of the SWI/SNF ATP-dependent chromatin remodeling complex (also known as the Mammalian BAF complex). This complex is essential for regulating chromatin remodeling and repair. Despite its critical role, the relationship between specific variations in SMARCA2 and the phenotypic spectrum of NCBRS remains inadequately explored. To bridge this gap and to efficiently translate any potential *SMARCA2* therapy into the clinic, it is important to fully understand the spectrum of *SMARCA2* mutations. Hence, we present clinical and molecular data from a large cohort of NCBRS patients, aiming to elucidate the genotype-phenotype correlations, but most importantly to identify reccurent variants or the regions of hotspot mutation.

Methods
We reviewed the clinical records of 155 NCBRS patients, comprising of 86 previously published cases and 69 newly-identifed and recruited patients. We used clinico-genetic data available from patients previously published, as well as recruited via GeneMatcher or enrolled in the Sanford Research CoRDS Rare Disease Registry. For genotype-phenotype correlations, we aim to analyze the distribution of variations across different domains of the SMARCA2 gene and correlate these with the observed clinical manifestations in order to further demonstrate the variability in the clinical phenotype associated with variants in this particular gene.

Results
Our cohort exhibits a wide phenotypic spectrum, including neurodevelopmental delay with varying degrees of intellectual disability, distinctive facial features, epilepsy, prominent interphalangeal joints, distal phalangeal abnormalities, and additional anomalies. We identified 68 variants (45 unique) within the SNF2 ATPase domain, one splice site variant, two truncating variants (large deletions), and two variants within the HAS domain. Further analysis is ongoing to delineate the impact of these variants on the phenotypic outcomes.

Conclusions
This study aims to provide deeper insights into the mechanisms underlying the phenotypic variability observed in NCBRS. By enhancing our understanding of the genotype-phenotype correlations, we hope to contribute to improved diagnosis and management, but most importantly to identify potential therapeutic targets and design further disease models and therapies for individuals affected by NCBRS.

ABSTRACTS

Topic: Neurodevelopmental Disorders / Developmental Neuroscience

EPNS25_754 - Genomic Landscape of Autism Spectrum Disorder in the Indian Population: Insights from Whole Exome Sequencing and Copy Number Variation Analysis

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Objectives

Autism Spectrum Disorder (ASD) is a neurodevelopmental disorder characterized by impairments in social interaction, communication, and repetitive behaviours. In this study, the limited availability of large-scale Whole Exome Sequencing (WES) was addressed and Copy Number Variation (CNV) was analysed in the children with ASD among Indian population. The study objective was to identify the specific genomic markers associated with ASD among Indian children and adolescents.

Methods

Children and adolescents aged 18 months-18 years fulfilling the diagnostic criteria for ASD, as per DSM-V, were screened. Those who fulfilled the inclusion criteria and provided consent were included, while those with known genetic etiology and neurometabolic disorders were excluded. Around 3-5 ml blood was extracted through venepuncture. Whole Exome Sequencing (WES) was performed and the data was analysed using a robust bioinformatics pipeline for variant identification, filtering, and annotation.

Results

Seventy-nine patients were enrolled in the study. A total of 637,681 unique variants were identified in the ASD cohort. After stringent filtering, 340 variants from a panel of 1,210 ASD-associated genes were prioritized. We identified 38 genes carrying pathogenic or likely pathogenic variants, including HMGCL, AGL, POGZ, ASH1L, PTEN, OTOG, MYBPC3, TSC2, and NRXN3. Variants in the OTOG gene were observed in four patients, while ASH1L variants were found in two patients. Additionally, CNV analysis of 67 samples uncovered 2,170 CNVs, of which five were classified as pathogenic or likely pathogenic. Comparative analysis with 100 Indian control samples identified 8,704 CNVs, of which 19 were significantly associated with ASD.

Conclusions

This research uncovers a distinct genomic landscape in ASD within the Indian population, laying the groundwork for targeted diagnostic and therapeutic strategies. Ongoing studies aim to further elucidate the role of structural variations, complemented by functional evaluations.

ABSTRACTS

Topic: Neurogenetics

EPNS25_755 - SCN2A-related developmental and epileptic encephalopathy: evidence of parental mosaicism in a case with seizures and paroxysmal motor events

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Objectives
SCN2A gene variants are linked to epilepsy and neurodevelopmental disorders, with parental mosaicism playing a key role in the transmission of these mutations. While most *SCN2A* mutations are *de novo*, recent studies suggest that mosaic variants, present in 3–6% of patients, are more common than previously thought. The aim of this study is to raise awareness within the medical community about the possibility of *SCN2A* mosaicism, to improve genetic counseling and help better address the needs of affected families.

Methods
We report the case of a patient with DEE-*SCN2A* inherited from a mother with a mosaic mutation. The clinical evaluation included neurological, developmental, electroencephalographic, and neuroimaging assessments. A systematic review of published cases of *SCN2A* mosaicism was conducted, focusing particularly on low-level mosaicism (<20% AAF), which is often missed by conventional sequencing techniques such as Sanger sequencing.

Clinical Case
An 11-year and 6-month-old boy diagnosed with developmental and epileptic encephalopathy (DEE) presents with paroxysmal involuntary movements, dystonic postures, episodic ataxia, mild dystonia, spasticity, and moderate intellectual disability. He was born to consanguineous Syrian parents and experienced neonatal seizures, feeding difficulties, and suspected hypoglycemia. By day 21, he began having paroxysmal episodes with respiratory changes, cyanosis, altered consciousness, and post-ictal phases. Seizures persisted throughout infancy and continued into childhood. The seizures were characterized by asymmetric posturing, ocular deviation, and right-sided involuntary movements, occurring weekly and partially controlled with valproic acid and phenobarbital. His current treatment regimen includes levetiracetam, clobazam, and valproic acid. On examination, he exhibited speech difficulties, oculomotor apraxia, cerebellar syndrome, and right-sided hemiparesis with hyperreflexia. Genetic testing revealed a likely pathogenic loss-of-function mutation in *SCN2A* (2:166237676, NM_001040143.2, c.4520A>T/p.(Lys1507Met), classified as likely pathogenic by the ACMG, with the mother being a carrier of a mosaic *SCN2A* mutation in peripheral blood.

Conclusion
SCN2A mosaicism impacts epilepsy and neurodevelopment, affecting recurrence risk. High-depth NGS is essential for accurate detection, especially in low-level mosaicism cases.

ABSTRACTS

Topic: Epilepsy: Medical and Surgical treatment

EPNS25_756 - Acetazolamide as a potential treatment for self-limited epilepsy with centrotemporal spikes (SeLECTS) in children: A retrospective observational study

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Objectives

Self-limited epilepsy with centrotemporal spikes (SeLECTS), also known as Benign Rolandic Epilepsy (BRE), is the most common epilepsy syndrome in childhood. There is ongoing debate regarding the most effective antiseizure medications (ASMs) for treating SeLECTS. This study evaluates, for the first time, the effects and side effects of Acetazolamide (ACZ) in children with SeLECTS whose seizure onset occurred between the ages of three and thirteen.

Methods

This retrospective observational study was conducted at a Pediatric Neurology Clinic in Mashhad from 2018 to 2021. We collected clinical data from 52 children with SeLECTS who consumed ACZ. The data included demographic information, age of seizure onset, age at the start of ACZ treatment, frequency of seizures before and after the prescription of ACZ, number of medications used before Acetazolamide, and any side effects experienced. Finally, SPSS version 26 was used to analyze the clinical data.

Results

We observed a positive effect of ACZ in controlling SeLECTS, with a significant reduction in both the number and severity of seizures. Forty-eight patients experienced no seizures following the prescription of ACZ. Two patients discontinued Acetazolamide due to nausea, vomiting, and skin sensitivity and 2 patients had mild side effects. Furthermore, there were no significant correlations between the age of seizure onset or gender and seizure frequency in patients who had no seizures after using ACZ (p-value > 0.05).

Conclusions

The study indicates that Acetazolamide could be an effective treatment for SeLECTS, even as a monotherapy in children, and is associated with mild side effects

ABSTRACTS

Topic: Epilepsy: Diagnosis and Investigations

EPNS25_757 - Clinical clusters of pediatric patients with status epilepticus: insights from a large single-center case-cohort study in Switzerland

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Objectives

This study assessed the clinical characteristics of pediatric patients admitted with status epilepticus (SE) to Switzerland´s largest tertiary-level pediatric hospital.

Methods

We conducted a retrospective case-cohort study analyzing 642 SE admissions from 467 patients. We applied a combination of traditional descriptive statistics and machine learning approaches. A k-clustering algorithm was used to identify distinct clinical subgroups, while LASSO regression tested whether clinical metrics could predict mortality.

Results

Significant age-related differences in SE etiology emerged: infants and younger children more often presented with acute symptomatic causes, whereas older children and adolescents were more likely to have preexisting epilepsy syndromes. Patients receiving out-of-hospital treatment had faster treatment initiation and better first-line therapy response. Shorter latency from SE onset to first-line treatment correlated with higher response rates and a reduced need for intensive care. Cluster analysis identified three distinct patient subgroups based on clinical presentation and management. At admission, two broad categories emerged: (1) younger patients presenting with SE due to an acute etiology and (2) older patients with more heterogeneous etiologies. These groups were further divided into: (i) younger patients with acute SE associated with an infection, including febrile SE ('Febrile seizure' cluster); (ii) younger patients with acute SE and a more severe in-hospital course ('Para-infectious' cluster); and (iii) older patients with an established epilepsy diagnosis ('Known epilepsy' cluster). Additionally, we identified key clinical predictors of mortality in pediatric SE: progressive semiology and a prior epilepsy diagnosis were associated with increased mortality risk, while infection-related SE was linked to lower mortality risk.

Conclusions

This study, reporting the largest pediatric SE cohort in Switzerland, offers valuable insights into the clinical presentation and management of pediatric SE.

ABSTRACTS

Topic: Cerebrovascular Disorders

EPNS25_758 - Morphometric data of infarcts and long-term cognitive consequences in children with arterial ischemic stroke in early life

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Objectives

The **aim** was to find a relationship between infarct size and cognitive outcomes at primary school age in children who suffered pediatric arterial ischemic stroke (PedAIS) in the first two years of life.

Methods

Cohort study, prospective design. 21 children (15 boys), PedAIS onset under 2 y.o. Brain MRI: 1st in acute period, 1.5T; the axial-plane slices, T1-, T2, DWI images; infarct area was manually delineated for each child in BrainVisa software. Total volumes of acute infarct and brain (mm^3), the infarction/brain volume ratio (%) was calculated.

Cognitive tests have been performed at the stage of long-term consequences when they started primary school at 8.8±1.2 y.o. We conducted the Raven's Colored Progressive Matrices (*non-verbal intelligence*), «The method for determination cognitive development» Zambatsavechene (*verbal intelligence*), Go/No-Go task (*cognitive inhibition*), The Corsi block-tapping test (*working memory capacity*).

Statistical analysis. RStudio software, descriptive statistics (median, interquartile range (IQR), range), Spearman's correlation with Holm–Bonferroni correction.

Results

Brain imaging: brain volume median 982599mm^3 (IQR 662088, range 319474-1375100); infarct volume median - 2841mm^3 (IQR 8977, range 409-102192); infarction/brain volume ratio median - 0.3% (IQR 1.4, range 0.04-22.9).
Raven's Matrices: median 66.7% (IQR 25.0, range 47.2-100.0), values above chance 16.67% (W=231, p<0.001). Test Zambatsavechene: median 69.0% (IQR 20.7, range 32.7-94.8), values above chance 20% (W=231, p<0.001). Go/No-Go task: median 95.0% (IQR 4.2, range 85.8-99.2), values above chance 50% (W=231, p<0.001). Corsi test: median 5 (IQR 1, range 4-7), values above 1 (W=231, p<0.001).
There was no significant correlation between the ratio infarction/brain volume and cognitive tests: Raven's Matrices (r=-0.37, p=0.099), Test Zambatsavechene (r=-0.19, p=0.404), Go/No-Go task (r=0.13, p=0.588), Corsi test (r=-0.18, p=0.427).
The correlation between the age of PedAIS onset (in days) was significant for infarction/brain volume ratio (r=-0,53, p=0.013), either for the Raven's Matrices scores (r=0.76, p<0.001).

Conclusions

Although PedAIS is presumed to be connected with significant cognitive dysfunction in the long-term outcomes, only an indirect relationship between the damage caused by an infarct in the brain and the long-term cognitive consequences was revealed in our small size pilot study. However, age of stroke onset may become a perspective marker for more subtle cognitive impairments such as non-verbal intelligence.

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ABSTRACTS

Topic: Neurometabolic Disorders

EPNS25_759 - Lentiviral hematopoietic stem cell gene therapy (atidarsagene autotemcel) for late juvenile metachromatic leukodystrophy (MLD): Interim analysis of a Phase III trial

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Objectives: Metachromatic leukodystrophy (MLD) is a rare lysosomal storage disorder caused by arylsulfatase A (ARSA) enzyme deficiency causing progressive demyelination and neurodegeneration. Atidarsagene autotemcel (arsa-cel), an autologous ex vivo hematopoietic stem cell (HSC) gene therapy (GT), showed favorable long-term efficacy and safety in early-onset MLD in prior studies. A Phase III clinical trial (NCT04283227) is evaluating the safety and efficacy of arsa-cel in pre-symptomatic or early-symptomatic Late Juvenile MLD (LJ-MLD) patients.

Methods: This ad hoc interim analysis summarizes engraftment, pharmacodynamic, and safety data.

By January 2025, six patients were enrolled and treated (4 pre-symptomatic and 2 early-symptomatic). One patient, who had undergone an allogeneic HSC transplant a year before enrolment, met eligibility criteria due to full-host chimerism and normal bone marrow (BM) findings.

Results: The median age at GT was 10.4 years (range 2.7–15.5 years). Mobilized peripheral blood, collected after 6–8 doses of G-CSF and plerixafor, was used as stem cell source, median yield was 34.3×10^6 CD34+ cells/kg (range: $30.3–37.7\times10^6$). All patients received myeloablative busulfan conditioning. The infused product had a median dose of 23.1×10^6 CD34+ cells/kg, with a vector copy number (VCN) of 2–5 per cell.

At a median follow-up of 27.8 months (range 12.6–34.3 months), all patients were alive. Five remained neurologically stable, while one early-symptomatic patient experienced initial progression followed by stabilization for 30 months. Adverse events were consistent with busulfan's known safety profile, with no treatment-related serious adverse events, malignancies, or replication-competent lentivirus observed.

All treated patients showed rapid engraftment of transduced cells. In the five patients with available data at 1-year post-GT, the median VCN was 0.33/cell (range 0.2–0-9) in peripheral blood mononuclear cells (PBMCs), with the rate of transduced BM progenitors ranging from 18.8% to 85.4%.

ARSA activity was restored to supranormal levels in PBMCs and to normal levels in cerebrospinal fluid at last follow-up, providing indirect evidence of functional ARSA enzyme in the central nervous system.

Conclusions: Early findings show short-term safety and pharmacodynamic efficacy of arsa-cel in LJ-MLD, and consistency with previous trials in early-onset MLD. Further follow-up will evaluate additional clinical endpoints, brain imaging, and long-term safety.

ABSTRACTS

Topic: Neurodevelopmental Disorders / Developmental Neuroscience

EPNS25_760 - To Explore the Association of Heavy Metals and Essential Micronutrients As Environmental Markers in Children with Autism Spectrum Disorder: A Cross Sectional Study.

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Objectives

Heavy metals have been implicated in the etiology of Autism Spectrum Disorder (ASD) through epigenetic mechanisms. Previous studies suggest a link between heavy metal exposure and epigenetic alterations in ASD. Additionally, structural DNA variations such as copy number variations (CNVs), insertions, and deletions contribute to disease susceptibility and progression. This study aimed to analyze heavy metal and essential micronutrient levels in blood, urine, hair, and nails of children with ASD and compare them with controls. Genomic and epigenomic changes were also investigated to establish a molecular connection between metal toxicity and genetic alterations in ASD.

Methods

This cross-sectional study included children aged 18 months to 18 years meeting DSM-5 criteria for ASD. Those with known micronutrient deficiencies, on chelating agents, exclusion diets, or chronic systemic diseases were excluded. Controls were children with IQ>70 on the Malins Intelligence Scale for Indian Children and without behavioral issues. Inductively Coupled Plasma Mass Spectrometry (ICP-MS) was used to measure 21 heavy metals and trace elements in blood, urine, hair, and nails. Genomic DNA was extracted from ASD samples and subjected to bisulfite conversion for DNA methylation analysis using the Illumina promoter array. Whole genome SNP analysis was performed using the Illumina Infinium Global Screening Bead ChIP Array (650K SNPs).

Results

A total of 500 ASD and 100 control subjects were enrolled (mean age: ASD 5.75±3.19 years, controls 7.31±4.23 years). Heavy metals were analyzed in blood (500 ASD, 60 controls) and urine (250 ASD, 30 controls). Significantly higher levels of Lead, Arsenic, Cadmium, Manganese, and Chromium were found in ASD subjects compared to controls ($P<0.001$). Methylation analysis (19 ASD subjects) identified 289 hypomethylated and 1132 hypermethylated promoter CpG sites. Hyper-methylation was prevalent in CETNP4, HMGA1, and RPAIN, while ALOXE3, OXCT1, and GLUD1 showed hypomethylation. SNP analysis revealed significant associations with the TAFA1 gene (rs9820086), which regulates inflammation, immune response, and neuronal function, suggesting a link between heavy metal exposure, inflammation, epigenetic modifications, and altered gene expression.

Conclusions

Levels of Lead, Arsenic, Cadmium, and Manganese were significantly elevated in ASD subjects. Epigenetic changes and specific genomic variants contribute to ASD pathophysiology.

ABSTRACTS

Topic: Neurometabolic Disorders

EPNS25_761 - Longitudinal analysis of anti-drug antibody response against Cerliponase alfa in CLN2 patients

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Objectives

Neuronal ceroid lipofuscinosis type 2 (CLN2) disease is a neurodegenerative lysosomal storage disorder caused by mutations in the TPP1 gene, encoding the lysosomal enzyme tripeptidyl peptidase 1 (TPP1). Affected children show first clinical symptoms between 1.5 and 4 years of age, including seizures, psychomotor decline, and loss of vision. Currently, intraventricular enzyme replacement therapy (ICV-ERT) with recombinant human TPP1 (rhTPP1, Cerliponase alfa) is the only approved treatment. It was shown to slow down the loss of motor and language function. Like in other ERT, immune reaction to the recombinant enzyme is a common adverse event and increases the risk of production of anti-drug antibodies (ADA) and subsequently loss of treatment efficacy. Aim of this study was to analyze drug-specific antibody response in biofluids of CLN2 patients receiving ICV-ERT as standard of care.

Methods

We developed a two-step assay consisting of a HEK293TGPI-TPP1-cell-based, flow-cytometry assay for highly sensitive screening purposes followed by serial-diluted ELISA for reliable titer-quantification. We prospectively observed a cohort of ten CLN2 patients before and during ICV-ERT with Cerliponase alfa for a follow-up time of twelve to up to 30 months of therapy duration. ADA response was analyzed in paired serum and CSF samples obtained before and every six months during treatment. These data were complemented by clinical disease progression parameters, like Hamburg LiNCL and Weill-Cornell score, as well as assessment of drug-related immune reactions.

Results

Six patients developed at least once an immune reaction to the ICV-ERT. Out of these, five developed an initial ADA response in serum and/or CSF that remained long-term in four patients. However, also three of the patients without clinical immune reaction developed ADA. Furthermore, all patients revealed a regression of motor and language function over time, independent of the presence of ADA.

Conclusions

Results from this study will help to improve understanding of the humoral immunological response to the recombinant enzyme, the presence of clinical immune reactions and the potential influence on treatment efficacy. This will be crucial for the prediction, treatment and prevention of immune reactions to ICV-ERT with Cerliponase alfa. In addition, it will help to improve individual patient risk assessments for future gene therapy approaches.

ABSTRACTS

Topic: Epilepsy: Medical and Surgical treatment

EPNS25_763 - Cannabidiol in pediatric patients with Lennox-Gastaut syndrome

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Objectives: Recently, a plant-derived, highly purified cannabidiol (CBD) formulation with a known and constant composition has been approved by the Food and Drug Administration and the European Medicines Agency (Epidiolex®) for the treatment of seizures associated with Lennox–Gastaut syndrome (LGS). This study presents a preliminary evaluation of the use of CBD in patients with LGS, a treatment-resistant epilepsy syndrome.

Methods Five patients diagnosed with LGS were included in this retrospective analysis. Demographic data, etiology, seizure characteristics, prior treatments, and EEG/MRI findings were recorded. All patients had previously used multiple anti-seizure medications without success. Some had undergone vagus nerve stimulation (VNS) or a ketogenic diet. CBD was administered orally at a starting dose of 5 mg/kg/day, and was maintained at 10 mg/kg/day.

Results: Among the five patients, two were female and three were male, with a mean age of 11.2 years (range: 9–14.5 years). All patients were diagnosed with Lennox-Gastaut Syndrome (LGS). The etiology was unknown in four patients, while one patient had a history of neonatal hypoglycemia. The earliest seizure onset was at four months of age, and all patients experienced multiple daily seizures. Seizure semiology included spasms, atonic, myoclonic, and generalized tonic seizures. Prior to cannabidiol (CBD) treatment, electroencephalograms (EEG) of all patients showed highly active generalized or multifocal epileptic abnormalities, and MRI findings were pathological. Multiple anti-seizure medications had been used without success. Three patients had undergone vagus nerve stimulation (VNS) and were followed up for at least one year, while one patient had been treated with a ketogenic diet. After six months of CBD treatment, patients were reassessed both clinically and with EEG. A reduction in seizure frequency was observed in all patients. In two patients, seizure frequency decreased to 1–2 episodes per month, while in three patients, it reduced to 1–2 episodes per week. EEG recordings of two patients showed no abnormalities, whereas a reduction in epileptiform activity severity was noted in the remaining three patients. No drug-related side effects were observed in any of the patients**.**

Conclusions This preliminary evaluation suggests that CBD may be an effective and well-tolerated treatment option for patients with LGS. Seizure frequency and EEG abnormalities showed improvement in all cases, and no adverse effects were reported. Further large-scale studies are needed to confirm these findings and establish long-term safety and efficacy.

ABSTRACTS

Topic: Neurometabolic Disorders

EPNS25_764 - Long-term and large scale analysis of NfL and GFAP as biomarkers in CLN2 patients treated with cerliponase alfa: Strengths and limitations

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Objectives

Neuronal ceroid lipofuscinosis type 2 (CLN2) disease is a pediatric neurodegenerative disorder caused by deficiency of the lysosomal enzyme tripeptidyl peptidase 1. Symptom onset is at age 1.5 to 4 years with language decline and seizures, followed by psychomotor regression and vision loss. The only approved therapy is intracerebroventricular enzyme replacement therapy (ICV-ERT) with cerliponase alfa, which slows down the decline in motor and language function. Neurofilament light chain (NfL) and glial fibrillary acid protein (GFAP) are biomarkers elevated in various neurodegenerative disorders. However, large scale and long-term data in CLN2 are lacking.

Methods

We analyzed NfL levels in 302 CSF samples and GFAP levels in 195 CSF samples of 54 CLN2 patients with late-infantile CLN2 phenotypes covering treatment periods up to 505 weeks. NfL- and GFAP-levels were correlated with treatment duration as well as the Hamburg CLN2 motor/language clinical rating scale (ML-score).

Results

In untreated patients before ICV-ERT, increased NfL levels showed a moderate correlation with lower Hamburg ML-scores start prior to ICV-ERT (Spearman correlation -0.518), which did not persist after treatment start. In contrast, GFAP showed no correlation with the disease stage at any point prior or during treatment. Throughout ICV-ERT with cerliponase alfa, NfL levels followed a biphasic course with highest levels prior to treatment and a rapid annual reduction of 52 % over the first two treatment years (95% CI [45%; 58%], $p < 0.001$). Subsequently, levels stabilized showing no annual change (0%, 95% CI [-7%; 7%], $p = 0.953$) at a mean NfL concentration of 647 pg/ml (SD 490.0; range 25 - 3417). GFAP showed a biphasic course as well: Over the first six years of ICV-ERT, statistical analysis of GFAP showed stable levels (average annual increase of 1% (95% CI [-6%; 9%], $p = 0.828$). Beyond six years of treatment, GFAP levels began to rise with an annual increase of 45% (95% CI [17%; 79%], $p = 0.001$).

Conclusions

These data show, that NfL may serve as a biomarker for monitoring initial treatment response in CLN2 disease but has limitations in tracking disease progression during long-term treatment. GFAP appears not to be a meaningful biomarker for monitoring initial treatment response. However, it might show relevance in later therapy stages. Overall, both biomarkers do not sufficiently embody clinical disease stages and therapy response over the entire treatment period and therefore cannot replace clinical scorings.

ABSTRACTS

Topic: Neuromuscular Disorders

EPNS25_765 - Relationship Between Trunk Control, Balance and Functional Skills in Ambulatory Children with Duchenne Muscular Dystrophy

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Objectives

Children with Duchenne Muscular Dystrophy (DMD) faced trunk control and balance problems. These problems are also reflected in functional skills. This study aimed to examine the relationship between trunk control, balance, and functional skills in ambulatory children with DMD.

Methods

Thirty-two boys with DMD between the ages of 5 and 12 (mean age: 8.59±2.14 years) were included. The Trunk Control Measurement Scale (TCSM), Pediatric Functional Reach Test (PFRT), Timed Up & Go Test (TUG), and Pediatric Evaluation of Disability Inventory (PEDI) were used for the assessments.

Results

There was a correlation between the children's PEDI-self-care score and TCSM-selective movement control (r=0.424; p=0.016), and PFRT (r=0.566; p=0.001). Also, the PEDI-mobility score and TCSM-static sitting balance (r=0.512; p=0.003), TCSM-selective movement control (r=0.518; p=0.002), TCSM-dynamic reaching (r=0.664; p<0.001), PFRT (r=0.350; p=0.049), and TUG (r=-0.600; p<0.001) were correlated. There was no correlation between the PEDI-social functions and trunk control and balance (p>0.05).

Conclusions

It is thought that maintaning trunk control and balance has an important role during functional skills in ambulatory children with DMD.

ABSTRACTS

Topic: Neurodevelopmental Disorders / Developmental Neuroscience

EPNS25_766 - Role of Gluten-Free-Casein-Free (GFCF) Diet in Children with Autism Spectrum Disorder :A Randomized Controlled Trial

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Objectives

The gluten-free casein-free (GFCF) diet is believed to influence neurochemical pathways through the gut-brain axis by reducing peptide impact. While some studies suggest behavioural improvements in children with Autism Spectrum Disorder (ASD), conclusive evidence remains insufficient. This study aimed to evaluate the effectiveness of the GFCF diet as an adjunct to standard treatment in improving core ASD symptoms.

Methods

This single-blinded, randomized controlled trial included children aged 3-12 years diagnosed with ASD based on DSM-5 criteria. Those on standard treatment for at least 12 weeks were eligible, while children receiving alternative therapy, with chronic systemic illness, or allergic to dietary components were excluded. The control group comprised children receiving standard treatment. The GFCF diet was administered for 24 weeks. Assessments, including the Childhood Autism Rating Scale (CARS-2), Applied Behaviour Checklist (ABC), Child Behaviour Checklist (CBCL), Children's Sleep Habits Questionnaire (CSHQ), and Development Quotient (DQ), were conducted at baseline and after 24 weeks. Resting-state functional MRI (fMRI) and structural imaging data were obtained from 15 children in each group at baseline and follow-up.

Results

A total of 104 children were enrolled (54 diet group, 50 control group). Five children from the diet group were lost to follow-up. Baseline scores for CARS-2, ABC, and CSHQ were similar between groups ($P \geq 0.05$). At 24 weeks, per-protocol analysis showed significant improvements in the diet group: CARS-2 ($P=0.009$), ABC ($P=0.029$), and CSHQ ($P=0.012$). Remission (CARS <30) was achieved in 14.2% of the diet group versus 4% of controls ($P=0.04$). Clinically meaningful change in CARS (≥4.5 points) was observed in 18.3% of the diet group compared to 4% of controls ($P=0.023$). Improvements in hyperactivity, attention problems, and sleep issues were greater in the diet group, with sleep issues significantly reduced ($P<0.01$). Intention-to-treat analysis confirmed improvements in CARS-2 ($P=0.03$) and CSHQ ($P=0.04$). No adverse events were reported. fMRI data is still under analysis.

Conclusions

The study suggests that eliminating gluten and casein from the diet may lead to significant behavioural and sleep improvements in children with ASD, demonstrating promising therapeutic potential.

ABSTRACTS

Topic: Movement Disorders/ Cerebral Palsy

EPNS25_767 - Unraveling Biological Mechanisms Underlying Pediatric Hyperkinetic Movement Disorders

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Objectives

To analyze the underlying biological mechanisms in children with genetic hyperkinetic movement disorders.

Methods

Retrospective analysis of 296 patients (median age of onset: 1.79yrs [0.5–4]; median age at last evaluation 11yrs [5-16], 54.8% males) with genetically confirmed hyperkinetic movement disorders, followed at two Spanish and Greek referral centres. Genetic diagnosis of single nucleotide and copy number variants was achieved by nuclear and mitochondrial sequencing methods. Metabolic pathways linked to causal genes were analysed using Reactome. Chi-square test was used to identify associations between clinical features and metabolic pathways.

Results

Patients were affected by dystonia (86,1%), chorea (8,1%), tonic upgaze (2%) and tremor/myoclonus (3,8%). Temporal pattern was chronic (62,2%), chronic with paroxysmal episodes (32,4%) or pure paroxysmal (3,7%). The clinical course was progressive in 40,9%. A neurodevelopmental disorder was present in 67.6% of cases. We identified 116 disease-causing genes, 10% of them (*SGCE*, *GNAO1*, *NKX2-1*, *ECHS1*, *PANK2*, *TH*, *KMT2B*, *RNASEH2B*, *ATP1A3*, *ADCY5*, *HPRT1*, and *PRRT2*) were observed in at least five patients each. The 116 genes were involved in the following biological pathways: mitochondrial/energy homeostasis (24,1%), nuclear gene expression and stress response (18,1%), lysosome-autophagosome (18,1%), synaptic transmission/channels (8.6%), structural elements (8.6%), dopamine homeostasis (6.9%), post-synaptic signaling (6.9%), calcium homeostasis (5.2%) and trace element deposition (2.6%). Analyzing phenotypic traits in relation to implicated biological pathways revealed multiple significant associations ($p<0.05$). Dopamine deficiency was associated with earlier onset (0.48yrs [0.24–0.92]), stable course, frequent paroxysmal episodes and developmental disorders. Synaptic and postsynaptic defects had also an earlier onset (0.33yrs [0.08–1.25], paroxysmal movement disorders and, in the case of postsynaptic defects, increased neurodevelopmental disorders. Structural defects presented later (2yrs [1.05–3]), with combined dystonia and normal neurodevelopment. Mitochondrial defects and trace element deposition were linked to complex dystonia, neurodevelopmental disorders and a progressive course.

Conclusions

The diverse genetic defects identified in our cohort were linked to the key metabolic pathways associated with dystonia, enabling correlations with the clinical phenotype.

ABSTRACTS

Topic: Neurodevelopmental Disorders / Developmental Neuroscience

EPNS25_769 - Global Prevalence of Complications and Comorbidities in Rett Syndrome: A Comprehensive Review of Literature

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Objectives

Rett syndrome (RTT) is a rare, genetic, neurodevelopmental disorder, primarily affecting females. While RTT is associated with complex complications and comorbidities impacting nearly all aspects of a person's life, quantitative estimates are lacking. A comprehensive literature review (CLR) was conducted to quantify the prevalence of RTT-associated complications and comorbidities.

Methods

The CLR was conducted by searching Medline, Embase, Cochrane Library, trial registries, and other evidence platforms between 01/01/2000-07/31/2024 for English language articles of complications and comorbidities among patients with RTT. Rates of behavioral (e.g., agitation), oral (e.g., dysphagia/chewing), musculoskeletal (e.g., scoliosis), respiratory (e.g., breathing disorders), sleep-related (e.g., apnea), and developmental (e.g., inability to walk) complications were examined. Additionally, rates of neurological (e.g., seizures), GI (e.g., gastroesophageal reflux), and orthopedic (e.g., fractures) comorbidities among others were analyzed.

Results

Of the 539 screened articles, 147 studies were eligible for full text extraction. Among behavioral complications, agitation was reported among 54%-57% of patients, with other complications being self-injury, anxiety, mood changes, and depression. Oral complications included dysphagia/chewing problems (24%-77%) and bruxism (21%-90%). Prevalence of musculoskeletal complications ranged from 9%-100% and 10%-35% for scoliosis and kyphosis, respectively. Respiratory complications included LRTI (18%-77%) and pneumonia (17%-38%). Developmental and sleep-related complications were also frequently observed. Epilepsy was the most common neurological comorbidity, occurring in 15%-91% of patients, with daily seizure frequency ranging from 3%-33%. Among GI comorbidities, 16%-83% and 16%-100% reported constipation and gastroesophageal reflux, respectively. Fractures (orthopedic comorbidity) affected 6%-65% of patients; higher rates occurred in more patients with high-severity (17%) than mild-severity mutations (13%). Nutritional, endocrinological, and cardiovascular comorbidities, among others, were also reported.

Conclusions

In this global CLR, behavioral, oral, and musculoskeletal complications, as well as neurological and GI comorbidities, were most observed among patients with RTT. These results demonstrate the significant burden of complications and comorbidities associated with RTT.

ABSTRACTS

Topic: Neurometabolic Disorders

EPNS25_770 - Real-world presymptomatic treatment in CLN2 disease: Learnings from families with multiple affected children

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Objectives

Neuronal ceroid lipofuscinosis type 2 (CLN2) disease is a neurodegenerative lysosomal storage disorder. Intracerebroventricular enzyme replacement therapy (ICV-ERT) with recombinant human TPP1 (Cerliponase alfa) is the only approved treatment. Data from clinical trials show significant increase of therapy efficacy in patients with treatment start < 2 years. Untreated children show first symptoms between 1.5 and 4 years of age, including seizures, followed by a rapid psychomotor decline and loss of vision.

Methods

We followed 14 families with two or more affected siblings with CLN2 disease, in which diagnosis of the oldest child led to an early diagnosis and therapy of the younger ones. In all siblings, we assessed therapy efficacy based on longitudinally collected disease progression scores, e.g. Hamburg Motor-Language (ML) score. In all treated ones we also assessed gross-motor, fine-motor, language and personal-social capabilities, reflected by number of passes in the respective Denver II Scale subdomains. For better comparability we normalized all data by the individual mean age of symptom onset in each family.

Results

The median time to an unrevealed Hamburg ML score of 0 (no function) increased from 35 months after symptom onset in untreated patients up to 102 months in postsymptomatically treated siblings. Presymptomatic siblings did not show a Hamburg ML score of 0 at all, whereas the longest observation time has been 118 months after symptom onset. Presymptomatic patients also showed much better function in Denver II Scale than postsymptomatic ones and even gained new capabilities over the course of development.

Conclusions

This study shows the advantages of presymptomatic treatment in CLN2 disease reflected by a longer period of preserved motor and language function as well as improved early childhood development. Therefore, it is crucial to diagnose the disorder as early as possible. Newborn screening pilot studies need to be brought more into the focus of NCL research.

ABSTRACTS

Topic: Neuromuscular Disorders

EPNS25_771 - The natural history of Duchenne Muscular Dystrophy patients in Singapore: A retrospective review in a single tertiary centre

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Objectives

Significant progress has been made in the management of Duchenne Muscular Dystrophy (DMD) in the past two decades. We aim to evaluate the differences in clinical care and outcomes of our DMD patients after the implementation of a multi-disciplinary clinic and coordinated care based on the 2010 and 2018 DMD Care Considerations.

Methods

A retrospective cohort study was conducted on 35 patients diagnosed with Duchenne Muscular Dystrophy, with comparison of those born before 2010 and those born between 2010-2020. Patients with Becker Muscular Dystrophy (BMD) were excluded. Data was collected and analysed using Fisher’s Exact test and two-sample t-test for categorical and continuous data respectively.

Results

There were 16 patients born before 2010 (mean current age 22 years) and 19 born between 2010-2020 (mean current age 9.1 years). 85.7% had a confirmed genetic diagnosis, although a higher proportion (94.7% vs 75%) occurred in the 2010-2020 cohort. The mean age of diagnosis was significantly lower in the later cohort (4.8 years vs 8.6 years). The proportion of patients who received steroids increased from 31.3% pre-2010 to 68.4% in 2010-2020, though the mean age of initiation in both cohorts was similar (6.3 years vs 6.5 years). Mean age at loss of ambulation was not significantly different (16 patients, 10.4 years vs 6 patients, 9.5 years). Most patients in the earlier cohort were on respiratory support (93.8%), underwent scoliosis surgery (50%; 3 patients refused) and were treated for cardiomyopathy (62.5%). Three patients who died in the earlier cohort did not survive past 20 years (mean age of death 19.3 years)

Conclusions

Advancements in DMD care were observed between 2010 and 2020, including earlier diagnosis, higher rates of genetic confirmation and increased steroid use. Despite these improvements, age at loss of ambulation was not increased. A larger national cohort study and longer follow up period will more clearly elucidate the impact of these changes. This will provide an important foundation for measuring clinical outcomes in the face of new emerging therapeutics.

ABSTRACTS

Topic: Epilepsy: Medical and Surgical treatment

EPNS25_772 - Vagus Nerve Stimulation Therapy for the Treatment of Seizures in Lennox-Gastaut syndrome

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Objectives: Lennox-Gastaut syndrome (LGS) is among the most severe epileptic and developmental encephalopathies. This retrospective study aimed to evaluate the effectiveness of adjunctive vagus nerve stimulation (VNS Therapy) in patients with LGS.

Methods: 55 pediatric patients with refractory LGS were included who were followed up at Gazi University Child Neurology Department between 2010 and 2024 in our study. VNS and medical therapy efficacy was evaluated based on seizure reduction, effective rate (percentage of cases with seizure reduction ≥ 50%), modified Early Childhood Epilepsy Severity Scale (E-Chess) score, and Grand Total EEG (GTE) score. The follow-up time points were 12 months after VNS and medical therapy. Pre- and postoperative data were compared and analyzed.

Results: A total of 55 patients were included in the study, of whom 63% were male and 37% were female, with a mean age of 14.7 years (range: 7–18 years). Vagus nerve stimulation (VNS) was implanted in 52% (n=29) of these patients. E-chess scores before medical treatment group and VNS surgery group were 13.81(12-15) and 14.11(12-15), respectively, while after 12 months of medical treatment and VNS surgery groups, it was 11.31(9-15) and 10.96,(8-14) ($p<0.01$). GTE score before medical treatment grup and VNS surgery grup was 13.96 (8-24) and 15.15(5-22), respectively, whereas after 12 months of medical treatment and VNS surgery, it were 10.23 (4-22) and 9.89 (3-17), ($p<0.01$). A statistically significant relationship was found between the efficacy rate and -chess scores after VNS surgery ($p<0.01$). No intraoperative complications or severe post-operative adverse effects were reported.

Conclusions: Our study shows that VNS can reduce the frequency and severity of seizure in patients with refractory LGS. VNS has a good application prospect in patients with refractory LGS. A clinical and surgical overview has been included to facilitate the use of VNS in LGS.

ABSTRACTS

Topic: Neurodevelopmental Disorders / Developmental Neuroscience

EPNS25_773 - First results of the intellectual development assessmentIn children with severe burn trauma at an early age

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Objectives

The intellectual development of young children with severe burn trauma hasn't been investigated thoroughly, and it is still unclear how combination of toxic and iatrogenic agents in those patients may affect cognitive skills in the developing brain.

The **aim** was to investigate long-term consequences of the level of intellectual development at primary school age children who suffered a burn injury of II-III degree under 3 years old.

Methods

Small cohort, case/control study. Study group: 14 children who suffered II degrees or more burn (boiling water, scald burn), burning area 20% of the total body surface area and more, age under 3 y.o. Control group: 21 children with no neurological or psychiatric diagnoses.

The Wechsler Intelligence Scale for Children-IV (WISC-IV) has been performed at the stage of long-term consequences at 8.8±1.0 y.o. in the study group and at 8.8±1.2 y.o in the control group.

Statistical analysis. RStudio software, descriptive statistics, Wilcoxon signed-rank test.

Results

The obtained intelligence indicators for burnt children: 107.5±14.0 for the general IQ, 107.4±15.4 for verbal IQ, 106.6±12.9 for non-verbal IQ.

The indicators of children in the control group: 120.3±11.0 for the general IQ, 121.3±10.5 for verbal IQ, 115.4±13.6 for non-verbal IQ.

The intergroup differences in the general IQ: W=191, p=0.0101, in verbal intelligence: W=198.5, p=0.0042, in non-verbal intelligence: W=153, p=0.2639.

Significant differences were found between the study and control groups in the subtests "Comprehension" (W=180.5, p=0.029), "Arithmetic" (193.5, p=0.0072), "Vocabulary" (W=190, p=0.0107), "Digit Span" (W=210, p=0.0009), "Coding" (W=202.5, p=0.0024).

Conclusions

A small size pilot study revealed the features of cognitive impairment following paediatric burn injuries. Results obtained using the Wechsler Intelligence Scale for Children-IV revealed significant differences in general IQ, verbal and non-verbal intelligence in the study group compared to the control group. We found that the most affected areas in the cognitive sphere in burnt children were vocabulary size and the ability to use it, as well as working memory, learning ability and processing speed.

ABSTRACTS

Topic: Epilepsy: Diagnosis and Investigations

EPNS25_774 - Clinical course and prognosis of childhood absence epilepsy

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Objectives: Our aim was to study the factors that can influence the prognosis of childhood and juvenile absence epilepsies (CAE/JAE).

Methods: Retrospective study was performed. Gender, age, perinatal and family history, age at seizure onset, results of EEGs and brain MRIs, the effectiveness of the different antiseizure medications (ASM) and the outcome of epilepsy were collected. EEGs were analysed with special interest, the duration and frequency of the 3 c/s spike/wave patterns during the whole EEG examination were measured accurately. Chi-square test was used to investigate the influences of different categorical variables on long-term outcome.

Results: 76 patients were included, 60 had CAE, 16 had JAE, 45 (59%) were females. The mean follow-up time was 7.1 years. 19 (25%) children had positive family history of epilepsy. 29 children had at least one brain MRI; 10/29 (34%) had abnormal findings: hippocampal abnormalities (6), other (4). Only 3/10 children with brain MR abnormalities were cured of epilepsy. The first choice of ASM was valproic acid (VPA) in 53/76 cases; ethosuximide (ETX) in 14/76, lamotrigine (LTG) in 9/76. 38/53 (72%) children with VPA therapy became seizure free. ETX was effective in 4/14, lamotrigine in 3/9 patients. 37/76 (48.7%) children required second-line ASM therapy. A new monotherapy was given to 26 children and bitherapy (a new ASM was added to the first choice ASM) was chosen in 11 cases. The second line monotherapy had higher effectiveness (65%), than the combination bitherapy (36%). 19/76 (25%) children needed third-line ASM. Those children whose background activity on the first EEG was abnormal were more likely to require a third-line ASM. After 3 years seizure-free status ASM was discontinued in 59 patients, 16 had seizure relapse (27%). Patients with a longer duration of total absence seizure at the first EEG examination were more likely to have relapse after ASM discontinuation. 52/76 (68%) of our patients remained seizure free after ASM withdrawal and 24 patients are seizure free with ASM.

Conclusions: Comparing to the published studies we found lower prevalence of positive family history and higher proportion of anomalies on brain MRI. CAE is considered to have good prognosis, nevertheless we found a 27% relapse rate after ASM withdrawal. Based on our data, valproic acid as a first-line ASM was effective in ¾ of our patients. When the first choice of ASM was not useful, a second-line monotherapy was more effective than an add-on combination therapy.

ABSTRACTS

Topic: Neurodevelopmental Disorders / Developmental Neuroscience

EPNS25_775 - Novel CYFIP2 frameshift variant linked to dyskinetic crises: functional studies show impaired cell motility

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Objectives: Variants in *CYFIP2*, a gene crucial for actin cytoskeleton regulation, are linked to neurodevelopmental disorders, including developmental and epileptic encephalopathies (DEE-65) and movement disorders. This study presents a case of a female patient with a *de novo* pathogenic *CYFIP2* variant, examining her clinical phenotype and the results of fibroblast-based functional studies.

Methods: Clinical evaluations included neurological, developmental, electrophysiological, and neuroimaging assessments. Functional studies utilized patient-derived fibroblasts to examine actin cytoskeleton organization and cell motility. Confocal and super-resolution imaging were used to analyze F-actin fluorescence, porosity, and fiber orientation. Live-cell imaging tracked migration parameters.

Results: The patient exhibited severe developmental delay, generalized hypotonia, and early-onset refractory epilepsy with focal and generalized seizures. Movement disorder features included dyskinetic and dystonic episodes, particularly affecting the orofacial and upper limb regions. Neuroimaging showed frontal-predominant cortical atrophy, white matter volume loss, and hypoplasia of the corpus callosum. Genetic testing identified a *de novo CYFIP2* variant (c.281_282insA/p.Gln95*). Fibroblast analysis revealed significant impairments in actin cytoskeleton organization and cell motility. Disrupted stress fibers, impaired lamellipodia and filopodia formation, and altered cell migration and adhesion were observed. These cellular abnormalities likely reflect the underlying mechanisms of *CYFIP2* dysfunction, which affects neuronal migration, axonal and dendritic development, and synapse formation, as seen in mouse models.

Pathogenic *CYFIP2* variants disrupt actin regulation, leading to altered neuronal architecture and synaptic connectivity, processes vital for neuronal migration, dendritic and axonal growth, and synapse formation. These disruptions affect cell mobility, adhesion, and intracellular trafficking, compromising cellular organization and communication.

Conclusions: This case emphasizes the critical role of *CYFIP2* in actin cytoskeleton regulation and its impact on neuronal function. Functional fibroblast studies provided insights into the cellular mechanisms underlying *CYFIP2*-related disorders. This study expands the phenotypic and genetic spectrum of *CYFIP2*-related disorders, contributing valuable information to the understanding of dyskinetic crises and actin dysregulation in these patients.

ABSTRACTS

Topic: Neurogenetics

EPNS25_776 - A Novel MECP2 Variant in a Male Patient: Expanding the Spectrum of Atypical Rett Syndrome

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Objectives

We aimed to present a novel MECP2 variant responsible for the very rare male Rett syndrome.

Methods

A male infant presenting with developmental delay and intractable seizures underwent clinical and genetic evaluation. Imaging tests revealed focal cortical dysplasia, and epileptic discharges were observed in the EEG. A novel MECP2 variant was identified with whole-exome sequencing (WES) analysis.

Results

A 1-year-old boy, born at 38 weeks of gestation as the second child of non-consanguineous parents, had an unremarkable perinatal and family history. At 9 months of age, developed seizures characterized by head drop episodes lasting 3–4 seconds, occurring approximately 10 times per hour. An electroencephalogram (EEG) performed at 10 months of age revealed epileptiform discharges, and initiated levetiracetam. Physical examination revealed no dysmorphic features, and neurological examination was unremarkable. Developmental assessment demonstrated delays in personal-social skills, as well as gross and fine motor functions. Brain MRI identified focal cortical dysplasia. Due to persistent seizures and new onset jerky seizures during follow-up, sodium valproate and topiramate were sequentially added to the treatment. Given the presence of global developmental delay, seizures, and a central nervous system developmental anomaly, genetic testing was performed. Chromosomal analysis and microarray testing yielded normal results, whereas whole-exome sequencing (WES) identified a c.506A>G (p.Glu169Gly) variant in exon 4 of the MECP2 (NM_004992.3) gene. The patient, shows normal motor and cognitive development, seizure-free for two years with sodium valproate and topiramate. Follow-up EEG recordings were normal.

Conclusions

Rett syndrome (RTT) is a neurodevelopmental condition that predominantly affects females. Mutations in the MECP2 gene are responsible for the majority of Rett syndrome cases, with approximately 95% of classic sporadic cases and 75% of atypical cases attributed to these mutations. Rett syndrome has three atypical forms: the preserved speech variant, the early seizure variant, and the congenital variant. We propose that the MECP2 variant identified in our patient is associated with an atypical form of Rett syndrome characterized by early-onset seizures. Given that Rett syndrome predominantly affects females, its occurrence in a male patient represents a rare and unusual case.

ABSTRACTS

Topic: Infectious and Inflammatory Diseases/ Neuroimmunology

EPNS25_777 - Neurophysiologic studies as a diagnostic and prognostic tool in acute flaccid myelitis

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Objectives

Acute flaccid myelitis (AFM) is a poliomyelitis-like syndrome that mostly affects children. Children commonly have severe and persisting deficits, even years after onset of disease. Diagnosis of AFM and estimation of its prognosis may be difficult. Limited data is available on the role of electromyography (EMG) and nerve conduction studies (NCS) in the diagnosis and estimation of prognosis in AFM. We aim to describe the neurophysiologic studies in a large cohort of patients with AFM and relate these to the timing of the investigations.

Methods

Patients with AFM were identified through a retrospective chart review at 11 sites from 4 different countries. Clinical features and results from additional studies, including microbiology studies, cerebrospinal fluid studies and magnetic resonance imaging (MRI) were collected. Complete data from all nerve conduction studies (NCS) and electromyography (EMG) studies were collected. Neurologic exam data was documented at presentation, at last follow-up, and at the time of each EMG/NCS wherever possible. Z-scores were calculated for NCS/EMG-results based on normal values from literature. Correlation between NCS/EMG and strength/ functional outcome was analysed with Spearman's rank test.

Results

In this cohort of 85 patients with probable or definite AFM, a typical pattern of decreased CMAP-amplitude with normal conduction velocity and normal sensory amplitudes in NCS was found. Furthermore, we found an EMG pattern of early and persisting spontaneous muscle fiber activity with absent units or decreased recruitment in affected muscles. CMAP at onset correlated well with muscle strength (r_s=0.558, p<0.001), as did the presence of acute denervation potentials (r_s=0.38, p<0.001) and decreased recruitment (r_s=0.61, p<0.001). CMAP amplitude, spontaneous muscle fiber activity and the level of motor unit recruitment at the first EMG were shown to be good predictors of functional outcome and strength at final follow-up.

Conclusions

The detailed description of EMG/NCS findings facilitate their use in the diagnosis of AFM, especially in settings where MRI is not possible, or late after onset when MRI abnormalities may have disappeared. Furthermore, early EMG/NCS may be used to facilitate estimation of prognosis.

ABSTRACTS

Topic: Neurological Emergencies

EPNS25_778 - Development of a clinical risk assessment tool for pediatric non-convulsive status epilepticus

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Objectives

Non-convulsive Status Epilepticus (NCSE) is a great mimicker in pediatric neurology, as its signs and symptoms may be very subtle, resembling diverse neurological conditions. The aim of this study was to (1) describe the history and clinical features of patients undergoing electroencephalographic (EEG) recordings to confirm or rule out NCSE; (2) identify risk factors and clinical features associated with the diagnosis of NCSE; (3) develop a clinical risk assessment tool.

Methods

single-center observational retrospective cohort study analyzing consecutive video-EEG recordings between 01/01/2019 and 01/10/2024. Data about clinical features, history, EEG and imaging findings were gathered. Descriptive statistics and multivariable logistic regressions were performed to identify risk factors and clinical features associated with the diagnosis of NCSE. The statistical significance level was set at $p<0.05$.

Results

353 EEG recordings from 269 patients (median age: 5.6 years) were included; 50.4% (n=178/353) were performed due to suggestive clinical features (mainly altered consciousness – 30.6%; subtle motor signs – 18.7%; abnormal verbal response – 17%); 49.6% of EEGs (n=175/353) were recorded to exclude NCSE in light of possible risk factors. A diagnosis of NCSE was established in 13.8% of EEGs (n=49/353). Significantly higher risk of NCSE was confirmed in patients presenting with behavioral changes (OR 2.97, 95% IC 2.1–3.8), subtle motor signs (OR 2.10, 95% IC 1.4–2.8), abnormal verbal response (OR 2.37, 95% IC 1.5–3.3) and acute clinical seizures (OR 2.17, 95% IC 1.3–3). The variables significantly associated with NCSE in a multivariable regression model (accuracy: 91%, area under the curve (AUC): 0.893, sensitivity: 71.8%, specificity: 97%) were used to develop an interactive clinical risk assessment tool (CLASP-NCSE).

Conclusions

The suspicion of NCSE is more likely to be confirmed in patients showing behavioral changes, altered speech, subtle motor signs and recent history of acute seizures. A better understanding of the signs, symptoms and risk factors closely linked to the diagnosis can help raise awareness about NCSE in everyday clinical practice. An interactive scoring tool encompassing these variables was developed to aid clinicians in prioritizing EEG recordings in case of limited capacity in the real-world setting. Further prospective studies are needed to validate the tool.

ABSTRACTS

Topic: Miscellaneous

EPNS25_780 - Building Bridges: A Dedicated ERN EpiCARE Working Group for Nurses and vEEG Technicians

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Objectives

Rare and low-prevalence epilepsies require a multidisciplinary approach to ensure optimal patient care. Nurses and video-EEG (vEEG) technicians play pivotal roles in these efforts.
Therefore, to enhance collaboration and education, ERN EpiCARE established a dedicated working group for these professionals, aiming to bridge clinical expertise, patient advocacy, and operational efficiency.

Methods

A survey was distributed to ERN-EpiCARE clinical centres, targeting nurses and vEEG technicians. It assessed their roles, duties, and available educational opportunities across European countries. Based on these insights, a one-day workshop was conducted to exchange practices and deliver targeted educational content.

Results

The survey received 114 responses from 39 different ERN-EpiCARE Health Care Providers, with 53% identifying as vEEG technicians and 47% as nurses across four nursing roles. Most respondents (66%) worked in epilepsy monitoring units, and over 40% had more than 10 years of experience. Awareness of educational opportunities was limited, with 60% either unaware of or unable to confirm the existence of relevant programs in their respective country. While almost all respondents performed EEGs, only 55% drafted reports for review. These findings informed the workshop agenda, which focused on exchanging local practices for seizure testing, pre-interpretation of EEGs, and advanced epilepsy care. Discussions included guiding families on rescue medications and adapting antiepileptic drug prescriptions based on side effects.

Conclusions

The survey and subsequent workshop underscored the importance and diverse expertise of nurses and vEEG technicians in managing epilepsies across ERN-EpiCARE Health Care Providers, revealing educational gaps and a need for improved knowledge-sharing.

Therefore, establishing a dedicated working group within ERN EpiCARE facilitates this exchange and collaboration, improves access to tailored educational programs, and enhances clinical and operational practices across European centres.

ABSTRACTS

Topic: Neuromuscular Disorders

EPNS25_781 - A comprehensive education and training programme for healthcare professionals in care and research for Duchenne muscular dystrophy developed from DMD Care UK and the DMD Hub.

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Objectives: The DMD Hub and DMD Care UK have pioneered the facilitation of expert care and clinical research across the UK for patients with Duchenne muscular dystrophy (DMD) and their families. However, recent work within these two collaborative projects has shown that we now need to address remaining discrepancies in care provision and access to clinical trials across the UK.

Methods: Key barriers to patients receiving the best quality care and access to research, are gaps in awareness and lacking appropriate levels of understanding about latest standard of care guidelines and clinical research in DMD. Knowledge of DMD care requirements is often limited to neuromuscular specialists, whilst multi-disciplinary specialists (respiratory, cardiac and emergency) and others responsible for crucial care delivery may be less informed.

Because a lack of access to expert care and clinical research carries significant consequences, DMD Care and the DMD Hub have developed a comprehensive, single, reliable source of up-to-date, tailored and accredited training for all aspects of DMD care and clinical research.

Results: We present here the first phase including core learning modules, launched in 2025 and free for all healthcare providers (HCPs) upon simple registration. Content is delivered online via a learning management system and in person through face-to-face workshops, is accredited and based on the needs identified by the Care and Hub networks.
We also outline plans for next steps of this education and training targeting different learning needs – including primary healthcare practitioners, community-based providers and tertiary specialists.

In addition to modules on physical aspects of multi-disciplinary care, we will develop an important and often overlooked component that covers psychosocial care needs including support at diagnosis, the impact of DMD on the central nervous system, screening, interventions and referral pathways. Also provided is, training and support for clinical trial teams for psychosocial considerations around trial participation.

Conclusions: This programme will address the need to provide harmonized and targeted training and education for healthcare professionals delivering care and research in DMD.
Although UK-based, this programme is available for healthcare practitioners in other countries, although content is currently delivered in English.

ABSTRACTS

Topic: Epilepsy: Medical and Surgical treatment

EPNS25_783 - The Effect of Ketogenic Diet on Zinc, Selenium, and Copper Levels in Children with Drug-Resistant Epilepsy"

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Objectives

The ketogenic diet (KD) is a well-established and effective nutritional therapy primarily used for the management of refractory epilepsy. This diet, characterized by its restriction of carbohydrate intake and high fat content, plays a significant role in reducing seizure frequency. However, it has been reported that long-term KD implementation may have adverse effects on certain micronutrients. Zinc, selenium, and copper are essential trace elements that play critical roles in various biochemical processes within the body. This study aimed to evaluate the changes in zinc, selenium, and copper levels in patients with refractory epilepsy undergoing KD.

Methods

This retrospective cohort study included 72 patients with refractory epilepsy undergoing KD treatment. Serum trace element levels were measured before and after one year of KD therapy. Baseline selenium and copper levels were assessed in 29 patients, while zinc levels were measured in 54 patients. After one year, these elements were reassessed in 48 (selenium/copper) and 67 (zinc) patients. Blood samples were analyzed using standard laboratory protocols.

Results

In this cohort, 48% of the patients were female, with a median age of 63.6 months at ketogenic diet (KD) initiation. The study revealed that after KD therapy, serum copper and zinc levels of the patients decreased slightly by %4 and %7,respectively, while selenium levels increased by %13. All patients were under the care of a registered dietitian at regular intervals and received dietary supplementation of zinc, selenium, and copper in accordance with World Health Organization recommendations. 10% of the patients had below-normal selenium levels at baseline.

Conclusions

Long-term ketogenic diet (KD) use is associated with decreased zinc and copper levels, impacting crucial antioxidant and immune functions. Therefore, the neurological and systemic consequences of these deficiencies in KD patients warrant consideration. These findings highlight the need for monitoring and supplementation during long-term KD therapy. The decrease in serum zinc and copper levels after KD therapy in our study is consistent with similar studies in the literature and suggests that KD may affect the absorption or metabolism of these minerals. This increase in selenium levels can be attributed to selenium supplementation administered to some patients to mitigate deficiencies observed in measurements taken at baseline and prior to the 1-year follow-up assessment. This indicates that patients should be given regular mineral supplementation during KD therapy.

ABSTRACTS

Topic: Neurodevelopmental Disorders / Developmental Neuroscience

EPNS25_784 - Transient Hypertonia in Non-Cerebral Palsy Infants at 4 Months as an Early Indicator of Autism Spectrum Disorder

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Objectives:
Developmental coordination disorder (DCD) is frequently associated with autism spectrum disorder (ASD) and is known to cause motor delays. While early ASD signs such as impaired eye contact are well-documented, motor phenotypes in early infancy often go unnoticed unless accompanied by neurological abnormalities. This can delay early intervention, and the connection between early motor signs and later DCD remains unclear.This study investigated whether transient hypertonia in Non-Cerebral Palsy Infants at 4 months could serve as an early sign of ASD. A retrospective analysis also explored the prevalence of hypertonia among infants later diagnosed with ASD.

Methods:
The prospective study included 15 full-term infants without perinatal abnormalities who attended 4-month check-ups between 2020 and 2023 at Deguchi Pediatric Clinic. Infants with hypertonia in the lower limbs and trunk, excluding cerebral palsy, formed the hypertonia group (n=7), while infants with normal tone were the control group (CTL, n=8). Development was assessed using Vineland Adaptive Behavior Scales (Vineland-II) and eye-tracking with Gazefinder (JVC Kenwood). ASD diagnoses were confirmed at age 2 using DSM-5, PARS-TR, and Vineland-II. Retrospective review identified cases of hypertonia among 408 infants. Ethical approval was obtained from Saniku Gakuin University.

Results:
In the prospective study, all 7 infants in the hypertonia group and 3 of 8 in the CTL group were diagnosed with ASD by age 2. Hypertonia resolved by 10 months in most hypertonia group cases, but social and motor delays persisted as shown by Vineland-II scores. Retrospective analysis found that 77 of 408 infants at 4 months had hypertonia, and 36 of these were later diagnosed with ASD.

Conclusions:
Findings suggest that transient hypertonia at 4 months may indicate an elevated risk of ASD, even if muscle tone normalizes later. Early recognition and intervention targeting motor development are critical. Further research will explore the potential of transient hypertonia as an early marker of DCD co-occurring with ASD.

ABSTRACTS

Topic: Epilepsy: Diagnosis and Investigations

EPNS25_785 - Unveiling epilepsy: the role of short video-EEG telemetry and epilepsy prediction tools in the diagnosis of paroxysmal episodes

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Objectives

To assess the diagnostic yield and accuracy of short video-EEG telemetry in pediatric patients presenting with suspected seizures/epilepsy after inconclusive findings from routine EEGs in wakefulness or sleep. To evaluate the performance of an epilepsy probability prediction tool.

Methods

Single-center retrospective observational study analysing all consecutive 2-day video-EEG telemetries performed between 2018 and 2023 to investigate suspected seizures/epilepsy. The risk of epilepsy was retrospectively, independently calculated by three blinded investigators using the Epilepsy Probability Risk Calculator. Descriptive statistics, associations, multivariate regressions and agreement analyses were performed. Statistical significance was set at $p<0.05$.

Results

133 telemetries with a median duration of 44 hours were included (133 patients, males: 52.6%, females: 47.4%, median age: 10 years). All patients had either previous routine EEG in wakefulness (57.35%) and/or sleep (77.96%). The telemetry confirmed or excluded the suspect in 84% of cases, a diagnosis of epilepsy was established in 46% of patients. An excellent agreement between the diagnosis at discharge from telemetry and at the last follow-up was noted (Cohen's k=0.891). During follow-up, 7 undiagnosed cases were eventually identified. Recording the events led to a higher diagnostic yield (56% vs 44%, OR 4.1, 95% IC 1.4-12, p=0.006), and events occurring with higher frequency (more than 7/week) were more frequently captured ($p<0.001$). Retrospective application of the Epilepsy Probability Risk Calculator score showed a moderate discriminative ability (AUC=0.717), a significant association with the diagnosis at the last follow-up ($\chi^2 = 16.674$, $p<0.001$), with moderate sensitivity (76%) and low-moderate specificity (55%) in predicting the diagnosis. The best performance was achieved in case of tail scores, such as risk of 0–20% (OR=0.177, 95% IC 0.066-0.490, $p<0.001$), and 80–100% (OR=4.148, 95% IC 1.750-9.834, $p<0.001$). Intermediate scores (20–80%) lacked significant predictive power for epilepsy (p=0.750): 86.67% of them were solved by the telemetry.

Conclusions

Short video-EEG telemetry is effective in unveiling epilepsy in case of pediatric paroxysmal episodes with no unequivocal ictal features. The use of clinical scoring systems may be effective to optimize and prioritize the access to the recording in scenarios with limited availability.

ABSTRACTS

Topic: Fetal and Neonatal Neurology

EPNS25_786 - Clinical presention of three new cases of KCNQ2 mutation – the role of genetics

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Objectives

In a substantial proportion, seizures in the first days of life, reflect neonatal-onset epilepsy, related to underlying metabolic or genetic disorders. Nonketotic hyperglycinemia (NKH) is an autosomal recessive inborn error of glycine metabolism. Surviving infants often have severe developmental delay and refractory seizures. KCNQ2 related disorders cause autosomal dominant neonatal epilepsies with wide phenotypic
heterogeneity, ranging from self-limited neonatal seizures with normal cognition, to early onset epileptic encephalopathy.

In this case series, we present three additional cases of KCNQ2 disease with different mutations and clinical course, and underly the importance of early genetic testing in neonatal seizures.

Methods

We describe data from three neonates with early onset seizures (100% males). Clinical characteristics, imaging, metabolic and genetic features were analyzed.

Results

All neonates were term. Seizures started on 2nd (patient 1 and patient 2) and 6th (patient 3) days of life. CNS infection, structural brain abnormality and hypoxic-ischemic encephalopathy were ruled out. On metabolic screening, increased CSF glycine level (154 umol/l, 15 umol/l and 21 umol/l in patient 1, patient 2 and patient 3, respectively) along with an elevated CSF to plasma glycine ratio (0.37, 0.078 and 0.05 in patient 1, patient 2 and patient 3, respectively), which was suggestive of NKH. However, genetic testing (Blueprint Genetics, Whole Exom Plus (patient 1) and Comprehensive Epilepsy Panel (patient 2 and patient 3)) revealed different heterozygous variants in KCNQ2 gene in all patients.

Conclusions

Advances in genetic medicine are increasingly expanding our understanding of neonatal-onset epilepsies and will continue to open doors for personalized medicine to optimize outcomes.

ABSTRACTS

Topic: Neurometabolic Disorders

EPNS25_788 - First real-life Experience with Arsa-cel in Metachromatic Leukodystrophy: Insights from Nine Cases

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Objectives

This study presents real-life data on Atidarsagene autotemcel (Arsa-cel) treatment outcomes in pediatric metachromatic leukodystrophy (MLD) patients in a routine clinical setting. Conducted at the first certified treatment center after EMA approval in 2020, this analysis provides insights into its application, efficacy, and safety outside clinical trials.

Methods

Between 2022 and 2024, nine MLD patients received Arsa-cel at the University Children's Hospital of Tübingen. Patients were identified via newborn screening (n=3), early disease signs (n=1), or family history (n=5). They were stratified by disease onset: late-infantile (n=2), early-juvenile (n=6), and late-juvenile (n=1). Two early-juvenile patients were early symptomatic; all others were presymptomatic at treatment. One late-juvenile patient received off-label treatment due to the unavailability of a matched donor for hematopoietic stem cell transplantation (HSCT). Treatment outcomes were assessed clinically and radiologically, with follow-ups ranging from 3 to 18 months.

Results

Treatment was well tolerated, with no severe adverse events post-discharge, and led to expected suprathreshold Arylsulfatase A (ARSA) levels in blood. All seven presymptomatically treated patients showed no clinical or radiological MLD signs at their last follow-up (1–19 months post-treatment). Of the two early symptomatic patients, one remained stable at short-term follow-up (3 months), while the other showed cognitive decline but stable motor function two years post-treatment. The latter had a high pre-treatment MRI score (15) compared to presymptomatic patients (0–1). Diagnosis age ranged from prenatal to 13.7 years, and treatment age from 6 months to 14.5 years. Newborn screening played a crucial role in early identification, enabling timely intervention to optimize treatment efficacy and prevent disease progression. This is the first analysis demonstrating Arsa-cel's safety and efficacy outside a clinical trial setting.

Conclusions

These findings confirm clinical trial results, demonstrating Arsa-cel's safety and efficacy. Early diagnosis and intervention are key to optimal outcomes, with presymptomatic treatment preventing disease progression. Implementing newborn screening is essential to identify patients early and maximize treatment benefits. Further long-term multicenter studies are needed to validate these observations and refine patient selection criteria.

ABSTRACTS

Topic: Infectious and Inflammatory Diseases/ Neuroimmunology

EPNS25_790 - Acute Disseminated Encephalomyelitis Profiles: Gender and Age Differences in Pediatric Demyelination

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Objectives

Acute disseminated encephalomyelitis (ADEM) is a rapid-onset inflammatory CNS disorder in children, causing demyelination, encephalopathy, and neurological deficits, often following infections. This study examines pediatric patients who had ADEM.

Methods

This 10-year retrospective study evaluated pediatric patients with Acute Disseminated Encephalomyelitis (ADEM), focusing on clinical, laboratory, and imaging profiles. The various profiles were assessed to determine age- and/or sex-based differences.

Results

The study reviewed 36 pediatric patients, with an average age of 6.08 years and predominantly male (61.1%). The interval between symptom onset and hospital admission averaged 7.5 days. Twenty-five percent had consanguineous parents, and various infections preceded symptoms. Clinical presentations included fever, nausea, vomiting, and seizures, with left facial hemiparesis being more common in girls (P-value = 0.023). Laboratory findings showed no significant cerebrospinal fluid (CSF) abnormalities, but girls had higher peripheral polymorphonuclear cell proportions (P-value = 0.021). Imaging revealed predominantly bilateral lesions in the brain, with older patients more likely to show lesions in the right parietal and occipital lobes (P-value = 0.015 and 0.04). Additionally, girls, particularly those who were older had significantly higher involvement of the cervical spine (P-value = 0.042 and 0.026).

Conclusions

This study highlights clinical, laboratory, and radiological features of ADEM in children, illustrating some variations by age and sex.

ABSTRACTS

Topic: Movement Disorders/ Cerebral Palsy

EPNS25_792 - Creating a reliable neuroimaging dataset for GNAO1 research: identifying structural brain abnormalities

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Objectives

GNAO1-related disorders (*GNAO1*-RD) are an ultra-rare condition, with nearly 290 reported cases in the literature. The associated symptoms encompass epilepsy, movement disorders, including dyskinetic seizures, psychomotor delay/intellectual disability, and gastrostomy use. Despite the growing recognition of *GNAO1*-RD, potential structural brain abnormalities have not been systematically studied due to limited data, often gathered in heterogeneous clinical environments. This study represents a first attempt at constructing a reliable neuroimaging dataset to explore the structural impact of *GNAO1* on brain development.

Methods

In this retrospective study, we included 35 patients diagnosed with *GNAO1*, with 24 patients from our institution and 11 from seven other clinical centers. We identified available T1-weighted MRI images for each patient. Image quality control involved visually inspecting each scan and ensuring that the resolution was sufficient for accurate brain tissue identification (resolution < 1.3 mm3). Due to clinical assessments being conducted at different timepoints, a total of 79 MRI sessions were available for analysis. Brain volume calculations were performed using a methodology specifically developed to be robust when analyzing heterogeneous neuroimaging samples from multiple centers.

Results

After quality control, 67 (84%) of the MRI images were deemed suitable for volumetric assessment. In a preliminary analysis of nine patients aged 4 to 8 years (mean age = 6.6 years), two brain structures showed significantly smaller volumes compared to age-matched controls: the cerebellar crus X (mean relative volume deficit = 76%) and the entorhinal cortex (mean relative volume deficit = 48%). Notably, volume deficits were observed bilaterally in both structures.

Conclusions

This study provides evidence that a sufficiently large and reliable neuroimaging database can be constructed using data collected in clinical practice. While the focus of this study is *GNAO1*-RD, this approach may also be applicable to other rare neurological disorders. Our findings suggest that *GNAO1* mutations may have a measurable impact on brain structure, particularly in areas associated with motor and cognitive functions, and warrant further exploration in larger cohorts. This research opens the door for future studies to refine the neuroimaging phenotype in *GNAO1*-RD and contribute to understanding its underlying pathophysiology.

ABSTRACTS

Topic: Movement Disorders/ Cerebral Palsy

EPNS25_793 - Unraveling the Natural History of GNAO1-Related Disorders: Insights from a Comprehensive Study

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Objectives: Pathogenic variants in *GNAO1* cause Developmental and epileptic encephalopathy 17, characterized by early-onset refractory epilepsy, developmental delay and/or intellectual disability, hypotonia, and movement disorders. Despite ongoing efforts to understand genotype-phenotype correlations, the heterogeneity of *GNAO1*-related disorders (*GNAO1*-RD) remains challenging. A recently developed severity score for *GNAO1*-RD aims to categorize patients, but a comprehensive exploration of natural history data is lacking.

Methods: Between March 2021 and December 2024, 20 individuals with *GNAO1*-related disorders harboring 22 distinct variants, including 5 novel variants (p.K46R, p.T48I, p.R209P, p.L235P, p.Q138*) were enrolled in this study. They underwent repeated clinical and neuropsychological assessments, 24-hour video-EEG monitoring, and brain MRI. Motor and language development were assessed using Vineland-II, Bayley-III, and GMFM-88, alongside a retrospective review of medical records. Dystonia, chorea, and stereotypies were evaluated with BFMDRS and AIMS. The GNAO1-related disorders severity score was applied annually.

Results: Our cohort exhibited wide variability in symptom severity and GNAO1-related disorders severity scores. Nineteen patients presented with developmental delay or intellectual disability and movement disorders, whereas one patient manifested a mild form of the disease, displaying certain traits of autism spectrum disorders. All patients experienced movement disorders, with 55% suffering from dyskinetic crises and 25% undergoing deep brain stimulation surgery yielding partial benefit. Epilepsy was prevalent in 50% of patients, with 66,7% meeting criteria for drug-resistant epilepsy. General stability in the progression over time was demonstrated through successive neuropsychological and clinical evaluations, with moments of worsening often related to dyskinetic crises and/or epilepsy decompensation. Remarkably, patients sharing the same *GNAO1* variant exhibited comparable evolution and severity scores.

Conclusions: Our comprehensive study sheds light on the intricate natural history of GNAO1-RD, emphasizing remarkable heterogeneity of clinical presentations. The uniform evolution and severity scores observed in patients sharing the same GNAO1 variant suggest that diversity in disease profiles arises from unique mechanisms. While patients showed a general stability in the progression and severity over time, it is important to note that transient exacerbations can occur, highlighting the complex nature of GNAO1-RD. This insight into the natural history of GNAO1-RD is crucial for identifying optimal therapeutic intervention windows and planning targeted clinical trials.

ABSTRACTS

Topic: Cerebrovascular Disorders

EPNS25_794 - Revealing the role of the optical coherence tomography for retinal damage detection in children with transient ischemic attack

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Objectives

Transient ischemic attack (TIA) is defined as a transient episode of neurological dysfunction resulting from focal brain, spinal cord, or retinal ischemia, without associated infarction or tissue injury. Trouble seeing in one or both eyes is considered to be symptoms of TIA in children. The aim of the study is to evaluate the optical coherence tomography (OCT) data as a possible tool in confirming visual symptoms in children with TIA.

Methods

Cohort study: 54 patients 10-17 y.o. with visual symptoms during TIA. TIA has been diagnosed under expert clinical assessment. No magnetic resonance imaging changes in brain and optical nerve (1,5 Tesla) have been found. All patients underwent anterior segment OCT (AS-OCT, RTVue 100, Optovue) within the next two to three months. Measurement of retinal optic nerve fiber layer (RNFL) thickness was performed in the area with a diameter of 3.45 mm centered on the optic nerve for 8 sectors on each eye. Only normative OCT database for RNFL for adults exists, therefore, we took the average values in each sector of the participants in our sample as normal values if they fell within the adult norm.

Results

All 54 patients (108 eyes) had transient mono- or binocular blindness, blurring or other options of visual impairment within a few minutes coexisted with transient neurological signs. 24 patients had normal RNFL thickness (44,4%) on both eyes, 15 patients (27,8%) had low RNFL thickness on one eye and 15 patients (27,8%) had low RNFL thickness on two eyes. Left-eyed sectors were affected more frequently than right (44 sectors vs 35 sectors accordingly). 19 patients (63,3%) had more than one affected RNFL area (6 patients - 2 affected sectors, 4 patients - 3 sectors, 9 patients - more than 3 segments). The most affected zone was a left lower nasal sector (n=16, 29,6%). We found a significant difference between the RNFL thickness in TIA and normal rate only in two sectors: 86,0±23 μm vs 126,2±22 μm for right inferior nasal sector (p=0,013) and 111,0±16 μm vs 145,2±16 μm for right superior temporal sector (p=0,0003).

Conclusions

According to the pilot OCT data we consider that vision impairment in children with TIA is a more serious condition than previously believed. The OCT data demonstrated in this pilot study might become the first step to develop the reliable set for TIA confirmation, differential diagnostics of sudden-onset vision loss in children and monitoring their condition.

ABSTRACTS

Topic: Neurological Emergencies

EPNS25_795 - Pediatric new onset status epilepticus: features and outcomes

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Objectives

Limited data is available on pediatric new onset status epilepticus (NO-SE), namely SEs occurring in people with no previous epilepsy diagnosis. The primary aim of the study is to describe the features and outcomes of pediatric NO-SE. The secondary aim is to identify possible predictors of outcomes.

Methods

single-center, observational, retrospective study. We included all consecutive pediatric patients (1 month-17 years of age) presenting between 2010 and 2022 with NO-SE. Information about semiology, etiology, EEG features, neuroimaging, response to treatment, diagnosis of epilepsy during 2-year follow-up or death were collected. The latest classification of SE from the ILAE was applied. Differences between groups and associations between variables were assessed using the Mann-Whitney U-test, the Chi-square test or Fisher's exact test. The statistical significance level was set at $p<0.05$.

Results

87 patients were included (median age: 3 years, 53% females). Prominent motor symptoms were seen in 67%, non-convulsive status (NCSE) was found in 33%, with autonomic SE accounting for one-third of NCSE cases. Acute and febrile etiology were the most frequent causes of NO-SE (31% and 24%, respectively). Refractoriness to treatment was noted in 14% of NO-SE, no deaths were seen. EEG before hospital discharge showed abnormal background activity or epileptiform discharges in 43% and 26% of patients. A diagnosis of epilepsy was established in 44% of cases with NO-SE during follow-up, most likely in patients with NCSE (OR 6.180, 95% CI 2.136-19.573, $p<0.001$) and less probably in patients with acute (OR 0.136, 95% CI 0.030-0.466, $p<0.001$) and febrile (OR 0.090, 95% CI 0.009-0.421, $p<0.001$) etiology. Autonomic SE was exclusively observed in patients who later developed self-limited epilepsy with autonomic seizures, accounting for 24% of post NO-SE epilepsy ($p<0.001$). Normal EEG at discharge was more frequently seen in patients without diagnosis of epilepsy during the follow-up (58% vs 29%, OR 0.300, IC 0.097-0.869, $p=0.018$).

Conclusions

pediatric NO-SE was frequently related to acute and febrile etiology, mainly occurring with prominent motor symptoms. Autonomic semiology and abnormal EEG at discharge were associated with higher risk of epilepsy after the acute event: these findings may be helpful to optimize the neurological follow-up of these patients. Prospective studies on larger cohorts are needed to confirm and expand the results.

ABSTRACTS

Topic: Neurometabolic Disorders

EPNS25_796 - Analysis of Outcomes in Krabbe Disease Patients Undergoing Hematopoietic Stem Cell Transplantation

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Objectives

To report the outcomes of three patients with early-infantile (EI), late-infantile (LI), and late-onset (LO) Krabbe disease (KD) following hematopoietic stem cell transplantation (HSCT) at 7 and 11 years post-treatment.

Methods

Clinical, radiologic and laboratory information from three patients with EI, LI and LO Krabbe Disease who underwent HSCT were analyzed retrospectively. Follow-up data was available for 7 (EI and LI) and 11 years (LO) post-HSCT. The outcomes of patients with EI and LI KD were compared with the clinical courses of affected older siblings who did not undergo HSCT. Informed consent was obtained from all subjects involved in the study. The study was conducted in accordance with Declaration of Helsinki, and approved by the Ethics Committee of the Medical Association of Hamburg (Germany) for studies involving humans (PV3782).

Results

All patients underwent allogeneic HSCT from a 10/10 HLA-matched unrelated donor following conditioning with Treosulfan/Fludarabin/Thiotepa. One patient experienced primary graft failure and was successfully re-transplanted immediately. No patient developed graft-versus-host disease and hematopoietic chimerism was full donor type at last follow-up.

The EI patient underwent HSCT presymptomatically at 57 days of age. Post-transplant, cognitive and motor development were delayed. Seven years post-HSCT, he is not able to walk without support and uses a wheelchair. He retains hand control, speech, and stable cerebral myelination. The untreated older sibling experienced rapid disease progression and died at 19 months.

The LI patient underwent HSCT presymptomatically at three months of age. Seven years after HSCT the patient maintains normal motor and cognitive function, though nerve conduction studies were abnormal. The untreated sibling experienced progressive neurological decline and died at 50 months of age.

The LO patient underwent HSCT at four years after showing visual impairment as the first manifestation of KD. Eleven years post-HSCT, motor and cognitive development remain age-appropriate, although visual impairment persists. MRI remains stable, and no peripheral neuropathy has been detected.

Conclusions

HSCT effectively halted central nervous disease progression in all three patients with KD, who were treated presymptomatically in the early forms or treated early symptomatically in the late onset form. Patients with EI and LI KD showed a significantly longer survival compared to their untreated siblings.

ABSTRACTS

Topic: Traumatic Brain Injury

EPNS25_798 - 6 Years of Concussion Clinic for Children and Adolescents: Recent achievements and future directions

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Objectives

Pediatric mild traumatic brain injury (mTBI) is a significant global health concern with approximately 300,000 cases/year in Germany. Unless the rate of intracranial complications is extremely low, Germany reports one of the highest rates of hospitalization for pediatric TBI worldwide. Most symptoms typically improve within days or weeks but a relevant number of patients experience persisting post-concussive symptoms.

Methods

We conducted a monocenter analysis comprising all patients presenting due to head injury to our emergency department (ED). In addition, we analyzed data of the nationwide hospital database and data from a hospital survey covering 18 pediatric ED in Germany. At our Concussion Clinic we implemented a standardized Concussion Care Pathway (CCP) to ensure thorough evaluation, personalized guidance, tailored follow-ups and personalized rehabilitation. CCP aims to reduce hospitalizations on behalf of structured care and parental guidance, and the prevention of long-term physical and mental impairments to maintain participation and quality of life.

Results

From 07/2020 to 12/2023 a total of 7,347 patients presented with head injuries to our ED. Of 1588 cases classified as mTBI 73% were hospitalized. The concussion team was involved in the care of 2,538 patients. 184 individuals were directly referred to the multimodal follow up and rehabilitation program.
The total number of TBI cases (<18 years) admitted to hospital across Germany from 2014 to 2019 yielded 618,577 with 600,309 being classified as abbreviated injury scale (AIS) 1. The hospital survey demonstrated admission rates between 19.1 and 93% (median: 76.0%).

Conclusions

Our data highlight the importance of paediatric mTBI in clinical practice and call for standardized assessments and highlight the significant demand for counseling and rehabilitation. To reduce hospitalization rate and offer appropriate guidance on "return-to-school/sport" decisions, while minimizing the risk of re-injury and long-term effects, reliable data and accurate tools are essential. In September 2025 the nationwide controlled clinical study "SaVeBRAIN.Kids" (funded by the Federal Joint Committee) will be initiated to assess measures to safely reduce mTBI hospitalization rates.

ABSTRACTS

Topic: Infectious and Inflammatory Diseases/ Neuroimmunology

EPNS25_799 - Autoimmune glial fibrillary acidic protein (GFAP) astrocytopathy: a systematic literature review with focus on age-specific features in children

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Objectives

We aimed to describe early clinical-radiological characteristics of GFAP astrocytopathy, with focus on age-specific features in children.

Methods

A systematic review following PRISMA guidelines and registered on PROSPERO (CRD42024505205) was carried out in PubMed, including adult or pediatric patients with GFAP astrocytopathy with individual patient data.

Results

A total of 546 patients (45.4% female) from 185 studies were included (median onset age: 36 years, range 0–103; 26.0% <18 years at onset).

Clinical syndromes with brain involvement ((meningo)encephalitis/encephalomyelitis) were slightly more frequent in children compared to adults (83.1% vs 61.2%), whereas isolated myelitis (1.5% vs 7.4%) and isolated optic neuritis were rarer (3.1% vs 8.0%).

The most frequent symptoms were headache (55.4%), fever (55.3%), weakness (46.6%), and encephalopathy (44.1%). Compared to adults, children had higher rates of fever (72.7% vs. 51.9%) and seizures (31.7% vs. 18.1%) at presentation, but lower rates of psychiatric symptoms (33.0% vs. 51.0%), movement disorders (28.3% vs. 52.7%), and sphincter dysfunction (23.3% vs. 52.7%).

Disease severity at onset was similar in both age groups (median mRS 3.4 vs. 3.2), as were ICU admission rates (33.0% vs. 36.1%) and mechanical ventilation (22.2% vs. 29.5%).

Neuroimaging showed supratentorial involvement (81.6%), cerebellar (22.3%), brainstem (33.2%), optic nerve (8.6%), and spinal involvement (60.0%). Compared to adults, children had more frequent cortical (51.3% vs 31.6%) and basal ganglia involvement (58.8% vs 29.5%), but rarer white matter abnormalities (56.4% vs 75.4%) and radial perivascular enhancement (16.8% vs 42.1%).

High-dose steroids were the primary acute treatment (90.2%), with IVIG used more frequently in children (75.0% vs. 44.3%). The disease was monophasic in 79.0%, with favorable outcomes (median mRS 1.4).

Conclusions

GFAP astrocytopathy is rarer in children than adults, but the identification of age-specific features may help recognize this newly described syndrome also in pediatric age. In particular, children more often appear to present with brain involvement and less frequently with isolated spinal or optic nerve involvement than adults. Fever and seizures are more common in children, while psychiatric symptoms, movement disorders, and sphincter dysfunction are less frequent than in adults. GFAP-related radial perivascular enhancement, reported frequently in adults, appears rarer in children.

ABSTRACTS

Topic: Neurological Emergencies

EPNS25_800 - CLASP-NCSE: CLinical risk ASsessment tool for Pediatric Non-Convulsive Status Epilepticus

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Objectives

the signs and symptoms of non-convulsive status epilepticus (NCSE) may be very subtle, and there is no available tool allowing to systematically assess the risk of NCSE based on presenting clinical features and recent history. The aim of this study is to describe and validate a clinical risk assessment tool for pediatric NCSE, CLASP-NCSE. This is a 0-7 scoring tool that uses clinical features (altered consciousness, subtle motor signs, abnormal verbal response and acute clinical seizures) to estimate the risk of NCSE.

Methods

this was a single-center retrospective observational cohort study at a tertiary centre for pediatric neurology and neurophysiology. The CLASP-NCSE score was calculated on patients consecutively referred for video-EEG recordings to confirm or rule out pediatric NCSE between 01/01/2019-01/09/2024 (n=371). Clinical data was collected using patient notes, a logistic regression was performed. The score was developed by using the odds ratios to weight the coefficients from the regression, converting them into a formula with a 0-7 score result. The CLASP-NCSE was then tested on patients undergoing EEGs between 01/10/2024-13/01/2025 (n=49), and performance metrics were calculated using the electroencephalographic diagnosis of NCSE as gold standard. The statistical significance level was set at $p<0.05$.

Results

The CLASP-NCSE score was significantly ($p<0.001$) predictive of NCSE, with high accuracy (0.980) and an area under the curve (AUC) of 0.984. Three risk categories for NSCE risk were identified (low, moderate, or high) depending on the CLASP score (0-2, 3-5 and 6-7, respectively). Key enhancements included simplified scoring guidelines and the addition of a visual dashboard.

Conclusions

the CLASP-NCSE score provides a user-friendly framework for systematically evaluating the risk of NCSE. The score is based on clinical features and history of presenting complaint in cases with possible or suspect ongoing NCSE. The tool may be helpful to prioritize the access to EEG recordings in case of limited capacity in the real-word scenario. A further, multi-center prospective validation on a larger population is needed, to assess interobserver reliability and to better define the risk bands.

ABSTRACTS

Topic: Movement Disorders/ Cerebral Palsy

EPNS25_801 - The added value of clinical neurophysiology in pediatric movement disorders

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Objectives

Diagnosing pediatric movement disorders (MDs) is challenging due to their heterogeneous and evolving presentations. While clinical neurophysiology (CNP) is a complementary diagnostic tool in adult MDs, its role in children remains underexplored. This study evaluated the feasibility and diagnostic contribution of CNP in pediatric MDs.

Methods

This retrospective observational study analyzed investigations using superficial electromyography (sEMG) and accelerometry, with or without EEG, performed in children with suspected MD at a tertiary movement disorder center. The conclusion of CNP examination (CNP diagnosis) was compared to the referral and final (made after CNP) clinical diagnoses. Descriptive statistics were used.

Results

Ninety-four CNPs were included (median age at CNP: 14 years, range 3–18). The indications for CNP were: confirm the clinical diagnosis (41%), establish the MD among suspected MDs (33%), characterize MD subtype (23%) or aid symptomatic treatment (3%). The referral diagnoses were myoclonus (82%), tremor (29%), dystonia (15%), chorea (9%), functional (9%) and tics (2%). All patients completed the CNP protocol, with interpretable results in 99% of cases despite artifacts (20%), uncooperative behavior (10%) and difficulty in following instructions (16%). The final diagnosis was available in all except 3 cases. The referral diagnosis, CNP diagnosis and final diagnosis aligned in most cases (61%). CNP contributed to refining the final diagnosis in 21% of cases, by changing the referral diagnosis or identifying a previously unrecognized MD. In 14% of cases, CNP diagnosis differed from the final diagnosis, mainly when there was a complex phenotype. In this group, the most disregarded CNP diagnoses was chorea (50%), followed by myoclonus and tremor.

Conclusions

This study underscores the value of CNP as a feasible tool for diagnosing pediatric MDs guiding the final diagnosis in 83% of the cases. However, the complex and frequent mixed phenotypes in children may lead to different CNP findings from clinical interpretation, necessitating close collaboration between neurophysiologists and clinicians. Future research should focus on standardizing protocols and improving the recognition of mixed phenotypes to enhance diagnostic precision and clinical applicability.

ABSTRACTS

Topic: Epilepsy: Medical and Surgical treatment

EPNS25_802 - Efficacy of corticosteroid therapy in the treatment of GRIN2A-related Epileptic Encephalopathy with Spike-Wave Activation in Sleep

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Objectives: Epileptic Encephalopathy with Spike-Wave Activation in Sleep (EE-SWAS) is characterized by psychomotor regression or stagnation occurring in parallel with abundant epileptic discharges during sleep. In addition to structural causes, GRIN2A is the main monogenic contributor to this syndrome. Corticosteroid therapy is the first-line treatment for EE-SWAS; however, its specific efficacy in *GRIN2A*-related EE-SWAS remains poorly studied. This study aimed to assess the therapeutic effectiveness of corticosteroids in this population.

Methods: We conducted a descriptive, retrospective, multicenter study from 2019 to 2023, including patients carrying a pathogenic/probably pathogenic *GRIN2A* variant who received corticosteroid treatment for epileptic encephalopathy before age 15. Clinical and EEG data were analyzed before and after treatment. Clinical improvement was assessed three months post-treatment based on cognitive and behavioral evaluations, including neuropsychological testing when available. EEG improvement was evaluated at one and three months post-treatment using both a qualitative severity score (0 = normal EEG, 4 = highly disorganized activity with generalized high-amplitude spikes) and a quantitative spike-wave index (SWI), with significant EEG improvement defined as a reduction of at least two grades on the qualitative scale and an SWI decrease of more than 50%.

Results: A total of 22 patients were included, with a mean age at EE-SWAS diagnosis of 5.5 years. Before corticosteroid therapy, 55% had pre-existing psychomotor delay, and 82% had epileptic seizures. Corticosteroid therapy led to cognitive and/or behavioral improvement in 81% of patients (18/22). Among the 18 with epilepsy, 16 (89%) became seizure-free. EEG improvement was observed in 68% (15/22), with five showing improvement within one month and four achieving complete EEG normalization. Five patients experienced relapse, characterized by language deterioration, EEG worsening, or psychomotor regression, three of whom improved after treatment prolongation or a second corticosteroid course. Three reported mild to moderate side effects. Overall, 59% exhibited both clinical and EEG improvement after the first corticosteroid treatment, an extended regimen, or a second treatment course, highlighting its potential benefit.

Conclusions: This is the first study to demonstrate the clinical and electroencephalographic efficacy of corticosteroid therapy in *GRIN2A*-related EE-SWAS. Our findings align with previous studies on corticosteroid efficacy in EE-SWAS, regardless of genetic cause. The identification of a pathogenic *GRIN2A* variant in a patient with EE-SWAS should not lead to an underestimation of potential pharmacological interventions. This population is at high risk of worsening preexisting neurodevelopmental disorders due to epileptic activity activation.

ABSTRACTS

Topic: Neurogenetics

EPNS25_803 - Clinical and Imaging Clues in Aicardi-Goutières Syndrome: A Pediatric Neurology Perspective

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Objectives

Aicardi-Goutières Syndrome (AGS) is a rare monogenic interferonopathy with wide phenotypic variability. Our aim was twofold: To characterize the clinical, radiological, and genetic profiles of patients and to assess diagnostic clues and pathway.

Methods

This retrospective study included six patients (Males: 2, Females: 4), diagnosed with AGS at a tertiary center between January 2010-December 2024. Comprehensive clinical evaluations, including neurological and systemic examinations were conducted alongside cranial magnetic resonance imaging (MRI), computed tomography (CT). Diagnosis was confirmed by molecular genetic tests in all patients.

Results

The median age at onset of complaints and the time of admission were 0.4 (0–24) month, and 8.2 (1.2–128.4) months, respectively. The median age of diagnostic delay was 43.5 (1-120) months. Presenting symptoms included delay in head control (n=2), seizures (n=2), abnormal gait (n=1), and prematurity with dysmorphic features (n=1). Microcephaly (n= 4) and nystagmus (n= 2) were additional presenting features. Pyramidal signs were observed in all, with cerebellar findings in one patient. Systemic features included scoliosis (n=2), panniculitis (n=1), hepatosplenomegaly (n=1), and elevated liver enzymes (n=1). Joint contractures (n= 2) and hypotonia (n= 2) were accompanying features. Cranial MRI showed exclusive white matter involvement in all patients, with additional cerebral atrophy (n=4), cysts (n=2), calcifications (n=3), and thin corpus callosum (n= 4). CT scans were available in three patients and demonstrated calcifications. Diagnosis was confirmed by whole-exome sequencing (WES) in all patients with homozygous variants in *SAMHD1* (n= 2), *RNASEH2B* (n= 1), *RNASEH2C* (n= 1), compound heterozygous variants in *SAMHD1* (n= 1) and *TREX1* (n=1). Out of 3 patients who were lost to follow-up, one was deceased. For the remaining three patients, the median follow-up duration was 2.5 (0.7–99.6) months. Ruxolitinib treatment was considered in three patients at ages of 9 months, 3 and 6 years, respectively.

Conclusions

Presentation of AGS may be with nonspecific signs and symptoms. Recognition of systemic involvement, clinical and neuroimaging clues serve as a tool for diagnosis. Accurate diagnosis for emerging therapeutic options, such as Janus kinase inhibitors, requires evaluation of outcome parameters and collaboration between pediatric neurologists and rheumatologists.

ABSTRACTS

Topic: Neuromuscular Disorders

EPNS25_805 - Report of five cases of Bethlem myopathy

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Objectives

Bethlem myopathy (BM) is a rare disease (~1 : 1 000 000) that is not well investigated to date. It represents the mild end of a spectrum of diseases with presumably identical genetic underpinning, which is a mostly dominantly inherited variant in the COL6A(1-3) gene. The produced collagen 6 is responsible for forming nests for muscular stem cells in the extracellular matrix, its defect leading to an overlap syndrome of muscular and connective tissue disorder. The goal of this work is to further elucidate genotypic-phenotypic correlation and the natural history of this disease.

Methods

Presentation of five cases affected by BM who are or were in care at the neuromuscular division of a neuropediatric outpatient center and followed for several years.

Results

We present five cases of children affected by BM. They were diagnosed at 2, 10, 14, 15, and after 16 years of age, respectively. Mutations were found within COL6A1 and COL6A3 (one case). Symptoms shared by the patients and typical for the entity are mildly to moderately increased creatine kinase levels, proximal weakness, distal joint contractures, mild to moderate walking impairments, two of them showing a markedly restricted range (45 m, 1 km). With the individual diagnosed the earliest due to gross motor developmental delay, crossed fingers and foot dysmorphia was present at birth. Other associated symptoms are muscular hypotonia, hyporeflexia, scoliosis, and respiratory function decline. There is no BM specific treatment and the described individuals do not take any supportive medication. On one patient, several tendon release surgeries have been performed on the lower limbs.
All individuals obtain supportive measures including regular physiotherapy and orthopedic visits. For (2),(3),(4), orthoses are implemented.

Conclusions

BM is a spectrum disease presenting with mild to moderate proximal muscle weakness as well as joint contractures. Individuals usually show impaired gait and respiration can also be affected, survival is generally not restriced.
The siblings (4) and (5), showing variations in the same subunit of the collagen 6 gene presented with similar symptoms as patient (1) whose variation differs in localization. Individuals (2) and (3), who share a parent, show a more severe affection.

ABSTRACTS

Topic: Neuromuscular Disorders

EPNS25_806 - A Case Series of Childhood Onset Hereditary Spastic Paraplegia

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Objectives Hereditary spastic paraplegia (HSP) is a progressive condition that can manifest either in its pure form, characterized by spastic weakness in the lower extremities, or in a complex form where additional features such as seizures, muscle atrophy, neuropathy, ataxia and intellectual disability may be present. Initial symptoms in early childhood often include delays in motor development, loss of walking ability and toe-tip walking. Our objective is to retrospectively present a group of pediatric patients diagnosed with HSP whose symptoms emerged in early childhood, highlighting both their clinical manifestations and genetic features.

Methods We performed a retrospective analysis of cases involving childhood-onset HSP that were monitored at the Division of Pediatric Neurology, Dokuz Eylul University School of Medicine. The recorded data encompassed clinical presentations, family histories, examinations, electrodiagnostic tests, neuroimaging findings, results of genetic tests, comorbidities and treatment regimens

Results A total of 22 patients (7 girls) from 18 families were assessed, with an avarage age of 11.1 years (ranging from 1 to 19 years). Only 2 patients exhibited pure HSP, while the remaining cases showed additional features such as epilepsy, intellectual disability, ataxia, and learning diability. Fifteen cases were diagnosed using NGS, identifying associated HSP with genes including *PLP1 (1), ZFYVE26 (5), GBE1 (1), ENTPD1 (1), SACS (2), SPAST (2), AMPD2 (1), AP4M1 (1), SLC1A4 (2), HSPD1 (1), GBA2 (1), SEPSECS (1), PRKCG (1)* and *mt-ATP6 (2)*.

Conclusions The majority of patients presented with the complex HSP clinic. The increased accessibility to NGS/WES has contributed to a higher rate of genetically confirmed diagnosis among patients.

ABSTRACTS

Topic: Neuromuscular Disorders

EPNS25_807 - Evaluating long-term treatment outcomes and health-related quality of life in patients with spinal muscular atrophy: Study design and conduct

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Objectives The survival and motor functioning in spinal muscular atrophy (SMA) have significantly improved since the advent of disease modifying treatments. This disease evolution with an emerging group of new survivors is the object of intense research. The overall aim of this study is to identify the long-term outcomes of patients with SMA in Sweden who have been treated with any of the approved disease-modifying treatments. Furthermore, to investigate prognostic factors affecting treatment outcomes as well as the patients' fatigue and health-related quality of life.

Methods This is a population-based longitudinal study that will be conducted in collaboration with the university clinics in Gothenburg, Stockholm and Skåne. All patients with SMA in Sweden who have received SMN-targeted treatment will be considered for enrolment. Data regarding disease diagnostics and phenotypic features will be collected both retro- and prospectively. Further analyses will focus on predicting factors influencing treatment response, including SMN2 copy number, age at onset, and treatment type. We will also examine the impact of growth metrics (e.g., height, BMI), scoliosis, lung function, and other interventions (e.g., surgeries) on motor function. Biomarker levels in plasma and cerebrospinal fluid will be analyzed for correlation with motor function changes. Additionally, patient-reported outcomes on quality of life, fatigue, and independence will be assessed, with an emphasis on understanding the correlation with motor function. Ethical approval has been granted.

Results The study protocol has been designed through a multicenter collaboration with representatives from the neuromuscular teams that systematically follow and treat children, adolescents and young adults with SMA in Sweden. Factors that were considered essential in the study design and conduct were (a) the collaborative approach to ensure high recruitment and participation rates; (b) the set-up for data collection in a safe, digital platform, i.e. REDCap; (c) the combination of clinical parameters with functional assessments and patient-reported outcomes; (d) the inclusion of dedicated study personal for continuous monitoring and support.

Conclusions Continuing to study long-term treatment outcomes will enable us to ameliorate the monitoring of this disease and help prevent disease complications. By correlating clinical and growth-related factors with motor function improvements, this study could enhance clinical decision-making and treatment strategies. The impact on patient's health and daily living is of great interest not only from the patient perspective but also to the society, as disease modifying treatments are expensive and the healthcare burden and life costs are highly demanding.

ABSTRACTS

Topic: Infectious and Inflammatory Diseases/ Neuroimmunology

EPNS25_808 - Time-lag to diagnosis and Relapses in Opsoclonus Myoclonus Ataxia Syndrome: 11-year data of 71 children

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Objectives: Opsoclonus Myoclonus Ataxia syndrome (OMAS) is a rare autoimmune disorder affecting young children. As with other diseases, a delay in diagnosis may impact course and prognosis. However, there is a lack of data due to its rarity.

Methods: This retrospective observational study reviewed data of children diagnosed with OMAS from a single center over 11 years (2014-2024). Those with at least six months of follow-up and treatment data available were included. Association with underlying tumor, time lag to diagnosis, therapy patterns, and disease course were studied. All except three (three drugs upfront), were treated with two drugs upfront using an escalating protocol

Results: A total of 81 children were identified with symptoms suggestive of OMAS. Ten were excluded (five had infection-associated OMAS and for five data was inadequate). Among 71 children (median age 18.5 months, IQR: 13-23), forty-seven (66.2%) had associated tumors. Four children with tumor-associated OMAS died. Of the remaining 67 children, followed up for a median duration of 37.5 months (IQR: 22-57), 29 had a monophasic course, 30 had an intermediate course with at least one relapse, and 8 had a chronic course. The median time lag to treatment was 4 weeks (2-6 weeks, range 1-40 weeks). The median relapses were 1 (IQR: 0-2, range 0-5). Of the 25/38 with relapsing or chronic course versus 18/29 (P=0.75) with monophasic course had tumors. There was no correlation between time-lag to diagnosis and relapses.

Conclusions: This study shows that two-thirds of OMAS are tumor-related. The time lag to diagnosis does not appear to impact the risk of relapse when at least two drugs are used up front.

ABSTRACTS

Topic: Neurogenetics

EPNS25_810 - GRIN2A-associated epilepsy and neurological disorder: a single center experience

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Objectives

The *N*-methyl-d-aspartate receptor (NMDAR) is an ionotropic glutamate receptor, and glutamate is the main excitatory neurotransmitter of the central nervous system. The *GRIN2A* gene encodes the GluN2A subunit of the NMDAR, a heterotetramer consisting of two GluN1 subunits and two GluN2 subunits. *GRIN2A*-related disorders encompass a broad phenotypic spectrum that includes developmental delay evolving to intellectual disability (DD/ID), epilepsy, speech and language disorders, movement disorders, and neuropsychiatric disorders. A history of epilepsy is present in nearly 90% of individuals with GRIN2A variants.

Methods

We retrospectively evaluated six consecutive patients (one male) with GRIN2A mutations according to demographic, clinical, imaging, genetic, and EEG findings. We also assessed the treatments and prognosis.

Results

The mean age of the patients was 12,6 years (min: 10-max: 16), and the mean age at presentation was 6.7 years (min: 2.5-max: 11). The patient with self-limited epilepsy with centrotemporal spikes (SeLECTS) had c.46C>G (p.Leu16Va) (novel variant). The patient with focal epilepsy, intellectual disability, and cafe au lait spots had c.2497_2499delinsG p.(Ile833AspfsTer44) (novel variant) frameshift variant. The other 4 patients had Epileptic encephalopathy with spike-wave activation in sleep (EE-SWAS). One of the patients with EE-SWAS had a 218.1kb deletion in the 16p13.2 region [arr[GRCh38]16p13.2(10116757_10334890)*1]. Other variants related to EE-SWAS were missense as: c.2278G>A (p.Gly760Ser), c.46C>G (p.Leu16Va) (novel variant), 2 patients with c.1592C>T (p.Thr531Me). Brain MRI was normal. The initial presenting symptom of the 4 patients was seizure. The initial presenting symptom was Speech delay and attention deficit-like symptoms in one patient each, The patient with speech delay also had EEG abnormalities and subsequently developed drug-resistant epilepsy. Although improvement in EEG findings in those who were receiving levetiracetam treatment was observed without immunotherapy with the addition of clonazepam treatment in 1 patient with SWAS, 2 of them received steroids and one of them received both steroid and IVIG. Permission for the use of memantine and IVIG was obtained from the Ministry of Health. Memantine treatment was started in 3 patients. One of these patients benefited from memantine, another one partially benefited, and the drug was continued, and one patient did not benefit from memantine. One patient has refractory seizures despite immunotherapy and memantine treatment.

Conclusions

The recognition of GRIN2A variants will increase precision treatment options. Characterizing the functional consequences of pathogenic variants will further enhance precision medicine approaches. Immunotherapy and memantine treatments may help prevent the devastating effects of the disease.

ABSTRACTS

Topic: Neurometabolic Disorders

EPNS25_811 - Altered autophagy involved in neurodevelopment and neurodegeneration: study of a cohort of patients with BPAN (Beta-propeller protein-associated neurodegeneration), new insights and phenotypes.

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Objectives: Several monogenic defects related to autophagy have emerged, including the *WDR45* gene, associated with the β-propeller protein-associated neurodegeneration (BPAN). Our aim is to describe the clinical and biochemical profile in BPAN patients.

Methods: Observational and clinical study in a cohort of pediatric BPAN patients. Clinical evaluation, biochemical, radiological, neurophysiological and genetic data were assessed. Autophagic markers in fibroblasts were investigated using western blot and immunofluorescence techniques.

Results: A total of 26 BPAN patients were assessed by the group in 2 sites, 4/26 males, ages ranging from 0.5-18 years. The main symptom at onset was global neurodevelopmental delay, associated with febrile seizures (n=4), language regression (n=2) and severe hypotonia (n=2). The age at onset was before 15 months in all cases. The evolution was variable, including different degrees of developmental delay/intellectual disability (23), epilepsy (21), different patterns of motor and movement disorders including early parkinsonian signs (17), sleep disorders (14) and behavioural issues (12). A systematic assessment of the dysmorphology were assessed, showing recognizable particular features. Elevated liver transaminases were present in 14 cases. Brain MRI showed T2/SWI hypointense signal in globus pallidus and sustancia nigra in 23/26 cases. The cohort showed novel pathogenic variants (15/26), most of them *de novo* in the *WDR45* gene, with the exception of one whose mother showed mosaicism for the *WDR45* variant. CSF studies were performed, showing alterations in the neurotransmitters profile in 4 patients. Neurofilament Lght chain levels were explored in plasma and CSF in 15 individuals, showing a significative correlation with the neurological phenotype. Fibroblasts studies showed alterations in markers compatible with a defect in the autophagic flux (LC3BI/II ratio, LAMP1 and p62).

Conclusions: We describe a cohort of BPAN patients, with a homogeneous and systematic assessment. A recognizable and particular phenotype is described in a subset of patients, including neurological, dysmorphic, biochemical, neuroimaging, and electrophysiological patterns. A potential biomarker is described, that showed an association with the neurological severity in this cohort. The cellular studies contribute to understand the pathomechanism that will allow the development of new therapeutical approches.

ABSTRACTS

Topic: Miscellaneous

EPNS25_812 - The Art of Paediatric Neurology

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Objectives

Paediatric Neurology is an ever changing fast developing field. Within this field a broad variety of individuals is in contact and discourse: health professionals, scientists, students, patients, parents, family members and many more. We aim to develop new methods of diagnosis, management, intervention and treatment of pediatric neurologic disorders and human development. We aim to understand as humans with our brains the human, the human´s development, childhood and the human´s brain itself with all its complexity and beauty.

Methods

During the EPNS fellowship 2024 in London inside The Tate Gallery of Modern Art talking to a Co-fellow about the future EPNS meeting in Munich the idea was born. The aim is to present results of neuropediatric diagnostics as artwork (e.g. close to the poster area). By showing selected EEG pattern, MRI and CT scans or other results of neuropediatric diagnostic methods as framed pictures and display images as artwork I want to invite people to change perspective, get a new point of view and start (thinking) creativity in a new way.

Results

The process of discovering a visual language within our field involves mastering the art of pediatric neurology, brain science, and creativity. It raises the question: who is the true "artist" when EEG patterns display brain activity? Is it the patient, the technician, the brain itself, or the pediatric neurologist interpreting and transforming the "lines"? How can we develop a visual language that effectively translates complex content into something universally understood? What imaging patterns do we, as humans, perceive as beautiful—the healthy or the pathological? How can we grasp the overwhelming complexity of neuronal networks, and how much information can we truly capture in images? There is much to be learned from art in this process.

Conclusions

Paediatric Neurology is an Art. Within our community of the EPNS we live culture. The city where the EPNS-congress is taking place is a vivid City of Art and Culture. During the challenging times in patient care, politics, science and life we should constantly worship the beauty of Neuropaediatrics in all it´s complexity and promote dialogue driven by art. That way we will find the creativity of our community to develop new ideas for future. The project of "The Art of Paediatric Neurology" wants to invite to start thinking in new ways and opening new horizons.

ABSTRACTS

Topic: Neurological Emergencies

EPNS25_813 - Basal Ganglia Stroke After Minor Head Trauma: A Single Center Experience

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Objectives

Basal ganglia stroke after minor trauma associated with mineralization of lenticulostriate arteries is a rare clinicoradiological entity seen only in infants. This study aims to present the clinical characteristics and notable features of patients who presented to the Pediatric Emergency Department of Marmara University Training and Research Hospital with basal ganglia stroke, subsequently diagnosed with mineralizing angiopathy after minor head trauma.

Methods

The medical records of five cases who presented with basal ganglia stroke after mild head trauma were retrospectively evaluated, noting risk factors, clinical courses, and treatment outcomes.

Results

Five children were included in this study (median age: 22 months, range: 9-50 months). Presenting complaints varied: right total hemiparesis in two cases, left arm paralysis in one case, and left total hemiparesis in two cases. Two cases had concomitant seizures and were treated with anti-seizure medications (one was treated with levetiracetam, while the other received phenobarbital). Minor head trauma was identified as the only common precipitating risk factor among all patients. A thorough evaluation was conducted for each, including magnetic resonance imaging and computed tomography (CT) of the brain, along with a detailed thrombosis workup. Investigations for prothrombotic risk factors and underlying vasculopathies yielded normal results. Cranial CT revealed calcification in the basal ganglia in all cases. Two cases received both anticoagulant and antiplatelet therapy (enoxaparin and acetylsalicylic acid), while two cases were treated solely with enoxaparin, and one case received only acetylsalicylic acid. The average treatment duration was one year. Two cases showed full recovery, while weakness persisted at varying levels despite ongoing physiotherapy in the other three cases. No recurrence was observed in any of the patients.

Conclusions

Basal ganglia stroke after minor head trauma is mostly associated with favorable neurological outcomes; however, exceptions do exist. Three of the five patients in our series continued to exhibit signs of mild weakness. There is currently no consensus on treatment guidelines. It is crucial to recognize this rare and unique clinical entity specific to infancy to prevent overtreatment and to plan precise medical interventions

ABSTRACTS

Topic: Neuromuscular Disorders

EPNS25_815 - Congenital myasthenic syndromes: phenotypic/genetic heterogenity, ngsCrucial contribution to diagnosis/treatment, a case series

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Objectives Congenital Myasthenic Syndromes (CMS) are a group of early-onset neuromuscular transmission genetic disorders affecting the neuromuscular junction, mainly classified as presynaptic, synaptic and postsynaptic. They present with great phenotypic and genetic heterogeneity. Therapeutic results vary according to the underlying mutation. Thirty-five genes have been reported with *CHRNE* mutations being the commonest.
Our objective is to present the genetic, phenotypic and treatment response of a series of CMS Greek pediatric patients.

Methods We retrospectively collected clinical, genetic and treatment response data of ten patients from three pediatric departments. CMS diagnosis was confirmed via whole exome sequencing.

Results All patients presented with oculomotor dysfunction and proximal muscle weakness of various severity. Eight patients had *CHRNE* related mutations: three were homozygous to pathogenic splice-site variant c.1219+2T>G and four to c.1327delG, all resulting in primary acetylcholine receptor deficiency and were treated with pyridostigmine; one was a compound heterozygote with c.1219+2T>G and a duplication mutation (c.1181_1187dup) responsible for slow-channel syndrome, and responded well to salbutamol. Two patients had compound heterozygous *DOK7* mutations and salbutamol was beneficial, while pyridostigmine administration prior to molecular diagnosis resulted in clinical worsening.

Conclusions *CHRNE* mutations c.1219+2T>G and c.1327delG were the most common mutations in this case series responding well to pyridostigmine. Pyridostigmine worsened symptoms in a *DOK7* mutation patient. Patients with *DOK7* mutations and slow channel related mutations -even in heterozygosity- benefited from salbutamol. Response to treatment varies according to the underlying mechanism which, in turn, signifies the importance of molecular diagnosis for choosing the appropriate treatment for CMS patients.

ABSTRACTS

Topic: Cerebrovascular Disorders

EPNS25_816 - Permanent hemiplegia in CACNA1A Variants: A Multi-Center Cohort Study

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Objectives
CACNA1A-related disorders encompass a spectrum of rare genetic conditions stemming from variants in the CACNA1A gene, encoding the P/Q-type calcium channel subunit. These mutations result in a wide spectrum of neurological manifestations, including severe neurological events with permanent hemiplegia. This multicenter observational study aims to characterize the clinical features, genetic variants, and pathogenesis underlying permanent hemiplegia in these disorders.

Methods
We retrospectively analyzed data from patients with pathogenic or likely pathogenic variants in the CACNA1A gene, referred to pediatric Neurology Centers.

Results
Nine patients, with a mean overall age of 14.8 years, presenting with permanent hemiplegia were included in the study. The mean age at onset of acute events was 3.6 years. Clinical manifestations were uniformly severe, marked by drug-resistant epilepsy in all cases. Ischemic stroke and stroke-like episodes were prevalent, affecting primarily parietal, temporal, and occipital regions. While some cases exhibited motor deficits attributable to stroke, others were consistent with Hemiconvulsion-Hemiplegia-Epilepsy syndrome (HHE). Genetic analysis revealed recurrent variants affecting transmembrane domains, particularly segments S4 and S5. Notably, recurrent gene variants were documented, suggesting potential genotype-phenotype correlations in stroke-like presentations.

Conclusions
This study delineates nine cases of patients with permanent hemiplegia, a rare clinical entity with limited prior documentation. The underlying pathogenesis likely involves neurovascular events, which, in some cases, are further complicated by HHE syndrome. Moreover, the occurrence of HHE syndrome should prompt genetic evaluation for CACNA1A variants. A deeper understanding of these conditions is essential for developing targeted preventive therapies, such as calcium antagonists, to reduce the frequency of these episodes and improve patient outcomes.

ABSTRACTS

Topic: Neuromuscular Disorders

EPNS25_818 - A Case Series of Pediatric Arthrogryposis Multiplex Congenita

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Objectives Arthrogryposis multiplex congenita (AMC) is defined by the presence of congenital joint contractures affecting two or more body areas. This condition displays significant phenotypic and genetic diversity.Our objective is to enhance the genetic diagnostic accuracy for AMC by incorporating WES analysis into routine clinical investigations.

Methods We performed a retrospective analysis of cases involving Pediatric AMC cases that were monitored at the Division of Pediatric Neurology, Dokuz Eylul University School of Medicine. The recorded data encompassed clinical presentations, family histories, examinations, electrodiagnostic tests, neuroimaging findings, results of genetic tests including panels and WES analysis, and comorbidities

Results Within the scope of ICGNMD Project, 500 samples from 170 families were included. AMC compatible clinic was present in 30 families. Seventeen cases were able to recieve a genetically confirmed diagnosis. *COL6A2, COL6A1, KLHL40, POMT1, POMGNT1, LAMA2, DNM2, IGHMBP2, SLC12A1, KMT2C, PIEZO2* were among the genes detected

Conclusions The etiology of AMC is extensive, and the inclusion of WES analyses has the potential to elevate the precision of genetic identification rates.

ABSTRACTS

Topic: Neurodevelopmental Disorders / Developmental Neuroscience

EPNS25_819 - Speech disorders in children: prenatal and perinatal risk factors

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Objectives

To identify prenatal and perinatal risk factors for speech development disorders. Clarification of the role of prenatal and perinatal risk factors for the development of central nervous system pathology and the subsequent formation of developmental disorders (primarily speech disorders) is relevant.

Methods

The longitudinal study included 525 children with specific and non-specific speech development disorders (324 boys, 201 girls, born between 2005 and 2021).

Inclusion criteria: a) the possibility of collecting anamnestic data; b) the presence of speech development disorders; c) neuropsychological and speech assessment results at different age.

Exclusion criteria: a) autism and autism spectrum disorders; b) epilepsy; c) cognitive epileptiform disintegration; d) presence of identified genetic syndromes; d) traumatic brain injury; e) childhood stroke.

The authors analyzed the anamnesis data related to the prenatal and perinatal periods of development, the results of neurological examinations during the first year of life in their correlation with data on the motor and subsequent speech development, the results of neuropsychological examination at different age.

Clinical research bases: Center for Speech Pathology at Kazan Federal University, A. Yu. Ratner Children's City Clinical Hospital No. 8, Pediatric Republican Clinical Hospital, Millenium Clinic.

Results

Of the 525 children, 322 (61.3%) were found to have specific speech disorders as a result of neuropsychological and speech status examination, while 203 (38.7%) had non-specific speech disorders comorbid with delays in the development of other higher mental functions. In total, perinatal central nervous system damage at the age of 0 to 12 months was recorded in 506 out of 525 (96.3%) children. The main prenatal and perinatal risk factors for the development of speech disorders revealed as a result of the study: threatened miscarriage; the presence of infectious diseases in pregnancy; childbirth at a gestational age of up to 36 weeks; hyperbilirubinemia in the neonatal and perinatal periods; cerebral ischemia in the neonatal and perinatal periods; perinatal pathology of the central nervous system (diffuse muscle hypotonia syndrome, pyramidal insufficiency syndrome). Specific risk factors for the development of complex speech developmental disorders (both receptive and expressive speech) have not been revealed, which leaves open the question of the etiology of impressive speech development disorders and the reasons for the increase in the number of children with this pathology in recent decades.

Conclusions

Pediatricians and neurologists need to be especially vigilant when identifying these risk factors, especially if they are combined with motor development delays.

ABSTRACTS

Topic: Cerebrovascular Disorders

EPNS25_821 - Varicella Zoster Virus as a Possible Trigger for Moyamoya Syndrome in Down Syndrome: A Report of Three Cases

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Objectives

Moyamoya syndrome (MMS) is a rare cerebrovascular disorder marked by progressive stenosis of the intracranial internal carotid arteries (ICA), increasing stroke risk, with Down syndrome (DS) being a known predisposing factor. Additionally, Varicella Zoster Virus (VZV) infection is a well-known risk-factor for stroke. We investigated VZV's potential role in MMS progression in DS patients.

Methods

A retrospective review of three DS patients with MMS and VZV from our center.

Results

Case-1: A 10-year-old girl with DS presented to the Pediatric Emergency Department (PED) with right hemiparesis and speech difficulties. Brain MRI revealed a recent ischemic lesion. Angiography was consistent with MMS complicated by acute thrombosis of the left middle cerebral artery (MCA). Past VZV infection was documented at 3-years-old. She underwent endovascular treatment. Laboratory and cardiological findings were negative. Cerebrospinal fluid (CSF) analysis revealed intrathecal anti-VZV antibodies. The patient was started on oral aspirin (ASA) and antiviral therapy. Neuroimaging follow-up showed progression of MCAs stenosis. Repeated CSF analysis revealed borderline CSF anti-VZV IgG levels and antiviral therapy was re-administered. Subsequent MRIs showed no new lesions. She remained on ASA and exhibited no residual motor deficits.

Case-2: A 12-year-old boy with DS presented to the PED with left hemiparesis and slowed speech. Neuroimaging revealed a stroke secondary to right ICA dissection. The patient underwent endovascular intervention and was started on antiplatelet therapy. Past medical history revealed mitral valve prolapse, hypothyroidism. He received VZV vaccination. CSF analysis demonstrated intrathecal VZV IgG synthesis. He was started on ASA and antiviral therapy. Four years later, he was readmitted to the PED with aphasia and right-sided hemiparesis. Brain MRI revealed new left MCA ischemic lesions. Angiography showed left ICA stenosis progression. Diagnostic workup ruled out infectious or autoimmune causes. He underwent successful revascularization surgery.

Case-3: A 9-year-old boy with DS presented to the PED with left hemiparesis and slurred speech. Brain MRI revealed recent right ischemic lesions. Angiography showed asymmetric ICAs stenosis, predominantly of the right. Past medical history included previous VZV infection when 3-years-old. CSF analysis revealed intrathecal VZV IgG synthesis. He received ASA and antiviral therapy. Follow-up angiography confirmed bilateral vasculopathy, with progression of the right ICA stenosis.

Conclusions

DS-associated vascular abnormalities may predispose these patients to MMS. DS and MMS association is rare but well-reported in literature. VZV infection or reactivation may act as a precipitating factor for MMS-like arteriopathy, particularly in DS underlying vascular fragility and immune dysregulation.

ABSTRACTS

Topic: Neurogenetics

EPNS25_824 - Whole Exome Analysis in Seronegative Autoimmune Encephalitis: Insights from a Single-Center Study

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Objectives

Autoimmune encephalitis (AE) is characterised by inflammation of the brain parenchyma leading to neurological dysfunction. It encompasses a variety of aetiologies, with autoimmune causes being prominent. The hallmark of AE diagnosis is the detection of specific autoantibodies such as anti-NMDA, anti-GAD or anti-GABA A/B. However, in seronegative AE, these autoantibodies are absent, making diagnosis difficult. Recent research suggests that genetic predisposition and underlying immune sensitivities may contribute to the pathogenesis of AE. In addition, seronegative AE raises questions about its true autoimmune nature or potential association with other underlying diseases.

Methods

This study included 20 paediatric patients (10 female, 10 male) diagnosed with seronegative AE at Kocaeli University Medical Faculty, Department of Paediatric Neurology between 2010 and 2024. Whole exome sequencing (WES) was performed to investigate genetic predisposition. Inclusion criteria were based on the diagnostic framework for probable autoimmune encephalitis, excluding cases with identified pathogenic antibodies. Clinical data, neuroimaging findings, cerebrospinal fluid (CSF) analysis and response to immunotherapy were also evaluated.

Results

In the 20 patients included in the study, the most common clinical features were altered mental status, seizures and psychiatric symptoms. Neuroimaging and cerebrospinal fluid (CSF) analysis did not reveal any significant abnormalities. Genetic analysis has been completed for 11 patients: variants were identified in RANBP2 (2 patients), TH (1 patient, homozygous), CLN8 (1 patient, compound heterozygous), RNF213 (1 patient, compound heterozygous), NLRP12 (1 patient), MVK (1 patient, compound heterozygous), ADGRV1 (1 patient), ATRX (1 patient, hemizygous), SCN11A (1 patient), and CAMTA1, CILK1, and TBP variants were detected simultaneously in 1 patient. The genetic study for the remaining 9 patients is ongoing.

Conclusions

Our study highlights the potential role of genetic factors in the pathogenesis of seronegative AE. WES emerged as a valuable tool in uncovering genetic predispositions, aiding in the differentiation of seronegative AE from its mimickers. These findings underscore the need for integrating genetic studies into the diagnostic algorithm of seronegative AE, ultimately improving diagnostic accuracy and guiding personalized treatment approaches. Further large-scale studies are warranted to validate these preliminary results.

ABSTRACTS

Topic: Neurogenetics

EPNS25_825 - Diagnostic yield of deep phenotyping and reanalysis of genetic studies in patients with childhood-onset neurological disorders.

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Objectives

It is estimated that 50% of patients with neuropaediatric pathology of genetic origin do not receive a conclusive diagnosis. Review of previous genetic studies, including reanalysis of sequencing data, together with updated deep phenotyping of patients have been proposed to increase the diagnostic yield by 5% to 15%. This study aims to assess the diagnostic yield achieved through the application of deep phenotyping and genetic studies reanalysis in a cohort of patients with childhood-onset neurological disorders without an established aetiological diagnosis.

Methods

Cross-sectional study. Inclusion criteria: patients with paediatric-onset neurological pathology with inconclusive previous genetic studies and possibility of updated clinical phenotypic assessment. Reanalysis of the clinical exome or phenotype-driven extension to other genetic studies.

Results

A total of 161 patients were included, of whom 113 cases have been completed, while 48 remain ongoing. Among the completed cases, 13 achieved a definitive diagnosis following a critical review of previous inconclusive genetic results and phenotypic correlation. Nine cases were resolved through clinical exome reanalysis, four through functional studies of candidate variants identified in the reanalysis, and four through non-exome diagnostic techniques. Additionally, 15 cases were diagnosed via whole exome sequencing, while 68 remain unresolved.

Conclusions

The overall diagnostic yield of genotype-phenotype reassessment was 28.3%, with clinical exome reanalysis accounting for 40% of these diagnoses. Notably, deep phenotyping following a thorough review of genetic results enabled a definitive diagnosis in an additional 11.5% of cases. Integrating comprehensive genotypic and phenotypic reassessment into routine clinical practice is recommended to enhance diagnostic yield, improve clinical management, and optimize the efficient use of molecular diagnostic techniques."

ABSTRACTS

Topic: Neurogenetics

EPNS25_826 - Familial TSC: is it better for children to be born to parents with known TSC?

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Background and Objectives

Tuberous sclerosis complex (TSC) is associated with benign growths, early-onset drug refractory epilepsy and poor neurodevelopment. Around 1/3 of cases are inherited. Presymptomatic EEG monitoring and early treatment aims to improve outcomes. Therefore, optimising early (pre-seizure) diagnosis of children with TSC is of utmost importance, such as through family history. We aim to better understand the inherited cases in our TSC clinic and explore the impact of having a known family diagnosis on the child's care.

Methods

Familial TSC cases were ascertained through the TSC clinic database from 2010 to 2024. Retrospective review of medical records was performed.

Results

We identified 15/160 (9%) families to have familial TSC. Two thirds (10/15) were paternally inherited, while one third (5/15) was maternally inherited.

In 3 families, the diagnosis was known and communicated to the medical team prior to the child's birth. Early EEG monitoring, counselling regarding seizure presentation and timely antiseizure medications were able to be instigated, potentially leading to a better neurological outcome.

In 6 families, the diagnosis of TSC was known in a parent, but was concealed or forgotten until the child presented with either seizures (5) or obstructive hydrocephalus secondary to subependymal giant cell astrocytoma (1).

In one family, a parent had a solitary renal angiomyolipoma, but a diagnosis of TSC was not considered until their child presented with prenatal cardiac rhabdomyomas.

In another, a child apparently had a de novo TSC2 variant following segregation, but the mother subsequently developed multiple renal angiomyolipomas. She is presumed to be mosaic.

In 4 families, the child was the proband, presenting with infantile seizures or antenatal cardiac rhabomyomas. The parents were apparently unaffected, but segregation of the genetic variant revealed they carried the same variant as their child. Subsequently, 3 of 4 parents had TSC features on imaging.

Conclusions

This case series highlights the importance of counselling individuals regarding recurrence risk in this autosomal dominant condition prior to transitioning out of paediatric care to allow for earlier monitoring and management of affected children. It also showed the variability in presentation amongst family members in TSC, and the importance of segregating genetic variants even in apparently unaffected parents, as it may have health and management implications.

ABSTRACTS

Topic: Neurometabolic Disorders

EPNS25_827 - Case-based Rare Disease CME Significantly Improves Competence in Differentially Diagnosing Pediatric Patients With Hypotonia or Missed Motor Milestones

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Objectives

A diagnosis of MCT8 deficiency is easily missed in paediatric/neurology practice due to poor familiarity with this rare disease and failure to order or adequately interpret thyroid function tests for babies with hypotonia, missed motor milestones and/or other red flags. To increase the recognition and diagnosis of patients presenting with potential MCT8 deficiency, we developed a CME-accredited interactive online case-based educational activity featuring 2 cases for learners to diagnose.

Methods

Physicians worked through 2 cases, answering questions along the way with evidence-based feedback regarding correct responses (Tonduti D, Bauer A. *Hypotonia and Failure to Thrive: What's Your Next Step?* Available at www.medscape.org/viewarticle/hypotonia-and-failure-thrive-whats-your-next-step-2023a1000x81). The education effects were assessed using a 3-question, repeated pairs, pre-assessment/post-assessment study design. One question assessed confidence. Differences from pre- to post-assessment were evaluated using McNemar's test. The activity launched in February 2024 and data were collected through mid-January 2024.

Results

1,878 neurologists and paediatricians participated in the education, with 1,056 completing both cases and all pre- and post-assessment questions. Significant improvements were seen, with 36/135 (27%) neurologists having correct responses at baseline, improving to 99/135 (73%) post case completion (P<.001). The corresponding figures for paediatricians were 276/921 (30%) pre-assessment vs 792/921 (86%) at post-assessment (P<.001). In particular, significant improvements were observed in physicians' ability to differentiate MCT8 deficiency from a condition with a similar presentation and select the right diagnostic tests, as well as in their knowledge of the burden of MCT8 deficiency for patients and their families.

After participating in the activity, 44% of neurologists and 60% of paediatricians had measurable improved confidence in their ability to diagnose MCT8 deficiency.

Conclusions

This study demonstrates the success of online interactive case-based education in improving knowledge, competence and confidence in diagnosing a rare condition associated with hypotonia.

ABSTRACTS

Topic: Epilepsy: Diagnosis and Investigations

EPNS25_830 - To identify early electro-clinical predictors of Global Disease Outcome (GDO) in children with epilepsy onset within the first year of life

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Objectives

To identify early electro-clinical predictors of Global Disease Outcome (GDO) in children with epilepsy onset within the first year of life.

Methods

We conducted a retrospective analysis of 549 patients who experienced epilepsy onset within the first year of life, selected from 3,606 children who underwent EEG between 2008 and 2020. Exclusion criteria: acute provoked seizures only and follow-up of less than one year. At the time of epilepsy onset, we collected data on neurological examination (normal/pathological), seizure type (focal, spasms, polymorphic), background activity (normal/pathological), EEG abnormalities (absent/focal/multifocal/diffuse), MRI results (normal/pathological), and age. GDO was derived through clustering analysis, which combined neurological examination, intellectual disability, and epilepsy outcomes at the last follow-up. It ranged from level 0, indicating a normal outcome, to level 3, signifying the most severe outcome. Levels 1 and 2 indicate an intermediate degree of disability.

Results

The average age of epilepsy onset was 4.02 months (range: 0–12), and the mean follow-up duration was 5.6 years (range: 1–14.7). All onset features had significant correlations with GDO ($p<0.05$). Pathological neurological examinations were correlated with levels 2 (17.49%) and 3 (28.96%). Focal seizures were linked to levels 2 (25.11%) and 3 (33.33%), while spasms (31.5%) and polymorphic seizures (47.86%) were associated with level 3. Pathological background activity and multifocal EEG abnormalities were associated with levels 2 (18.48%, 11.66%) and 3 (27.14%, 18.58%), respectively. Pathological MRI was correlated with levels 2 (11.48%) and 3 (12.75%). An earlier age of onset was associated with level 3 (mean: 2.24 ± 3.2 months).

Conclusions

Electro-clinical features at epilepsy onset correlate with GDO levels and can predict disease severity. These findings highlight the prognostic value of early assessments in guiding management and predicting outcomes.

ABSTRACTS

Topic: Infectious and Inflammatory Diseases/ Neuroimmunology

EPNS25_831 - Myelin oligodendrocyte glycoprotein antibody associated disease (mogad) in children –experience of threecenters

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Objectives MOGAD is a rare, relatively newly described demyelinating disorder of the CNS, presenting with various phenotypes such as optic neuritis (ON), transverse myelitis, acute demyelinating encephalomyelitis (ADEM), cortical encephalitis etc. Clinical presentation, disease course and prognosis differ among adults and children, as the latter demonstratea rather indolent and diffuse initial attack, better recovery, fewer relapses, and less need for chronic immunomodulation therapy. Our aim is to retrospectively present a case series of children in the MOGAD spectrum from three Pediatric Neurology Centers.

Methods 16 children (8 males, 8 females) from the Pediatric Neurology Departments of the Children's Hospital "P. & A. Kyriakou", "Attikon" University Hospital and the Pediatric Department of "PA.G.N.I." are included. Demographic data, clinical presentations, disease course, treatments given, relapses and disease prognosis are presented

Results Median age at disease presentation was 9 years old (3.5 – 15 years).The most frequent initial clinical presentation was ADEM (37.5%) followed by optic neuritis (25%). Other initial clinical manifestations included: four patients (25%) with cerebral (ADEM-ON, FLAMES, FUEL) and cerebellar syndromes, one with NMOSD and one with combined central and peripheral demyelination (CCPD). All patients were treated with intravenous methylprednisolone at initial episode. 37.5% of them required additional intravenous immunoglobulin administration, while two (12.5%) required also plasmapheresis. Almost all patients experienced complete recovery after induction therapy. All received oral prednisolone for a median of 3 months (1–6 months). Disease relapsesincluding ADEM, ON, cerebral and cerebellar syndromes and CCPD occurred in 6 patients (37.5%). They received maintenance treatment with Rituximab (3 patients) or MMF (mycophenolate mofetil) and responded well, except for the FUEL patient, who relapsed on Rituximab and remains asymptomatic under MMF treatment.

Conclusions MOGAD presents clinical heterogeneity in children. Clinical phenotypes are enriched as our knowledge expands regarding this entity. Although most patients present with monophasic disease course which responds well to steroids, a significant proportion will relapse. The majority of patients with recurrent MOGAD respond well to maintenance therapy.

ABSTRACTS

Topic: Movement Disorders/ Cerebral Palsy

EPNS25_832 - Alternating Hemiplegia of Childhood Rating Scale: creation and validation of a disease specific clinical outcome measure

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Objectives

To present a specific clinical outcome measure for Alternating Hemiplegia of Childhood (AHC), developed in the setting of a granted project focused on the identification of possible candidate treatments.

Methods

The AHC scale has been designed by 4 experts in AHC and revised by 2 experts in movement disorders. It is divided into 4 parts: Paroxysmal Score (6 subscores: the Paroxysmal Dystonia Index, the Paroxysmal Plegic Index, the Paroxysmal Mixed Index, the Ocular Abnormalities Index, the Autonomic Abnormalities Index), Epilepsy Score, Non Paroxysmal Score, Adaptive Score. The Non Paroxysmal Score rates muscle tone, dystonia, parkinsonism, other movement disorders, gait, dysarthria, swallowing, psychiatric features, cognition/psychomotor development, language. The Adaptive Score addresses feeding, dressing, handwriting, hygiene and socialization. From October 2022 to November 2023 the scale has been tested by 4 raters on 48 Spanish, French and Italian individuals with a clinical diagnosis of AHC: 22 males and 26 females (mean age: 18.6 yrs [SD: 12.4], range 2-48 yrs). Patients have been examined according to a standardized video protocol. In the Italian and French cohort, the Burke-Fahn-Marsden Scale (BFMS) has been administered to determine the interrater-reliability.

Results

The statistical analysis has shown a good interrater-reliability both on global scores and single items (Intra-class Correlation Coefficient -ICC ranging from 0,95 to 0,99). A significant correlation has been observed on 31 patients between the AHC total Score and the BFMS (rho=0.58; $p<0.001$). As far as Internal Consistency is concerned, an excellent correlation has been found between the Non Paroxysmal Score and Adaptive Score (r=0.74; $p<0.001$), the AHC Total Score and the Paroxysmal Score, the Non Paroxysmal Score, the Adaptive Score and with both subscales of the BFMS ($p<0.001$). Thera has been no statistically significant correlation between Paroxysmal e Non Paroxysmal Scores (r=0.21; $p=0.15$).

Conclusions

The interrater-reliability of the AHC scale is "almost perfect", according with Landis and Koch Criteria (P above 0.81). Construct validity and internal consistency are good, they confirm that AHC Paroxysmal and Non Paroxysmal features are independent and that, in adult age, the disease "burden" is linked with non paroxysmal, chronic features and impaired adaptive abilities. The AHC scale appears to be a promising tool for outcome measure and genotype-phenotype correlation.

ABSTRACTS

Topic: Neurodevelopmental Disorders / Developmental Neuroscience

EPNS25_834 - Precision Therapy Approaches in Pediatric Patients with Monogenic Neurodevelopmental Disorders

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Objective/Hypothesis

In patients with monogenic neurodevelopmental disorders (mgNDDs), clinically relevant precision therapies can be identified through structured research of medical and genetic databases.

Methods

At the Center of Rare Developmental Disorders, kbo-Kinderzentrum Munich, a structured online search using 14 databases is carried out for every genetic diagnosis. In this retrospective observational study, we analyze the precision therapies found, offered and carried out in pediatric patients with mgNDDs presenting 01/06/2021–31/12/2024. Therapy approaches are divided into CNS-directed and non-CNS-directed approaches, as well as approved therapies, interventional clinical trials and off-label targeted therapies. In-center initiated off-label therapies are evaluated for effectiveness.

Results (preliminary, data-cut on 15/01/2025)

Database searches were carried out for 221 NDD genes (376 patients). CNS-directed precision therapy approaches could be identified for 57/221 mgNDD genes (26%): 10 approved therapies for 7 mgNDDs (3%), total of 65 interventional clinical trials for 31 mgNDDs (14%), and 62 off-label targeted therapies for 47 mgNDDs (21%). 54/376 patients received a precision therapy (14%): an approved targeted therapy in 2/375 patients (0.5%), an investigational product within an interventional clinical trial in 4/375 patients (1%), and an off-label targeted therapy in 49/375 patients (13%). Out of the 44 off-label therapies initiated at our center, the effectiveness could be evaluated in 25 cases, 15 therapy evaluations were still in progress and 4 treatments could not be evaluated for other reasons at the time of the data-cut. Positive effects leading to a long-term treatment, documented through developmental tests and/or quality of life questionnaires were documented in 18/25 cases, no or minimally positive effects in 7/25 cases. The therapy acceptance was high (90%).

Conclusions

Structured database searches revealed clinically relevant precision therapy options for pediatric patients with mgNDDs. Approved targeted therapies and enrollments in interventional clinical trials were significantly less common (0.5-1%), than drug-repurposing (13%). Drug-repurposing, although certainly not able to heal all symptoms, seems to be an available and potentially beneficial therapeutic option in this cohort. Further studies in a larger cohort for each mgNDD and consequently applied test batteries are necessary to decide on the clinical relevance of the identified drug-repurposing options.

ABSTRACTS

Topic: Neuropsychiatric Disorders / Functional Neurological Disorders

EPNS25_835 - Brain dismorphism in in adolescents with conduct disorder and psychopathic traits

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Objectives We found electrophysiological differences specifically related to the influence of sex on psychopathic traits. .

Methods The resting electroencephalography (EEG) activity and low-resolution brain electromagnetic tomography (LORETA) for the EEG spectral bands were evaluated in 38 teenagers with conduct disorder (CD). The 25 male and 13 female subjects had psychopathic traits as diagnosed using the Antisocial Process Screening Device. All of the included adolescents were assessed using the Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition, Text Revision (DSM-IV-TR) criteria. The visually inspected EEG characteristics and the use of frequency-domain quantitative analysis techniques are described

Results Quantitative EEG (QEEG) analysis showed that the slow-wave activities in the right frontal and left central regions were higher and the alpha-band powers in the left central and bitemporal regions were lower in the male than the female psychopathic traits group. The current source density showed increases in paralimbic areas at 2.73 Hz and decreases in the frontoparietal area at 9.37 Hz in male psychopathics relative to female psychopathics

Conclusions These findings indicate that QEEG analysis and techniques of source localization can reveal sex differences in brain electrical activity between teenagers with CD and psychopathic traits that are not obvious in visual inspections.

ABSTRACTS

Topic: Neurodevelopmental Disorders / Developmental Neuroscience

EPNS25_837 - Homozygous MDGA2 loss-of-function variants cause developmental and epileptic encephalopathy

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Objectives: Developmental and epileptic encephalopathies (DEEs) encompass a diverse group of disorders caused by pathogenic variants in genes that impair normal brain function. However, a substantial proportion of DEE patients remain without a definitive genetic diagnosis. As part of our SYNAPS project, we aimed to identify the genetic causes of DEE in unsolved cases from our Queen Square cohort of individuals with neurodevelopmental disorders.
Methods: Through the SYNAPS project and GeneMatcher, we identified four families carrying homozygous *MDGA2* variants. Proband-only whole exome sequencing (WES) was performed for all families, and variants and inheritance were confirmed by Sanger sequencing in available family members. We also examined the biochemical, cellular and ligand-binding criteria of MDGA2 nonsense variants using a mammalian cDNA expression vector.
Results: In this study, we identified homozygous variants in *MDGA2* on five individuals with DEE from four unrelated families. The homozygous *MDGA2* variants include two nonsense variants, one splice variant and a homozygous deletion of exon 3. Notably, patients with the various *MDGA2* variants exhibited similar clinical phenotypes, marked by severe early-onset DEE, severe neurodevelopmental impairment, regression of acquired milestones, abnormal movements, a progressive disease course, and distinctive dysmorphic features, strongly suggesting that there is a causative relationship between *MDGA2* loss-of-function mutations and DEEs. Systematic functional studies showed that the tested nonsense variants of MDGA2 displayed impaired membrane transport and, in comparison to wild-type MDGA2, lacked the ability to negatively modulate synapse number, synaptic transmission, and synaptic strength at glutamatergic synapses in cultured hippocampal neurons.
Conclusions: Collectively, our results provide compelling evidence that *MDGA2* loss-of-function is associated with a new autosomal recessive DEE and emphasize that MDGA2 may be a relevant therapeutic target for mitigating the symptoms of DEEs.

ABSTRACTS

Topic: Neurogenetics

EPNS25_838 - Impact of Everolimus treatment in Tuberous Sclerosis Complex

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Objectives: Tuberous sclerosis complex (TSC) is a syndrome caused by a mutation in the TSC1 or TSC2 gene with multiple organ involvement manifested by various benign and malignant tumors with different localizations. TSC is an important cause of epilepsy and autism, as well as lung and kidney disorder in adults and children. Secondary to mutation in TSC genes, inhibition of the mTOR pathway is impaired, resulting in aberrant cell proliferation. As a result, mTOR inhibitors, including Everolimus, have significant therapeutic potential in the treatment of tuberous sclerosis.The aim of this study is to highlight the effects of Everolimus treatment on children with Tuberous Sclerosis.

Methods: This study is a retrospective analysis of the medical data recorded electronically and on paper files of TSC cases hospitalized in our clinic in the last 4 years from January 2020 until december 2024 (search keywoeds: TSC, Tuberous sclerosis complex). We reviewed the main characteristic signs of Tuberous Sclerosis, emphasizing the evolution of patients on Everolimus treatment.

Results: Of the 76 patients hospitalized during the above mentioned period, 35 had subependymal giant cell astrocytoma (SEGA), 36 had cardiac rhabdomyomas, 37 angiofibromas, 72 had epilepsy, 24 autism, and renal imaging changes were noted in 32 patients. The 29 patients who received treatment with mTOR inhibitors were further evaluated - thus 27 patients were included in the national program on the presence of SEGA criterion and 2 for drug-resistant epilepsy. In 17 patients out of the 27 treated with Everolimus, the SEGA volume decreased, while in 7 patients it was stationary, and in 3 cases it continued to evolve. In 6 patients the frequency and duration of epileptic seizures decreased, and renal angiomyolipomas improved in 4 patients.

Conclusions: At present, the occurrence of SEGA or drug-resistant epilepsy are criteria for inclusion in the National Program of Everolimus treatment, but it is necessary to evaluate the evolution of the patient from all points of view, both the progression of SEGA over time and the changes in the various signs present in this tuberous sclerosis complex (epilepsy, angiofibromas, autism, renal changes). Everolimus treatment has a positive effect on SEGA but also on renal lesions and epilepsy.

ABSTRACTS

Topic: Epilepsy: Diagnosis and Investigations

EPNS25_839 - Lennox-Gastaut Syndrome criteria: linking clinical and electroencephalografic features

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Objectives The International League Against Epilepsy (ILAE) had recently revised Lennox-Gastaut Syndrome (LGS) diagnostic criteria, emphasizing the importance of electroencephalographic features, but not specifying the duration of Generalized paroxysmal fast activity (GPFA). Regardless of their duration, GPFA have been correlated with increased epileptic activity, but there was no evidence about their correlation with clinical criteria. We aimed to identify electroclinical differences among patients with LGS clinical criteria referred to our center.

Methods We analysed electroencephalographic criteria with descriptive statistics and clinical features with regression techniques. We marked GPFA if duration was longer than one second, Generalized Polyspike Train (GPT) if shorter (Conrad EC et al. Using Generalized Polyspike Train to Predict Drug-Resistant Idiopathic Generalized Epilepsy. J Clin Neurophysiol. 2022 1;39(6):459-465).

Results Among 90 patients identified, 28 had GPFA, 13 had GPT, 23 had Slow-Spike-and-Wave (SSW) complexes but had not GPT and GPFA, 26 had none (Null). GPT+GPFA group differed from SSW+Null because of an higher mean age of onset (1.83 vs 0.98 years, p-value 0.005), more frequently genetic etiology (51% vs 31%, p-value 0.047) and shorter seizure-free intervals (one-year seizure-free 2% vs 18%, p-value 0.015).

The GPFA group compared to remaining subjects had less cognitive (86% vs 97%, p-value 0.051) and motor impairment (39% vs 63%, p-value 0.034), but more psychiatric comorbidities (39% vs 18%, p-value 0.028). They had higher seizure burden than GPT group (weekly seizures 82% vs 38%, p-value 0.005). We found a trend towards more spasms in GPFA group than others (54% vs 27%, p-value 0,056).

Conclusions The GPFA group presents worse epilepsy, but less cognitive and motor impairment compared to those without LGS criteria. The GPFA+GPT group presents more frequently genetic etiology and higher mean age of onset than SSW+Null. These data suggest a correlation between clinical and electroencephalographic criteria, which could be relevant for patients' selection/stratification.

ABSTRACTS

Topic: Movement Disorders/ Cerebral Palsy

EPNS25_840 - Repetitive neuromuscular magnetic stimulation as novel intervention for children and adolescents with upper motor neuron syndrome

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Objectives

Due to impaired or missing selective motor control in patients with upper motor neuron syndrome (UMNS) neurorehabilitation is often limited. Neurostimulation has emerged as an approach for enhancing motor function by externally activating the respective muscles. This study examines repetitive neuromuscular magnetic stimulation (rNMS) targeting the tibialis anterior muscle (TAM) combined with functional physiotherapy (frNMS).

Methods

In this prospective study twelve children (8.9 ± 1.6 years) and ten adolescents (14.15 ± 1.8 years) affected by UMNS underwent one week of conventional physiotherapy followed by one week of frNMS training targeting the TAM. Clinical outcome measures including walking speed, strength of the ankle dorsiflexors and plantar flexor spasticity as well as patient reported outcomes were measured at baseline and after each study week.

Results

frNMS was found to be a safe method (no AEs in >84% of the sessions) with no sessions omitted due to adverse events (AE). The most common AE was a tingling sensation at the stimulation site (7.1% of the children's and 23% of the teenagers' sessions). 100% of adolescents and 83.3% of children would repeat and recommend the treatment. Therapists positively evaluated its practicability. On an individual level, measurements demonstrated clinically meaningful effects on the strength of ankle dorsiflexor in 4 adolescents and 5 children. For ankle plantar flexors spasticity, a decrease was observed in 4 adolescents and 4 children. Improvements in the Gait Outcomes Assessment List were observed for 24 items from the patient's and for 22 items from the caregivers' perspective. The 10 Meter Walking Test demonstrated no change for both age groups.

Conclusions

frNMS can be considered a well-tolerated, feasible and safe intervention. These findings underline the importance of further large-scaled, controlled studies to explore muscular and central effects and underlying mechanisms to establish frNMS as a therapeutic option for neurological conditions, particularly in the rehabilitation of congenital or acquired brain injuries.

ABSTRACTS

Topic: Neurodevelopmental Disorders / Developmental Neuroscience

EPNS25_841 - The Neurodevelopmental Challenges of Stuttering in Preschool Children: A Study from Uzbekistan

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Objectives: More than 70 million people, are suffering from logoneurosis. Numerous hypotheses on the psychophysiological mechanisms and causes of stuttering highlight the need for further in-depth study of this speech disorder. This study aims to determine the degree of severity of central nervous system neurological disorders in children with stuttering.

Methods: A study was conducted on 20 children with logoneurosis aged 5-7 years (13 boys and 7 girls). All children underwent examinations using commonly accepted neurological methods and assessments of higher mental functions using a special test card (Kondratyev S.Yu., 2010, and Noskova O.V., 2017).

Results: Analysis of neurological changes in the examined children revealed convergent strabismus in 2 children, enuresis in 4 children, hypotonia in 15 children, hypertonicity of tendon reflexes in 13 children, and impaired coordination of movements in 7 children. There was statistically significant difference between boys and girls ($P > 0.05$, using one way ANOVA followed by Tukey HSD test). The results of the study of higher mental functions using a special test card revealed a decrease in attention and memory in 20 children, a decrease in abstract thinking in 17 children, and changes in the emotional sphere (appearance of fear, anxiety, aggression, avoidance of communication) in 20 children.

Conclusions: The neurological symptoms in the examined children were characterized by a scattered localization, indicating the absence of a specific lesion center. Specifically, there are disturbances in the pyramidal and extrapyramidal control of the speech motor system and disruptions in higher mental functions.

ABSTRACTS

Topic: Neurometabolic Disorders

EPNS25_842 - Neuronal ceroid lipofuscinosis – pre-treatment versus post-treatment era

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Objectives: The neuronal ceroid lipofuscinoses (NCLs) are a heterogeneous group of neurodegenerative lysosomal storage disorders primarily affecting the brain and the retina of children and young adults. While various therapeutic strategies are currently being explored, there is presently one clinically approved drug that has been shown to effectively attenuate the progression of CLN2 disease (cerliponase alfa, a lysosomal enzyme infused into the brain ventricles of patients with CLN2 disease). The aim of this study is to show how the emerging diagnostic and therapeutic methods have changed the management and prognosis of our clinic's NCL patients.

Methods: This is a retrospective analysis of the medical data recorded electronically and on paper files between January 2005 and December 2024 of the patients diagnosed with neuronal ceroid lipofuscinosis. There were included the patients with a clinical picture of NCL that refused or couldn't perform any diagnostic tests, but also those who performed either skin/conjunctiva biopsy or genetic testing. The following are some of the most important data assessed: demographic data, age of onset, early and late symptoms, evolution, global developement, laboratory and MRI findings.

Results: There were 28 cases of NCL, 13 of them had a NCL clinical picture, but no biopsy or genetic tests were performed, 3 of them had a suggestive skin/conjunctiva biopsy, 12 of them were genetically tested (6 with NCL7, 6 with NCL2). The onset of symptoms was at different ages: in 19 cases at 3-4 years old, at 1-2 years in 7 children, in one child at 6 years, and in another case at 12 years. In 15 patients the onset was with seizures, while ataxia, cognitive and motor deterioration were the first symptoms in 13 children. All children had cerebellar atrophy on MRI. Out of the 6 patients diagnosed with CLN2, 4 received intraventricular infusions with cerliponase alfa, with slower symptom progression.

Conclusions: In the last 20 years diagnostic and therapeutic options in NCL have significantly developed. Even though NCL remains a challenging pathology with a decreased life expectancy, the enzyme replacement therapy improves the quality of life in children with CLN2. The high clinical suspicion and the better access to genetic testing increases the chance of an early treatment in children with NCL. Furthermore, the ongoing research in the pathophysiology and treatment options in NCL allows us to hope for a better prognosis for our little patients in the future.

ABSTRACTS

Topic: Infectious and Inflammatory Diseases/ Neuroimmunology

EPNS25_843 - Higher fitness levels associate with higher brain volume and lower lesion volume in youth with Multiple Sclerosis

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Objectives

Previous studies have shown that higher levels of cardiorespiratory fitness (CRF) are associated with greater hippocampal volume and cognitive function in rodents and healthy adults. We seek to explore this connection in youth with Multiple Sclerosis (MS) Our objectives were to determine the relationship (1) between CRF and brain lesional volume, and (2) between CRF and regional brain volume in youth with MS.

Methods

Youth with MS (≤ 19 y/o) were recruited from the Hospital for Sick Children (Toronto, CA). CRF levels were assessed by performing a cardiopulmonary exercise test on a cycle ergometer, assessing peak oxygen consumption (VO_2 peak), maximal heart rate and maximal workload (watts). MRI scans of MS patients were performed following a standardized protocol. De-identified FLAIR MRI sequences were processed using FreeSurfer version 7 (Massachusetts General Hospital, Harvard Medical School). A semi-automated segmenting tool (3D Slicer) was used to determine the lesion volume (cm^3) on FLAIR MRI sequences closest in time to the performed exercise test. To compare the CRF levels of our youth with MS with a healthy Canadian population of youth, the 'New Reference Values for Cardiopulmonary Exercise Testing in Children' (Blanchard et al.) were used to calculate z-scores. Descriptive and correlational statistics were performed (JASP 0.19.1.0).

Results

33 youth with MS (26 F; median age 16.3 years, IQR 1.91) were included. The MS group had z-scores indicating lower fitness levels when compared to normative values (mean z-score for VO_2 peak -1.2, max HR -1.3, and max workload -2.2). Higher lesion volume was associated with lower VO_2 peak z-scores (r=-0.363, p=0.038). The higher the volume in the whole brain and the thalami the higher the VO_2 peak values (r=0.526, p=0.002 and r=0.417, p=0.02, respectively) and max workload values (r=0.495, p=0.005 and r=0.362, p=0.045, respectively). Maximum workload was also higher in youth with greater hippocampal dentate gyrus volume (r=0.439, p=0.014).

Conclusions

Youth with MS have lower CRF levels in comparison to normative data from healthy children. Higher fitness levels are associated with higher dentate gyrus head volume and lower lesional volume in youth with MS. Higher fitness may be protective in MS, but the directionality of this relationship is unknown due to the cross-sectional nature of this study. Future longitudinal studies are needed.

ABSTRACTS

Topic: Epilepsy: Diagnosis and Investigations

EPNS25_845 - Epileptic and neurodevelopmental outcome at 24 months after neonatal hypoxic-ischemic encephalopathy

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Objectives

This retrospective, dual-center Italian study assessed the incidence, electroclinical features, and risk factors for post-neonatal epilepsy in neonates with hypoxic-ischemic encephalopathy (HIE) treated with therapeutic hypothermia (TH). Although previous studies have examined risk factors, few have investigated their relevance at different time points.

Methods

We included neonates with HIE2 and HIE3 who underwent TH. Neurological examination and General Movements were assessed before and after TH. Conventional EEGs (cEEG) were performed within 6 hours of life and after TH (72 hours to 10 days). Brain MRI was conducted within 30 days. Developmental outcomes were evaluated at 24 months using Griffiths Mental Development Scales. Polygraphic EEG was performed at 3-9-12-24 months and annually thereafter. The median follow-up duration was 48 months. Epilepsy was classified based on ILAE criteria.

Results

We enrolled 159 patients. Patients with epilepsy were 15/159 (9.4%): 9/159 (5.6%) with onset before 24 months (range 1-21 months); among them, 8 patients' onset was before 6 months of age, 4 of them in the first month of life. These 4 patients presented later with Infantile Epileptic Spasm Syndrome (IESS). Seizures' onset was after 24 months in 6/159 individuals (3,7%). At the last follow-up, all 15 patients have focal epilepsy. Global development was normal in 4 patients, and in 11/15 was pathological (10/15 <2DS; 1/15, <1DS). Identified risk factors for post-neonatal epilepsy included: MRI lesions involving the basal ganglia and thalamus ($p < 0.0001$), encephalopathy ($p = 0.0008$), previous neonatal seizures ($p = 0.0014$), severe anomalies on the cEEG recorded after 6 hours of life ($p = 0.0032$) and after hypothermia ($p = 0.0071$).

Conclusions

Our study confirms post-neonatal epilepsy after HIE2/3 is rare and generally well-controlled. MRI and early EEG are key predictors. High-risk patients should be screened for IESS in early months and continue long-term neurological follow-up beyond 24 months.

ABSTRACTS

Topic: Epilepsy: Medical and Surgical treatment

EPNS25_846 - Focal seizures evolving to epileptic spasms: similar semiology, different etiology and treatment in 2 cases

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Objectives

The coincidence of focal seizures and epileptic spasms has been described previously, especially when an underlying structural lesion is present. Early treatment of epileptic spasms is important to prevent further neurodevelopmental regression and therefore combination of vigabatrin and corticosteroids/ACTH are considered first line therapy. Underlying etiology can help guide therapy, but is often not known at time of presentation. Here we present 2 cases with focal seizures evolving to epileptic spasms with a different etiology and different response to treatment.

Methods

Patient records, brain MRI and EEG recordings of these 2 patients were reviewed retrospectively.

Results

The first patient presented at the age of 2 months with focal seizures arising from the right frontal region with secondary generalisation. Brain MRI was normal. Treatment with phenobarbital was initiated, but one month later, developmental regression occurred, as well as recurrent seizures. On ictal video-EEG recording, focal to secondary generalised seizures ending in a cluster of clinical and electrographical spasms was seen. Corticosteroids were started, followed by levetiracetam and vitamin B6, but without effect. Given the focal onset of the seizures, a trial with carbamazepine was initiated, after which EEG normalised and seizures disappeared. The patient regained positive developmental improvement. Trio WES analysis revealed a de novo likely pathogenic variant in *GRIN1*.

The second patient was diagnosed prenatally with right frontal closed loop schizencephaly lined by polymicrogyric cortex. Genetic testing (micro-array and trio-WES analysis) remained negative. At the age of 16 months focal seizures arising from the right frontal region with evolution to a cluster of spasms were seen on ictal video-EEG monitoring. The combination of focal seizures alone and focal seizures with evolution to spasms, without hypsarrhythmia, at > 1 year of age, led us to the initiation of carbamazepine, which was not effective. Seizures were well controlled after treatment was switched to vigabatrin.

Conclusions

Epileptic spasms occurring around 6 months of age are mostly seen as part of infantile epileptic spasms syndrome, for which early treatment is important to improve neurodevelopmental outcome. Although in general the first line treatment option is a combination of vigabatrin and ACTH/steroids, alternative options might be effective in selective cases. Focal seizures evolving to epileptic spasms might have a common cellular mechanism for seizure initiation, as proposed by Traub et al in 2019. Alternative treatment strategies might therefore be considered, even including sodium channel blockers as illustrated in the first example.

ABSTRACTS

Topic: Epilepsy: Diagnosis and Investigations

EPNS25_847 - E/I regulation in neurodevelopmental disorders: EEG investigation of children with GNAO1-related disorders

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Objectives: Gαo, encoded by the GNAO1 gene, is a subunit of a heterotrimeric guanine nucleotide-binding protein expressed in the brain. It plays a pivotal role in regulating neuronal excitability and neurotransmission. Patients with variants in GNAO1 exhibit a spectrum of epileptic and non-epileptic phenotypes, including severe developmental delay, hypotonia, and movement disorders. Given the intricate nature of cortical networks, a delicate coordination of excitatory and inhibitory inputs is essential for normal information processing. Changes in either direction of the excitatory/inhibitory (E/I) ratio may lead to neurodevelopmental disorders. This study aims to analyze E/I ratio changes in children with GNAO1-related disorders (GNAO1-RD) and correlate these alterations with the severity of the overall clinical presentation and specific symptoms.

Methods: We conducted an observational study involving 12 children with GNAO1-RD caused by pathogenic variants and 36 age-matched, typically developing controls (TDC). EEGs were recorded during eyes-closed rest. Clinical evaluations included scales for epilepsy, movement disorders, motor and language development, and an overall severity score. Molecular assessments of *GNAO1* variants used bioluminescence resonance energy transfer (BRET) assays. Quantitative EEG measures included spectral power, aperiodic exponent, long-range temporal correlations (LRTC), and functional E/I ratio (fE/I). Statistical analyses incorporated permutation tests and cluster-based enhancements.

Results: Children with GNAO1-RD exhibited elevated delta power and reduced alpha power compared to TDC. Higher delta power correlated with more severe epilepsy and pronounced molecular dysfunction, while lower alpha power was associated with overall clinical severity. Stronger alpha and beta-band LRTC were observed in GNAO1-RD, reflecting altered network dynamics. Reduced alpha-band fE/I ratios suggested a network state dominated by inhibition, potentially compensating for hyperexcitability. Developmental differences were evident as age-related decreases in delta power observed in TDC were absent in GNAO1-RD.

Conclusions: This study identifies quantitative EEG abnormalities in GNAO1-RD, characterized by increased delta power, decreased alpha power, and disrupted network dynamics indicative of an inhibition-dominant state. These findings align with molecular dysfunction caused by GNAO1 variants, highlighting the role of GNAO1 in maintaining E/I balance. The results provide neurophysiological insights into GNAO1-RD pathophysiology and suggest potential biomarkers for assessing disease severity and therapeutic interventions.

ABSTRACTS

Topic: Epilepsy: Diagnosis and Investigations

EPNS25_850 - Using TSC neuroradiological features on early MRI as biomarkers of epilepsy and developmental outcome at 5 years – a single-centre cohort study

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Objectives

Cortical tubers, subependymal giant cell astrocytomas (SEGA) and subependymal nodules (SEN) are the neuroimaging hallmarks of Tuberous Sclerosis Complex (TSC). Previous studies suggest that imaging-based biomarkers may useful in predicting outcomes in TSC. Our study aims to describe the prevalence of these neuroimaging markers and to correlate them with epilepsy and developmental outcomes at 5 years.

Methods

This is a retrospective single-centre cohort study of children with TSC who had MRI brain performed between 18-36 months. Tubers, SEN, SEGA, cerebellar and radial migration line involvement were quantified for each scan. Seizure outcome at 5 years was categorised as either poor (at least monthly seizures) or favourable (<monthly). Drug resistant epilepsy (DRE) was defined as having trialled more than 2 antiseizure medications. Developmental outcomes comprised of adaptive function assessed using the Vineland-III and a diagnosis of Autism Spectrum Disorder (ASD) before 5 years. Neuroradiological markers were compared between epilepsy and developmental outcome groups. Fisher’s exact test, unpaired t-test, odd ratios, Pearson correlation and binary logistic regression were performed. Receiver operating characteristic (ROC) curves were used to investigate the diagnostic accuracy of radiological variables.

Results

All 39 children had cortical tubers with a median of 20.5 (IQR 29 – 33). There was no difference between tuber counts of the poor seizure outcome group compared with the favourable seizure outcome group. However, children with DRE had higher total tuber count (31.5 vs 9.5, p=0.0007) and SEN count (9.0 vs 7.0, p=0.004) compared to children without DRE. Children with impaired adaptive function had more total tubers (33.0 vs 22.0, p=0.026) and frontal tubers (15.0 vs 11.0, p=0.023) than children with age-appropriate adaptive function. Children with ASD had more total tubers (32.0 vs 25.5, p=0.049) and frontal tubers (14.5 vs 11.0, p=0.013) than children without ASD. Multivariable logistic regression showed DRE is associated with higher cortical tuber count independent of early onset of seizures. However, tuber count was not a significant predictor of adaptive function or ASD at 5 years in the presence of poor epilepsy outcome. ROC curve results showed having more than 22.5 tubers was associated with a likelihood ratio of 4.4 for developing DRE (sensitivity 73%, specificity 83%).

Conclusions

Total tuber count on early MRI may be useful as a predictor of DRE, but did not independently predict impaired adaptive function and ASD at 5 years. Poor epilepsy outcome is a significant risk factor for both developmental delay and ASD.

ABSTRACTS

Topic: Movement Disorders/ Cerebral Palsy

EPNS25_851 - Functional repetitive neuromuscular magnetic stimulation of the gluteal muscles as a novel therapeutic approach for children and adolescents with bilateral spastic cerebral palsy

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Objectives: Minors with bilateral spastic cerebral palsy (BSCP) experience motor impairments caused by the triad of limited selective motor control, muscular weakness and spasticity. A novel therapeutic approach combines non-invasive neurostimulation by repetitive neuromuscular magnetic stimulation (rNMS) with conventional physical exercises. Here we present first real-world experience with functional rNMS (frNMS).

Methods: In this prospective study 8 patients aged 10.4 ± 2.5 years with BSCP (GMFCS level II-III) received frNMS targeted to gluteal muscles (12 sessions in 3 weeks). The Canadian Occupational Performance Measure (COPM) interview was conducted at baseline and at follow-up after 6 days and 6 weeks following the last frNMS session. Assessments included: 10-m- and 6-min-walking-test and GMFM-66 at baseline and within 6 days after the last intervention. The Gait Outcome Assessment List (GOAL) was completed at baseline and 6 weeks after the last session.

Results: COPM reported clinically important improvements of performance for 28% and satisfaction for 42% of mobility-related tasks evaluated by caregivers at least once during the follow-up period. On an individual level, 4 patients and 3 caregivers indicated improvements in at least one domain of the GOAL, respectively. The total score of GMFM-66 improved significantly by 1.4% ($p = 0.002$), as did the score in domain E (walking, jumping, and running (2.6%, $p = 0.021$)). In addition, a clinically meaningful enhancement was observed in domain D (standing (1.9%, $p = 0.109$)). There was no improvement in gait speed or distance walked during the 6-minute walking test. In 77.1% of sessions, no adverse events occurred. In 16.7%, participants reported tingling sensations, in 6,3% feelings of pressure, warmth, or cold and in 5,2% brief pain. The frNMS intervention was well-accepted (100% adherence) and highly feasible (97.9% protocol compliance). All participants would repeat the frNMS intervention, and 87.5% would recommend it to others.

Conclusions: frNMS is a promising approach for young patients affected by BSCP, due to its non-invasiveness and good acceptance aiming at improving mobility and participation. To further investigate the effects of frNMS, larger-scaled studies are warranted.

ABSTRACTS

Topic: Epilepsy: Medical and Surgical treatment

EPNS25_852 - Heart and weight: two essential parameters to monitor under fenfluramine – A monocentric french cohort of 23 Patients

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Objectives

Fenfluramine (FFA) is a serotonin-releasing agent approved in France for the treatment of Dravet syndrome (DS) in 2020 and Lennox-Gastaut syndrome (LGS) in 2022. This treatment requires specific monitoring due to its potential cardiological risks (pulmonary arterial hypertension and valvulopathy) and concerns regarding its possible impact on growth. We report on weight, height and BMI curve evolution and cardiological follow-up in patients receiving FFA for these two indications.

Methods

We analyzed weight changes and echocardiographic findings in 23 patients treated with FFA and followed in Marseille since 2017.

Results

Seventeen patients have DS, and seven have LGS. Treatment was initiated at an average age of 9.5 years (median: 6.5 years; range: 2 years to 20 years and 9 months). The average treatment duration is 3.5 years (median: 2 years and 4 months; range: 6 months to 7 years and 10 months). Eighteen patients were treated for at least one year, and ten patients for more than three years. No abnormalities were detected in the cardiac ultrasounds performed according to recommendations. Seventeen patients experienced weight loss due to loss of appetite from the introduction of FFA. Eleven patients had weight loss three months after initiation, while four showed insidious weight stagnation. Two patients experienced sudden weight loss after more than 1.5 years of treatment. Five patients discontinued FFA after an average treatment duration of 2.3 years (median: 1 year and 10 months). For four patients, weight loss led to treatment discontinuation, regardless of seizure frequency reduction. Weight loss appears to be more pronounced in patients with LGS than in those with DS.

Conclusions

FFA affects weight gain in 75% of patients, necessitating dietary monitoring and counseling. No cardiac abnormalities were observed.

ABSTRACTS

Topic: Neuromuscular Disorders

EPNS25_853 - The Role of Wearable Inertial Measurement Units (IMUs) to Assess Motor Performance in Patients with Juvenile Myasthenia Gravis (JMG): a pilot study

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Objectives: JMG presents challenges in clinical monitoring and treatment response assessment due to the rarity of the condition and lack of validated tools for this age group. Wearable devices utilizing IMUs are electronic tools designed to measure body acceleration and rotation, during ambulatory conditions. Preliminary studies have already demonstrated their applicability in children with rare neurological diseases. Consequently, they could provide a practical approach for quantitatively characterizing movement complexity in children with JMG.

The objectives of this study are:

- To evaluate the feasibility, reproducibility and accuracy of IMU-derived motor data as a clinical monitoring tool in JMG.

- To analyze the correlation between IMU-derived motor data and Quantitative Myasthenia Gravis (QMG) scale scores.

Methods: Children (<18 yo) diagnosed with JMG were prospectively enrolled. Clinical and anamnestic data were longitudinally collected in a dedicated database. QMG assessment scales were administered, and gait recordings were performed using IMU sensors applied to the lumbar and malleolar regions during self-selected speed walking and tandem walking. Spatio-temporal parameters, their variability, and nonlinear metrics of trunk kinematics were computed and compared with those of an age-matched control group (112 subjects, 6–25 yo). Subsequently, IMU-derived gait parameters were compared with the QMG scale scores. The Kruskal-Wallis test was used for statistical analysis (p-value <0.05).

Results: A total of 35 gait recordings were obtained from 8 patients with JMG, aged 5 to 18 years, during a follow-up period of 6 to 24 months. Gait analysis revealed increased stride time, with prolonged stance and double support phases observed in both normal and tandem walking. Moreover, nonlinear metrics demonstrated a diminished ability to organize gait patterns. IMU-derived parameters were more significantly altered in patients with more severe phenotypes, as reflected by higher QMG scores.

Conclusions: Motor difficulties in children and adolescents with JMG can be detected through gait analysis using IMUs. Gait alterations correlate with QMG scale scores. Therefore, IMUs can be useful as an additional assessment tool for the clinical monitoring of MG patients and for assessing their response to treatment, even in younger patients.

ABSTRACTS

Topic: Miscellaneous

EPNS25_856 - SynGO-Clinic: A Pilot Study Mapping Synaptic-Related Neurological Disorders Through Biochemical and Neurobiological Pathways

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Objectives: In recent years, numerous synaptic-related neurological disorders have emerged, with clinical symptoms guiding diagnostic and therapeutic approaches. However, given the significant role of metabolism in neuronal function, it is essential to explore common biochemical and neurobiological pathways underlying these disorders. Understanding these shared mechanisms may help identify overlapping treatment strategies for disorders with similar phenotypic presentations.

Methods: This study analyzed 20 genes associated with neurological phenotypes, each with over 60 reported patients. A literature review of patient cohorts and Human Phenotype Ontology coding was conducted to identify and classify unique symptoms. Additionally, the biological processes involving these genes were reviewed and categorized into 18 main functional groups, clustering them into 18 main categories, divided into three groups: neurodevelopmental, neurodegenerative, and mixed pathways. Statistical analyses included Chi-square tests for symptom frequency comparisons and ANOVA with Tukey's post-hoc tests for mean differences ($p<0.05$). The study investigated three key questions: (1) whether synaptic localization influences symptoms, (2) whether gene expression timing correlates with symptom onset, and (3) whether shared biological pathways contribute to similar symptomatology.

Results: The cohort included 1,648 patients (mean age: 12.56 years; 52.5% male). Infantile-onset patients showed significantly higher rates of involuntary movements ($p<0.05$), motor delay ($p<0.0001$), and hypotonia ($p<0.0001$). Hypertonia was more common in middle-aged individuals. Behavioral abnormalities, sleep disturbances, and language impairments were more frequent in infantile and childhood-onset cases compared to young adults ($p<0.005$). Synaptic localization influenced symptom presentation ($p=0.0028$). Postsynaptic mutations were associated with atypical behavior, sleep abnormalities, motor delay, hypotonia, and language impairment, whereas presynaptic mutations were linked to cognitive decline, involuntary movements, and hypertonia. Pathway analysis further distinguished neurodevelopmental disorders, primarily associated with seizures, developmental delays, and behavioral abnormalities, from neurodegenerative pathways, linked to CNS atrophy, involuntary movements, and communication deficits ($p=0.0008$).

Conclusions: This study highlights the importance of integrating rare neurological diseases to improve pathophysiological understanding. Distinct symptom profiles were identified based on synaptic localization and biochemical pathways, underscoring the need for a SYNGO-Clinic approach to bridge clinical phenotypes with synaptic biology. These findings provide a framework for future research and targeted treatments for synaptic-related disorders.

ABSTRACTS

Topic: Neuromuscular Disorders

EPNS25_857 - DMD Care UK: A successful collaboration between the clinician and patient communities, improving standards of care in Duchenne muscular dystrophy

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Objectives
DMD Care UK is a collaborative initiative between the John Walton Muscular Dystrophy Research Centre at Newcastle University and Duchenne UK, embedded in the UK North Star Network. It is funded by Duchenne UK, Duchenne Research Fund and Joining Jack. This national initiative aims to enhance and standardise care for everyone with Duchenne muscular dystrophy (DMD) in the UK by providing practical, consensus-driven guidelines and empowering individuals with DMD to actively participate in their care.

Methods
Working groups (WGs) comprising neuromuscular clinical experts, specialists, and patient representatives have been established to address various aspects of multidisciplinary care for DMD. To enhance and standardise care for individuals with DMD in the UK, each WG has developed practical guidelines using a consensus-driven approach, based on the comprehensive 2018 international care recommendations for DMD, along with other available clinical evidence, expert opinion, and patient experience. Once consensus is reached for a specific area of care, the guidance is submitted for endorsement by the relevant national body. The guidelines are then published in peer-reviewed journals, ensuring credibility and scientific value.

Results
DMD Care UK comprises 13 working groups, each dedicated to a specific aspect of care. Across the project, we engage over 130 clinical experts and more than 25 patient representatives, who contribute their knowledge and experience to develop, review, and refine consensus-driven materials. This initiative extends beyond neuromuscular clinicians, involving a range of specialists, including cardiologists, respiratory specialists, endocrinologists, physiotherapists, and psychologists. Each working group also includes patients or patient representatives to ensure a patient-centered approach. Currently, four guidelines—covering Bone and Endocrinology, Cardiac, Respiratory, and Emergency Care—have been published and endorsed, each accompanied by Patient and Family Guides to make the information more accessible to the patient community. Upcoming guidelines will address Physical Therapy, Corticosteroids (including vamorolone), Psychosocial care, and Orthopaedics. Other working groups are in the early stages of reviewing current evidence and tailoring the 2018 published international standard of care to align with UK-specific guidance.

Conclusions
The initiative continues to expand, developing guidance, responding to the impact of novel therapies, and effectively communicating information to both clinicians and the patient community. By standardising and improving care while collecting data on care delivery, the project is gaining valuable insights into the impact of care on patient outcomes, identifying gaps and opportunities in current care provision, and enhancing the trial readiness of the UK DMD population.

ABSTRACTS

Topic: Neurometabolic Disorders

EPNS25_859 - Importance of including α-Mannosidosis in a combined testing protocol with MPS in patients suspected of a Mucopolysaccharidoses

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Objectives

Alpha-Mannosidosis is an ultra-rare inherited disorder caused by a deficiency in α-mannosidase, leading to the accumulation of oligosaccharides in lysosomes, which damages organs and tissues. Mucopolysaccharidoses (MPSs) are a group of progressive lysosomal storage diseases (LSDs) caused by enzyme deficiencies that prevent the breakdown of glycosaminoglycans, leading to multi-system impairments. Both conditions share overlapping clinical symptoms, including respiratory infections and skeletal abnormalities, making differential diagnosis by phenotype challenging.

Methods

To improve early identification of alpha-Mannosidosis, we developed a novel diagnostic panel that simultaneously measures enzyme activities for six MPS types and α-mannosidase in a single Dried Blood Spot (DBS) using tandem mass spectrometry. In a previous retrospective study of over 1000 DBS samples submitted for MPS diagnostics, the frequency of alpha-Mannosidosis in this cohort of symptomatic patients was found to be notably high (4 cases out of 1000).

Results

Building on these findings, a prospective study was initiated in September 2022, and over 7,700 samples have since been evaluated for both MPS and α-mannosidase enzyme activities. Among this cohort, 46 samples showed low or borderline α-mannosidase activity, and 22 of these have been genetically confirmed as alpha-Mannosidosis. These results suggest that alpha-Mannosidosis may be underdiagnosed, and emphasize the importance of incorporating α-mannosidase testing into a combined diagnostic approach for MPS and related disorders.

Conclusions

This integrated diagnostic panel provides a valuable tool for earlier detection of alpha-Mannosidosis, improving diagnostic accuracy and patient outcomes.

ABSTRACTS

Topic: Infectious and Inflammatory Diseases/ Neuroimmunology

EPNS25_860 - Early antiseizure medication tapering in children and adolescents aged 2-18 years with single calcified or granular-nodular parenchymal neurocysticercosis in a low-risk subgroup identified by risk assessment: a pilot prospective Intervention study

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Objectives

A recent meta-analysis reported no difference between antiseizure medication (ASM) duration of 6,12, and 24 months on 1–1.5-year cumulative incidence of seizure recurrence after stopping ASM in single parenchymal neurocysticercosis (NCC). Currently, ASM is stopped after 6 months if the cyst resolves, however, there is no consensus regarding the duration of ASM in calcified or granular nodular NCC. The objective of the study was to estimate seizure recurrence in a low-risk group of calcified NCC for seizure recurrence (identified by clinical, EEG, and MRI criteria) post early (6-9 months or 12-15 months) anti-seizure medication tapering.

Methods

A group of single calcified or granular nodular parenchymal NCC with low risk for seizure recurrence was identified by literature review based on clinical (<3 seizures after starting appropriate ASM), EEG (normal within a week before tapering of ASM), and MRI brain (granular nodular or calcified NCC <1 cm without perilesional edema) parameters. Those seizure-free for either 6-9 months or 12-15 months were consecutively enrolled from January 2022 to January 2024. ASM was tapered over 2-3 months and all the patients were followed for seizure recurrence.

Results

Overall, ASM was tapered in 33 patients (mean age 9.5±2.4 years, 69.7% males). On a median follow-up of 10 (IQR:5-14) months post-tapering, the incidence of seizure freedom was 87.9% (95% CI: 61.8-96.6) with 12.1% having breakthrough seizures (95% CI: 3.4-28.2). Serial seizures and status epilepticus before starting ASM were significantly associated with seizure recurrence (hazards ratio:11.5 and 8 respectively, p=0.04). There was no significant difference in seizure recurrence between the 6-9 and 12-15-month groups.

Conclusions

The risk of seizure recurrence with early tapering (6-9 or 12-15 months of seizure freedom) of ASM in single calcified or granular nodular, low-risk parenchymal NCC is comparable to tapering after 24 months of seizure freedom (as mentioned in the literature). A prior history of serial seizures and status epilepticus increases the likelihood of breakthrough seizures. Early tapering can minimize ASM-related adverse effects and health costs related to prolonged ASM use and recurrent hospital visits.

ABSTRACTS

Topic: Neurometabolic Disorders

EPNS25_861 - High-Risk Population Testing for Metachromatic Leukodystrophy (MLD) in the Central and Eastern European (CEE) region

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Objectives

Lysosomal storage disorders (LSDs) are a heterogeneous group of genetic conditions caused by defective lysosomal metabolism, leading to substrate accumulation and a wide spectrum of non-specific clinical manifestations. These challenges often result in delayed diagnosis or missed cases. The advent of gene therapy for metachromatic leukodystrophy (MLD) has underscored the importance of early diagnosis in this rare disease. Increased awareness and the implementation of targeted screening programs are critical to facilitating timely diagnosis and treatment initiation.

Methods

Between January and March 2024, 77 paediatric neurology clinics across six Central and Eastern European (CEE) countries (Bulgaria, Croatia, Czechia, Hungary, Romania, and Slovakia) were invited to participate in a pilot screening initiative for MLD. Clinics were introduced to the availability of MLD testing kits provided by a medical diagnostic laboratory. A three-tiered screening protocol was utilized. Initial analysis of sulfatide isoforms (C16:0, C16:0-OH, C16:1-OH) was performed using tandem mass spectrometry. Samples with elevated sulfatide levels underwent secondary testing for arylsulfatase A (ARSA) enzyme activity. Confirmatory molecular diagnostics included sequencing of the ARSA, SUMF1, and PSAP genes. A total of 38 centres expressed preliminary interest in participating in the program.

Results

Ten centres actively utilized the testing kits out of 38 centres with interest. By December 2024, 33 tests had been performed. Several rare diagnoses were identified, including one case of MLD, one carrier of Multiple Sulfatase Deficiency (MSD), and one infant with Phelan-McDermid syndrome who underwent testing for MLD. Two tests were conducted following an index case of MLD in a sibling. Both tests were negative in the siblings.

Conclusions

This screening initiative highlights the feasibility of implementing targeted testing programs in CEE countries, potentially reducing diagnostic delays for MLD. Further collaboration and expansion of such programs may improve early diagnosis and enable timely access to advanced therapies. Ultimately, global newborn screening programmes are essential for the timely diagnosis of inherited metabolic diseases and for access to disease modifying treatment.

ABSTRACTS

Topic: Epilepsy: Diagnosis and Investigations

EPNS25_862 - Brain Imaging Findings and Etiology of Infantile Seizures in Infants Admitted to Namazi Hospital, Shiraz, Iran, with a 2-Year Neurological Follow-Up: A Cohort Study

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Objectives

To investigate the prevalence, etiologies, and brain imaging findings of infantile seizures in neonates admitted to Namazi Hospital, Shiraz, Iran, and to assess their neurological outcomes over a 2-year follow-up period.

Methods

This retrospective cohort study was conducted at Namazi University Hospital from September 2019 to September 2020. It included neonates diagnosed with seizures during NICU admission. Data were collected on demographics, clinical history, and brain imaging results (ultrasound, MRI). Etiologies of seizures were categorized, and neurodevelopmental outcomes were assessed using the Ages and Stages Questionnaire (ASQ) during a 2-year follow-up.

Results

Among 2,153 neonates admitted, 56 (2.6%) experienced seizures. Brain imaging identified hypoxic-ischemic changes in 41.8% of cases, intracranial hemorrhage in 4.0%, and other structural abnormalities contributing to seizure etiology. Metabolic and infectious causes were confirmed in 7.9% and 13.5% of cases, respectively. Unknown etiologies represented 31.8% of cases. Lower gestational age and birth weight were significantly associated with hypoxic-ischemic encephalopathy (HIE). At the 2-year follow-up, 29.2% of infants showed neurodevelopmental delays, with abnormal imaging findings, recurrent seizures, and HIE as key predictors.

Conclusions

Hypoxic-ischemic encephalopathy is the leading cause of infantile seizures in this cohort, highlighting the critical role of brain imaging in early diagnosis and intervention. Timely identification and management of at-risk infants can reduce long-term neurological sequelae.

ABSTRACTS

Topic: Epilepsy: Medical and Surgical treatment

EPNS25_863 - Adjunctive use of cenobamate for pediatric refractory epilepsy: a single-center retrospective study

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Objectives Epilepsy is one of the most common disorders in childhood. However, approximately one-third of patients do not achieve seizure freedom despite multiple antiseizure medications. Drug-resistant epilepsy (DRE) leads to worse quality of life, increased risk of unexpected death, and impaired neurodevelopment and cognitive function. Cenobamate has shown positive results in adult patients, however data on its use in children remain limited. This study aimed to report our center's experience with the efficacy and safety profile of Cenobamate as an adjunctive therapy in children with refractory epilepsy.

Methods We retrospectively evaluated the outcome of pediatric patients with DRE treated with Cenobamate in our department. Collected data included age, diagnosis, concomitant medication, seizure type, frequency and duration, median drug dose, and treatment-emergent side effects.

Results Cenobamate was started in 38 patients with a median age of 11 years (2-18). The etiology of epilepsy was genetic in 12 patients, structural in 7, both structural and genetic in 1 patient, and idiopathic in 17 patients. Before initiation of therapy, an average of 4 (range 1–12) antiseizure medications (ASM) were prescribed per patient. 14/38 patients were previously treated with the ketogenic diet, and 2/38 patients underwent VNS surgery. 27% (10/38) of the children had focal seizures, 37,8% (14/38) generalized seizures, and 35.1% (13/38) experienced both. 37.8% (14/38) of patients had epileptic encephalopathy. At the time of the study, the median treatment duration was 4 months, with a median dose of 1.79 mg/kg/d (range 0.52-4).

Cenobamate treatment reduced the total number of seizures per day in a statistically significant manner ($p<0.05$). Seizure frequency was reduced by>50% in 58% (22/38) patients, and seizure freedom was achieved in 4. Additionally, fewer patients required rescue medication after treatment initiation, 24.3% vs 16.2%. Regarding outcomes unrelated to epilepsy, daily life improved in 45.9% of patients, and 37.8% showed psychomotor progress. In 69.4% of patients, the doses of other antiepileptic drugs used alongside Cenobamate were reduced, while 32.4% had one or more ASM permanently discontinued.

Adverse effects occurred in 39.5% (15/38) patients, including somnolence, gastrointestinal symptoms, increase in seizure frequency, dizziness, and allergic reaction/exanthem, which were mostly self-limited. Dose reduction was needed in 2, and treatment was discontinued in 5 patients.

Conclusions Cenobamate demonstrates a safe, well-tolerated, and effective profile, achieving significant seizure reduction or freedom in children with DRE. These results are in line with adult published data, making cenobamate a novel ASM for treating refractory epilepsy.

ABSTRACTS

Topic: Miscellaneous

EPNS25_866 - Living with Developmental and/or Epileptic Encephalopathies: insights into quality of life of families and children

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Objectives

Few studies focus on the quality of life (QoL) of children and adolescents with Developmental and/or Epileptic Encephalopathies (DE/EE/DEE) and their families. Understanding determinants of QoL in these patients is crucial to deliver targeted interventions. This study aims to assess the personal and familiar QoL in a pediatric population with DE/EE/DEE and identify factors related to QoL reduction.

Methods

This is a single-center longitudinal observational study. Pediatric patients (age: 1 month-17 years) with DE/EE/DEE referred to our epilepsy center between February and December 2024 were included. QoL was assessed with PedsQL questionnaires (Epilepsy Module, Family Impact Module, copyright Mapi Research Trust), completed by one parent in inpatient or outpatient setting. Data on personal and epilepsy history were collected. The modified Rankin Scale (mRSC) and the pediatric Cerebral Performance Category Scale (PCPCS) were used to assess motor and neurological functions. Mann-Whitney U tests, Chi-square tests, correlation and linear regression analyses were used to identify predictors of lower QoL. Statistical significance was set at $p<0.05$.

Results

Ninety patients (52 males; median age: 10 years) were enrolled. The median patients' QoL was 42/100, with lower scores in items related to cognitive and executive functions. The median QoL of families was 55/100; the most affected areas were challenges in daily activities and health-related concerns. Patient QoL was significantly reduced in cases of daily seizures ($p=0.014$), motor and gastrointestinal comorbidities ($p=0.023$, $p=0.010$), sleep disturbances ($p=0.025$), and drug-resistant epilepsy ($p<0.001$). Family QoL was lower in patients with multiple pediatric intensive care unit (PICU) admissions ($p=0.019$) and drug-resistant epilepsy ($p=0.010$). Significant correlation was found between patient QoL and mRSC scores ($r=-0.0337$, $p=0.003$), number of medications ($r=-0.0354$, $p=0.001$) and age at epilepsy onset ($r=0,372$, $p<0.001$). Linear regression found patient QoL and recurrent PICU admissions as predictors of lower family QoL (adjusted $R2=0.346$, $p<0.001$). Drug-resistant epilepsy and gastrointestinal comorbidities were predictors of lower patient QoL (adjusted $R2=0.291$, $p<0.001$).

Conclusions

The study highlights the burden of DE/EE/DEE on QoL for patients and their families. QoL predictors may be the focus of targeted interventions to reduce the caregiving burden and improve patients' overall wellbeing.

ABSTRACTS

Topic: Neuromuscular Disorders

EPNS25_868 - Neurocognitive Profiles in Duchenne Muscular Dystrophy: Insights from the Multicenter EU-Funded BIND Study

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Duchenne muscular dystrophy (DMD) is the most common muscular dystrophy in childhood, affecting over 25,000 individuals in Europe. It results from mutations in the DMD gene that prevent the production of dystrophin, a protein essential for muscle and brain function. While progressive muscle weakness is the hallmark of DMD, around 50% of individuals also experience central nervous system (CNS) co-morbidities, including intellectual disability, autism, Attention Deficit Hyperactivity Disorder (ADHD), and Obsessive Compulsive Disorder (OCD). These co-morbidities are driven by deficiencies in dystrophin isoforms in the brain, with severity depending on mutation location.

Objectives: The EU-funded BIND project, launched in 2020, aimed to improve understanding of brain involvement in Duchenne and Becker muscular dystrophies (DMD/BMD). Seven neuromuscular centers across six EU countries collaborated to assess behavioral, cognitive, and neuropsychiatric issues in the largest DMD/BMD cohort to date. The study investigated how mutations affecting different dystrophin isoforms influence neurobehavioral outcomes and developed a screening tool for early detection of patients at risk of neuropsychiatric conditions.

Methods: This study combined online parent-report questionnaires and in-person cognitive assessments.

Results: Preliminary data from 253 DMD patients revealed two distinct performance clusters in cognitive areas such as memory, executive function, processing speed, and general intelligence. Patients with mutations affecting only Dp427 primarily clustered in the high-performance group (71%), while 91% of those with Dp140 mutations fell into the low-performance cluster. The BIND screening tool, developed to evaluate key developmental areas commonly affected in Duchenne, demonstrated high sensitivity and specificity in identifying at-risk patients. Data collected from over 800 patients, including participants from underrepresented regions, validated the tool's effectiveness.

Conclusions: These findings emphasize the critical role of dystrophin isoforms in neurodevelopment and the importance of mutation-specific profiling for predicting cognitive outcomes. By integrating data from a large multicenter cohort and developing a practical screening tool, the BIND project offers a framework for early diagnosis and personalized management of neuropsychiatric co-morbidities, improving clinical care and long-term outcomes for affected individuals.

ABSTRACTS

Topic: Neurometabolic Disorders

EPNS25_869 - Cataplexy beyond narcolepsy: a comprehensive review

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Objective Cataplexy, defined as a transient episode of skeletal muscle weakness without loss of consciousness triggered by emotions, is a characteristic feature of narcolepsy type 1. However, it can also occur in other medical conditions, like Niemann Pick type C, or as an adverse effect of medication. In this study, we aim to describe various conditions associated with cataplexy without narcolepsy, and to explore potential links in pathogenesis including neurotransmitter disturbances.

Methods We describe a case of 8-year-old twins with monoamine A/B deficiency due to atypical Norrie disease with cataplexy, illustrated by videos. Furthermore, we performed a comprehensive literature review following the PRISMA guidelines via the PubMed and Embase databases using search terms related to cataplexy without narcolepsy, secondary causes, neurotransmitter disorder, and drug-induced cataplexy.

Results After screening 754 articles, we included 96 publications describing 20 different conditions associated with cataplexy without narcolepsy. These conditions could be categorized into genetic disorders (n=13), medication side effects (n=4), secondary cataplexy due to structural lesions (n=2), and primary cataplexy. A direct link with monoamine neurotransmitter (dys)function was found in two genetic disorders (atypical Norrie disease and combined sepiapterin reductase and methylmalonyl-CoA epimerase deficiency) and 1 drug related side effect (clozapine).

Conclusions Cataplexy can occur in many different conditions beyond narcolepsy. It is important to be aware of this, both from a diagnostic as from a therapeutic/ prognostic point of vue. In several conditions, a link to monoamine neurotransmitter dysfunction or imbalance is likely. Further research into underlying mechanisms might improve the recognition and management of cataplexy in diverse clinical contexts.

ABSTRACTS

Topic: Infectious and Inflammatory Diseases/ Neuroimmunology

EPNS25_870 - Descriptive Study of Pediatric Patients Diagnosed with Multiple Sclerosis in a Tertiary Hospital

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Objectives

To describe the clinical, radiological, and therapeutic characteristics of a series of pediatric patients diagnosed with relapsing-remitting multiple sclerosis (RRMS).

Methods

A retrospective descriptive study was conducted on pediatric patients (≤18 years) diagnosed with RRMS between January 2017 and December 2024 in the Pediatric Neurology Department of a tertiary hospital. Clinical variables (age at onset, initial manifestations, medical history), radiological findings (demyelinating lesions, gadolinium enhancement), and therapeutic approaches (acute-phase treatments and disease-modifying therapies) were analyzed. Disability was assessed using the EDSS scale at the end of follow-up.

Results

Eight RRMS patients (4 males and 4 females) were included, with a mean age at onset of 12.1 ± 2.7 years. No family history of neurological or autoimmune diseases was recorded. Two patients had comorbidities: one with mild chronic kidney disease due to renal agenesis, poorly controlled hypertension, obesity, and metabolic syndrome; another with short stature and celiac disease.

The initial clinical manifestations were: hemispheric relapses (n=4) associated with spinal cord relapses (n=2), optic neuritis (n=2), brainstem/cerebellar relapses (n=2), pure spinal relapse (n=1), and one asymptomatic case at diagnosis. Five patients had positive oligoclonal bands in cerebrospinal fluid (CSF). Neurofilament analysis in CSF was performed in two patients. Serum and CSF testing for antineuronal, neuronal surface, and antimielin antibodies (anti-MOG), as well as microbiological studies, were negative. Brain MRI at disease onset showed demyelinating lesions in 100% of cases, with gadolinium enhancement in 62.5%.

In the acute phase, all patients except one received high-dose corticosteroids, with two requiring plasmapheresis. Disease-modifying therapy was initiated in all cases, with therapeutic escalation in two patients due to radiological progression. Currently, 4 patients are on fingolimod, 2 on rituximab, and 2 on natalizumab. Adverse effects were reported in three cases: two patients developed hypertransaminasemia, and one experienced diarrhea secondary to fingolimod. The disease evolution period ranged from 3 months to 7 years.

The final EDSS score was 1.5 in two patients, 1 in one patient, and 0 in the remaining ones. No new clinical relapses were documented in any case.

Conclusions

Early treatment with disease-modifying therapies is essential to reduce inflammatory activity, prevent relapses, and minimize disability accumulation in pediatric patients with RRMS.

ABSTRACTS

Topic: Epilepsy: Diagnosis and Investigations

EPNS25_871 - Early Childhood Absence Epilepsy: electroclinical features, prognosis and genetics in 27 patients with Absence Epilepsy < 3 years

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Objectives

Early-onset absences in children are a rare entity. We describe a cohort of 27 patients (20 girls) presenting absences with onset before the age of 3 years, trying to determine EEG patterns, prognosis and genetics.

Methods

A retrospective study of clinical and electroencephalographic characteristics, course of epilepsy, treatment response, cognitive development, and genetic results through analysis of the genetic panel for monogenic epilepsies (PAGEM).

Results

Median absence onset age was 21 months (6 to 36 months) with median follow-up of 10.8 years. 20 patients have absences accompanied by eyelid myoclonia, 9 of them have axial myoclonia. Absences are characterized by 3 Hz spike-and-wave discharges in 13/27 patients, and 10/27 have polyspike-and- wave discharges since the first EEG. 8/27 have a family history of epilepsy. During follow-up, 9 patients present other types of seizures: generalized tonic-clonic seizures in 7 patients, evolution towards Lennox-Gastaut syndrome in 2 patients. 19/27 develop pharmacoresistant epilepsy. 8 children have motor delay and 15 patients speech delay- among them 4 never acquired language. Cognitive development is normal in 11/27, while 16/27 show moderate intellectual disability, with 10 children attending special education institutions.

24 patients underwent genetic tests, pathogenic mutations were identified in 19 children: SYNGAP1 (3/19), CHD2 (1/19), GABRG2 (1/19), KCNA2 (1/19), RORA (1/19), RORB22 (1/19), SCN1A (1/19), SLC6A1 (6/19), YWHAE (1/19), YWHAG (2/19). No glucose transporter deficiency is found.

Conclusions

The semiology of seizures and the EEG patterns are more complex than those found in typical absences. The prognosis can be poor; the majority of patients develop a drug- resistant epilepsy and exhibit intellectual disability. Genetic analyses seem to be indispensable and can play a crucial role in better characterizing the clinical phenotypes and providing improved patient care.

ABSTRACTS

Topic: Neuromuscular Disorders

EPNS25_872 - Sensory Profile and Behavioral Problems in Children with DMD

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Objectives

Duchenne Muscular Dystrophy (DMD) is a progressive neuromuscular disorder characterized not only by motor impairments but also by cognitive, behavioral, and sensory processing difficulties. While behavioral problems in children with DMD are well documented, their sensory processing profiles remain underexplored.This study aims to investigate the sensory processing patterns of children with DMD and their association with behavioral problems.

Methods

A total of 34 children diagnosed with DMD were assessed using the Sensory Profile (SP) to evaluate sensory processing patterns, while behavioral problems were measured using the Strengths and Difficulties Questionnaire (SDQ). Correlations between sensory processing difficulties and behavioral problems were analyzed.

Results

The mean age of the participants was 8.5 ± 3 years. The distance covered in the 6-minute walk test was significantly correlated with multisensory processing ($r = 0.526$, $p = 0.036$), sensory processing related to endurance/tone ($r = 0.696$, $p = 0.003$), modulation of movement affecting activity level ($r = 0.681$, $p = 0.004$), and emotional/social responses ($r = 0.527$, $p = 0.036$) on the SP, as well as the emotional difficulties scale of the SDQ ($r = -0.680$, $p = 0.007$). Furthermore, sensory processing difficulties were strongly associated with increased emotional problems, hyperactivity, and social difficulties.

Conclusions

This is the first study to investigate the sensory profile of children with DMD and its relationship with behavioral problems. Our findings suggest that sensory processing difficulties and emotional challenges may be linked to disease severity in children with DMD. Additionally, sensory processing deficits appear to be associated with behavioral problems, highlighting the need for a comprehensive approach in their assessment and management. A deeper understanding of these sensory-behavioral interactions could inform targeted interventions aimed at enhancing daily functioning and overall quality of life for children with DMD.

ABSTRACTS

Topic: Neurometabolic Disorders

EPNS25_873 - Global Screening for Mucopolysaccharidoses: Differential Diagnosis and Prevalence Patterns Across Europe and the Middle East

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Objectives

Mucopolysaccharidoses (MPSs) are a group of chronic, progressive lysosomal storage disorders (LSDs) characterized by multi-system impairments. These conditions are caused by deficiencies in specific enzymes responsible for the breakdown of glycosaminoglycans (GAGs), leading to their accumulation in various tissues, including the arteries, eyes, skeleton, joints, skin, ears, teeth, respiratory system, spleen, liver, central nervous system, bone marrow, and blood. The clinical manifestations of MPSs vary depending on the affected enzyme and the level of enzymatic activity, ranging from mild to severe forms that can result in early mortality.

Methods

This study presents data on the differential diagnosis of MPSs using a single Dried Blood Spot (DBS) for screening across a high-risk population, comprising over 20,000 samples from more than 60 countries. The enzymes tested include MPS I (α-L-Iduronidase), MPS II (Iduronate-2-sulfatase), MPS IIIB (N-α-Acetylglucosaminidase), MPS IVA (N-Acetylgalactosamine-6-sulfate-sulfatase), MPS VI (Arylsulfatase B), and MPS VII (ß-Glucuronidase). A total of over 2,000 MPS-positive patients were confirmed, with the highest incidences observed in MPS I, MPS VI, and MPS IVA. Significant differences in distribution were noted based on geographic regions, with Europe and Africa showing similar patterns of MPS distribution, while the Middle East displayed divergent patterns, particularly for MPS I, MPS IVA, and MPS VI.

Results

The performance of the combined testing algorithm was validated, demonstrating its suitability for reliable and simultaneous diagnosis of multiple MPSs. Established cut-off values indicated that approximately 80% of MPS-like phenotypes exhibited normal enzyme activity, while 20% underwent genetic confirmatory testing. For biochemically negative MPS samples, differential diagnoses, including α-mannosidosis or mucolipidosis, should be considered.

Conclusions

Our findings underscore the importance of global MPS screening initiatives to reduce the time to clinical assessment and treatment initiation. The proposed workflow offers a reliable, efficient diagnostic tool and represents a valuable alternative for national newborn screening (NBS) programs.

ABSTRACTS

Topic: Neuromuscular Disorders

EPNS25_874 - Consensus statement on the orthopaedic management of hip displacement in Spinal muscular atrophy in the United Kingdom

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Objectives

Spinal muscular atrophy (SMA) is a genetic neuromuscular disorder caused by bi-allelic deletions or pathogenic variants in the *SMN1* gene, with SMA Type 1 being the most severe form. It leads to early muscle weakness, failure to meet motor milestones, and limited survival without ventilatory support. Disease-modifying therapies (nusinersen, risdiplam, and onasemnogene abeparvovec) have improved survival and motor outcomes but have also created new challenges in orthopaedic care. Managing hip pathology in children with SMA remains controversial, with approaches ranging from conservative to aggressive surgical interventions. To address this, a Delphi consensus exercise was conducted in the UK.

Methods

The process included two rounds that involved 45 participants (paediatric neurologists, orthopaedic surgeons, neuromuscular/orthopaedic physiotherapists and advocacy representative) from 19 leading paediatric neuromuscular centres. Round 1 involved a questionnaire with 16 statements, resulting in consensus on six statements and further discussion of seven. Round 2, conducted during an in-person meeting, allowed for live voting and modification of statements based on participant feedback. Family input gathered by advocacy representatives also informed the discussions.

Results

The final consensus includes 13 approved statements addressing key aspects of hip management in SMA. Recommendations emphasize the importance of individualized, multidisciplinary assessments and proactive strategies to prevent hip dislocation, particularly in children expected to achieve higher motor abilities, while acknowledging the lack of current evidence and the need to collect long-term data. Recommendations also included timeline on when starting radiographic surveillance, radiographic data to monitor and orthopaedic approach to painful hips. The consensus also highlighted the importance of including clinical and radiological data in the national SMA Reach UK registry and prioritizing the development of evidence-based guidelines for both conservative and surgical approaches. The potential role of less invasive approaches was highlighted as an option to be considered for selected cases.

Conclusions

This study emphasizes the importance of multidisciplinary collaboration and individualized care in optimizing orthopaedic management for SMA patients. By addressing gaps in clinical practice, the consensus recommendations provide a foundation for consistent, evidence-based care while promoting research and audit initiatives.

ABSTRACTS

Topic: Neuromuscular Disorders

EPNS25_875 - Interim Data Following 24 Weeks of Treatment with WVE-N531 in the Phase 2 Open-label FORWARD-53 Study

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Objectives: WVE-N531 is an investigational splicing oligonucleotide with phosphoryl guanidine (PN) chemistry currently being developed as a potential therapy for patients with Duchenne muscular dystrophy (DMD) amenable to exon 53 skipping. FORWARD-53 is an ongoing Phase 2 open-label study designed to evaluate the safety, tolerability, pharmacodynamics, pharmacokinetics, and clinical effects of WVE-N531 in boys with exon 53-amenable DMD.

Methods: All participants received 10 mg/kg intravenous infusions of WVE-N531 every other week (Q2W) for 48 weeks. Muscle biopsies are taken after 24 and 48 weeks of dosing. The primary endpoint is dystrophin protein levels as measured by western blot.

Results: WVE-N531 demonstrated positive interim results following 24 weeks of Q2W dosing (N=11; age 5-11; 10 ambulatory and 1 non-ambulatory). In a prespecified analysis of ambulatory participants, mean absolute muscle content-adjusted dystrophin expression was 9.0%, and mean absolute unadjusted dystrophin was 5.5%, with high consistency across participants as measured by western blot; 89% of ambulatory participants achieved muscle content-adjusted dystrophin levels of at least 5%. Dystrophin expression was quantified from two isoforms.

The mean WVE-N531 skeletal muscle concentration of ~41,000 ng/g combined with the 61-day tissue half-life supports monthly dosing going forward. Furthermore, data showed meaningful improvement in serum biomarkers for muscle health, such as creatine kinase, with localization of WVE-N531 in myogenic stem cells and regeneration of myofibers. WVE-N531 was safe and well tolerated; all treatment-related adverse events were mild, with no serious adverse events, no discontinuations, and no oligonucleotide class-related events.

Conclusions: Interim data from the Phase 2 FORWARD-53 study highlight the therapeutic potential of WVE-N531 in DMD. The FORWARD-53 trial is ongoing and all participants have elected to continue treatment in the planned extension portion of the study with monthly dosing of WVE-N531. We expect to deliver the 48-week FORWARD-53 data and receive feedback from regulators on a pathway to accelerated approval in the first quarter of 2025.

ABSTRACTS

Topic: Neurometabolic Disorders

EPNS25_876 - Basal ganglia involvement in phenylketonuria

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Objectives: The purpose of this study is to highlight this rare neuroimaging finding through cases report to increase awareness and improve diagnosis
Phenylketonuria is a disorder of amino acid metabolism caused by an inborn error in the phenylalanine hydroxylase gene
Non treated, the main clinical features are progressive irreversible neurological impairment associated in most cases by fair-hair, fair-skin, and blue-eyes
Imaging findings in literature were similar between pediatric and adult populations comprising symmetric periventricular white matter hyperintense on T2-weighted imaging and diffusion-weighted imaging

Methods: We report two pediatric cases with the classical clinical and biochemical presentation of phenylketonuria, and atypical neuroimaging features which brain MRI indicated basal ganglia involvement with normal appearance of white matter

Results: Patient 1
18 months old female, first of consanguineous parents with no specific history referred to our consultation for progressively worsening mental retardation
His psychomotor development appeared normal during the first months of life. At the age of 8 months, he developed psychomotor regression
On physical examination, he presented communication difficulties;No eye tracking
she is fair-haired, fair-skinned with brown eyes she has slight dystonia of the lower limbs ;his limb muscle tone and strength were normal, and had normal tendon reflexes
Brain MRI
Bilateral and symmetrical signal abnormality of T2 hyperintense and diffusion involving the pallidum, the subthalamic dentate nuclei and the tegmentum of the brainstem No white matter involvement
Blood and urine amino acid chromatography shows a high level of phenylalanine
Blood phenylalanine concentration was 1700 mmol/L.
Other metabolite screening was normal
Treatment was initiated with phenylalanine restricted diet
Patient 2
14 month old boy with unremarkable family, pregnancy, and delivery history
his parents are not consanguineous
the patient was referred to our consultation for delay in psychomotor acquisitions
On examination:
He had Fair skin; golden white hair; no eczema
Generalized hypotonia with loss of head control, eye tracking, and social smile,
tendon reflexes were normal .
Brain MRI; bilateral and symmetrical hypersignal T2 ; T2 flair of the basal lenticular and caudate basal ganglia
Blood phenylalanine concentration was 1000 mmol/L.
Other metabolites screening was normal

Conclusions:
Phenylketonuria is a treatable inborn error of amino acid metabolism
Brain MRI usually showed typical abnormalities in supratentorial white matter; isolated basal ganglia compromise is exceptional and deserves to be highlighted

ABSTRACTS

Topic: Neurodevelopmental Disorders / Developmental Neuroscience

EPNS25_877 - Phenotypic Profiles of 216 Children with Specific Language Impairment based on Family HIstory

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Phenotypic Profiles of 216 Children with Specific Language Impairment (SLI) based on Family history

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Objectives: SLI is a disorder of language acquisition in children with otherwise normal development. Familial aggregation and twin studies suggest a substantial genetic contribution. The broad spectrum of SLI subphenotypes necessitates a comprehensive phenotypic characterization of affected individuals and their families.

Methods: We included n=216 children with SLI (150 monolingual, 66 bilingual) aged 2 to 6 years in our study. Of these, 102 children were assessed between 24 and 42 months, 101 children between 43 and 59 months, and 12 children between 61 and 70 months of age. Nonverbal IQ was measured using the SON-R, while expressive and receptive vocabulary were assessed with the AWST-R and SETK. Additionally, grammar and phonology were periodically reassessed. Individual and family history data were collected through personal interviews with parents. We obtained information on primary and secondary affected relatives (biological parents, siblings, aunts, uncles, and grandparents) regarding speech, language, reading, and spelling disabilities.

Results: The male-to-female ratio was 3.1:1. A positive family history was found in 79% of cases, with fathers being affected twice as often as mothers and three times as often as siblings. Between the ages of 2.0 and 3.5 years, the phenotype was homogeneous across all children, characterized by very limited vocabulary and either no sentences or only very short two- to three-word combinations. From the age of 4 years, as vocabulary expanded and children began forming sentences, distinct subphenotypes could be identified. Based on the severity and specific areas of language impairment, we categorized the following subgroups: morphosyntactic-phonology syndrome, grammar type (G-SLI), phonology disorder, and verbal dyspraxia. Two subtypes had a significantly higher prevalence of positive family history: verbal dyspraxia (99%) and phonologic type disorder (85%), compared to grammar type disorder (71%) and morphosyntactic-phonology syndrome (79%).

Conclusions: The high familial occurrence of all subtypes, particularly Verbal Dyspraxia, supports the hypothesis of underlying genetic factors. The availability of DNA samples provides an opportunity to identify these genetic factors through linkage and association studies.

ABSTRACTS

Topic: Movement Disorders/ Cerebral Palsy

EPNS25_880 - Phenotypic complexity as a key predictor of DBS response in children beyond etiology

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Objectives: To evaluate efficacy and safety of Deep Brain Stimulation of the Globus Pallidus Internus(GPi-DBS) in children with different forms of dystonia.

Methods: Longitudinal study of dystonic patients who underwent GPi-DBS from 2020 to 2024. Surgery candidates were selected by a multidisciplinary team. Directional electrodes were inserted in the GPi using a stereotactic frame and microelectrode recording, and connected to a rechargeable generator. Surgery complications were collected. Patients were evaluated pre-/post-DBS using clinical dystonia (BFM) and myoclonus scales (UMRS). Scores were compared using Wilcoxon signed-rank test.

Results: Thirty four patients with segmental/generalized dystonia underwent DBS surgery at a mean age of 11.9 years (4-20). Dystonia was classified as isolated (n=8**),** combined (n=10) or complex (n=16). Aetiology was genetic (n=22, *TOR1A, GLB1, SGCE, IMPDH2, GNAO1, ATP8A2, GCDH, HPRT1, KMT2B, DHDDS, PDHA1, NKX2-1*), idiopathic (n=3, negative exome) or acquired (n=9). Eight patients had MRI basal ganglia lesions.

Six patients (17.7%) presented surgical complications (atrophic scar (n=2), wound infection, broken wire extension, and hemorrhage (n=2)), four of which required a second surgery. All complications resolved satisfactorily during the first-year follow-up.

After 31.2 (7-56) months of follow-up, there was a significant improvement in dystonia (n=32, BFM-motor pre/postDBS: 36 vs 15.8, p<0.0001; BFM-disability: 12.5 vs 7.5, p=0.0002). Significant improvements were observed in patients with isolated (BFM-motor 67.9%; BFM-disability 47.5%), combined (BFM-motor 68.9%; BFM-disability 56.5%) and complex dystonia (only for BFM-motor 24.1%). Patients with isolated/combined forms had significantly better outcomes than complex forms. Myoclonus-dystonia patients (combined group) also showed significant improvement in UMRS (n=8, Motor pre/postDBS 46 vs 30.3, p=0.0078; Questionnaire 11.5 vs 6, p=0.02).

Four out of eight children with dystonia due to hypoxic-ischemic encephalopathy had an improvement in BFM of 26-75%, including one cerebral palsy and three delayed-onset dystonia patients.

Conclusions: This study demonstrates that dystonia phenotype is a predictor of DBS response beyond etiology, with isolated and combined dystonia having better results than complex phenotypes. Among children with perinatal hypoxic-ischemic encephalopathy, those with delayed dystonia have an excellent response to DBS similar to genetic isolated dystonia forms.

ABSTRACTS

Topic: Neuromuscular Disorders

EPNS25_881 - Effects of Zolgensma (Onasemnogene Abeparvovec) and Nusinersen on swallowing functions in SMA Type 1 patients: A single centre experience

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Objectives: This study compares the swallowing status of spinal muscular atrophy (SMA) patients treated with only Nusinersen versus those who received Zolgensma (Onasemnogene Abeparvovec) after Nusinersen.

Methods: The study included 13 SMA patients with two SMN2 copies. Group 1 (n=6) received only Zolgensma following Nusinersen, and Group 2 (n=7) were treated with only Nusinersen. Swallowing abilities were evaluated using the Pediatric Eating Assessment Tool (PEDI-EAT-10), Oral and Swallowing Abilities Tool (OrSAT), and Neuromuscular Disease Swallowing Status Scale (NdSSS). Flexible Endoscopic Evaluation of Swallowing (FEES) was performed on consenting patients, and additional scales (Murray Secretion Scale, Rosenbek Penetration-Aspiration Scale, and Yale Pharyngeal Residue Severity Rating Scale) were used. Motor function was assessed with CHOP-INTEND and the Hammersmith Functional Motor Scale (HFMSE).

Results: The mean age of Group 1 was 48±15.1 months (83% male) and of Group 2 was 47.1±23.3 months (57% male) ($p>0.05$) when swallowing functions were evaluated. Median age at first Nusinersen dose was 120 months (Group 1) and 87.5 months (Group 2) (p=0.36). Zolgensma treatment was given at a mean age of 19.8±7.02 months after receiving a mean 6.8±2.7doses of Nusinersen. The NdSSS scores were 5±1.7 (Group 1) and 4.2±2.4 (Group 2) (p=1), while PEDI-EAT-10 scores were 5.8±6.2 (Group 1) and 18.7±13.4 (Group 2) (p=0.19). CHOP-INTEND and HFMSE scores were similar in both groups (p=0.39 and p=0.94, respectively). Oral feeding only was more common in Group 1 (57.1%) compared to 33.3% in Group 2. FEES revealed that Group 2 patients had started oral feeding at varying levels, while Group 1 patients, who were all tube-fed, had not. The median RPAS score was 2 for Group 1 and 5 for Group 2. Swallowing therapy continued in 66.6% of Group 1 patients after Zolgensma, but only in 14.2% of Group 2 patients.

Conclusions: Patients treated with Zolgensma after Nusinersen showed better swallowing function compared to patients on only Nusinersen. A higher rate of ongoing swallowing therapy in Group 1 may have influenced these results. Gross motor development is not predictive for swallowing functions.

ABSTRACTS

Topic: Cerebrovascular Disorders

EPNS25_882 - Risk factors and outcome in neonatal arterial ischaemic stroke: data from the Italian Registry of Infantile Thrombosis, an Italian multicentric study

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Objectives

We describe the multicenter cohort of patients with neonatal arterial ischemic stroke (NAIS) enrolled in the Italian Registry of Infantile Thrombosis (RITI), with focus on risk factors and potential early factors associated with outcome.

Methods

The RITI is a retrospective and prospective registry collecting neonatal/pediatric patients with systemic/cerebral thrombosis. We selected the subgroup with NAIS (occurred between 0-28 days of life). Univariate regression analysis was used.

Results

We identified 181 NAIS patients NAIS (56.2% males). Maternal/placental/pregnancy factors included medically assisted procreation (4.8%), twin pregnancy (3.0%), IUGR (4.5%), maternal infections in pregnancy (16.1%) or peripartum (10.1%), diabetes (10.8%), hypertension (4.5%). Delivery factors included prolonged rupture of membranes (>18 hours; 10.9%), urgent caesarean section (31.4%), 5-

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minute Apgar index <7 (10.6%). Neonatal age-specific factors were reported in 46.5%, including: need for resuscitation at birth (27.1%), or for mechanical ventilation (19.4%), hypoxic ischemic encephalopathy (11.6%), hypothermia (9.3%).

In 12.4%, NAIS was clinically silent, whereas in the remaining 87.6% clinical manifestations included seizures (79.4%), hyporeactivity (23.5%), hypotonia (16.1%), irritability (11.0%).

Strokes were multiple in 32.5%, left-sided in 62.0%, and bilateral in 15.0% (25/169). The middle cerebral artery territory was most frequently involved.

At last follow-up (median 21 months, IQR 13-45), no AIS relapses occurred. Neurological deficits were reported in 38.8%, and post-stroke epilepsy in 12.0%; of these, 86.7% also had seizures in the acute phase.

At univariate regression, factors significantly associated with neurological deficits at last follow-up were maternal age at the time of conception ≥32 years (p=0.031); urgent caesarean section: (p<0.001); lower gestational age (p=0.033); neurological deficits at discharge (p<0.001); epileptic seizures at last follow-up (p=0.008). Factors significantly associated with post-stroke epilepsy at last follow-up were need for assisted ventilation in the acute phase (p=0.001); brainstem involvement at MRI (p=0.037); longer admission duration (p=0.050).

Conclusions

Factors associated with NAIS include age-specific features, different to those in children. The identification of factors associated with poor outcome and epilepsy may help provide adequate counseling and tailor follow-up, rehabilitation and treatment strategy.

ABSTRACTS

Topic: Neurogenetics

EPNS25_884 - Partial loss of FITM2 function causes Hereditary Spastic Paraplegia

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Objectives: To report a previously unknown hypomorphic allele of FITM2 associated with an early-onset, complex hereditary spastic paraplegia (HSP) phenotype

Methods: In the index case, WES reanalysis identified two compound heterozygous variants in FITM2. Using a genotype-first approach and analyzing DNA data from leading genetic labs, we found two more cases with a similar phenotype and biallelic FITM2 variants. Clinical features, complementary tests, and follow-up data were collected. Cryo-electron microscopy was used to assess the impact of the G100R mutation and map the identified mutations onto the predicted FIT2 structure. Human dermal fibroblasts from controls and patients were obtained to measure FITM2 mRNA and protein levels. WT, H185-fs, G100R, and catalytically inactive FIT2 mutants were overexpressed in Expi293F GnTI- cells, and microsomes were isolated for enzymatic assays to measure specific activity as a fatty acyl CoA diphosphatase. To assess protein function, ER morphology and stress response, FIT2 WT and mutant G100R were expressed in FIT2 knockout SUM159 mammary carcinoma cells. UPR target transcript levels (BiP and Atf3) and protein localization were investigated using fluorescence microscopy. We also tested if the mutant proteins could rescue the phenotype in scs3Δ yeast.

Results: Both families presented an early-onset progressive complex HSP associated with cerebellar ataxia. The variant G100R was detected in both families. In Family 1, the additional variant was H185-fs, whereas in Family 2, was R180-Ter. No large, shared regions of homozygosity were found.

The H185-fs and R180Ter mutations both result in inactive enzyme, while the G100R mutation introduces a charged arginine side chain into TM3, causing significant steric hindrance with neighboring residues. Further characterization of G100R mutant using patient and control fibroblasts, showed that it leads to reduced FIT2 protein levels, while FITM2 mRNA levels remain similar. Assays of microsomes for acyl-CoA diphosphatase activity revealed that FIT2 G100R exhibited lower activity than the WT protein, in proportion to its expression levels. Using FIT2 KO SUM159 mammary carcinoma cells, we demonstrated that the FIT2 G100R variant results in lower levels of FIT2 enzyme compared to the WT protein, and that this reduction in FIT2 levels leads to ER dysfunction. Finally, in scs3Δ yeast, expression of WT human FIT2 rescued inositol auxotrophy, whereas FIT2 H185-fs and FIT2 H155A failed to rescue this phenotype, and FIT2 G100R only partially rescued it.

Conclusions

We demonstrate that complex HSP is a newly recognized clinical manifestation of *FITM2* mutations, expanding the range of associated conditions.

ABSTRACTS

Topic: Neuromuscular Disorders

EPNS25_885 - Understanding Neurodevelopmental and Psychiatric Burden in Duchenne Muscular Dystrophy: Evidence from the BIND Study

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Objectives Duchenne muscular dystrophy (DMD) is an X-linked neuromuscular disorder caused by dystrophin deficiency, leading to progressive muscle degeneration and early mortality. While its physical manifestations are well-documented, there is increasing recognition of the neurodevelopmental and psychiatric burden in affected individuals. However, systematic large-scale evaluations remain limited. The Brain Involvement in Dystrophinopathies (BIND) project, aimed to characterise neuropsychiatric comorbidities in a prospective multi-centre study children and young people with DMD

Methods A total of 238 boys with genetically confirmed DMD (aged 5-17 years) were assessed using the Development and Wellbeing Assessment (DAWBA) and the Strengths and Difficulties Questionnaire (SDQ). Participants were stratified by dystrophin isoform expression (Dp427+, Dp140+, Dp140-, Dp71-), and their neuropsychiatric profiles were compared with a matched cohort of children with intellectual disability of genetic origin (IMAGINE-ID, *n*=470) and UK population norms

Results Findings revealed that 21% of participants meet DSM-5 criteria for at least one neuropsychiatric disorder, with ADHD (8.4%), anxiety disorders (7.9%), and autism (6.7%) being the most prevalent. Importantly, genotype-phenotype correlations were observed. ADHD was more common in individuals with mutations affecting Dp427 alone, whereas autism was significantly more frequent (14.3%) in those with mutations involving Dp140. Anxiety disorders were particularly elevated (37.5%) in those lacking all the isoforms. While the overall prevalence of neurodevelopmental disorders was lower in DMD than in the IMAGINE-ID cohort, children with DMD exhibited significantly higher levels of emotional and behavioural difficulties compared to UK population norms. Additionally, differences in reported neurobehavioural challenges across study sites suggest potential cultural influences on parental reporting and clinical recognition of neurodevelopmental conditions in DMD

Conclusions We provide robust evidence of the substantial neuropsychiatric burden associated with DMD and reinforce the need for systematic screening and targeted interventions. The identification of genotype-phenotype associations highlights the potential for personalised clinical management strategies tailored to both neuromuscular and cognitive needs. With increasing life expectancy in DMD, addressing these neurodevelopmental and psychiatric comorbidities is critical for optimising quality of life. Integrating mental health care into standard clinical management could improve long-term outcomes for individuals with DMD and their families. This study underscores the necessity for a multidisciplinary approach that bridges neurology, psychiatry, and psychosocial care to provide holistic and patient-centred support

ABSTRACTS

Topic: Neuromuscular Disorders

EPNS25_886 - Motor evolution in lama2-rd: a natural history cohort

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Objectives: To assess the two-year evolution of motor function in patients diagnosed with LAMA2-related muscular dystrophy (LAMA2-RD) using the MFM-32 scale for patients older than six years and the MFM-20 scale for children aged 2 to 6 years.

Methods: This is a prospective, longitudinal, observational natural history study conducted in Spain. Annual evaluations (clinical data, motor function scales, muscular ecography, elastography) of patients with molecular diagnosis confirmation of LAMA2-RD. Data was recorded in the RedCap database. Results of MFM motor scale are analyzed through linear mixed models and visualized through heatmaps to explore patterns and relationships.

Results: A total of 26 patients (age range: 3 months to 53 years; 89% unable to walk independently at the time of the first evaluation) with confirmed molecular diagnoses of LAMA2-RD were evaluated. An overall annual decline (2.3%) in MFM scores was observed and severe phenotypes (20 patients; scores ranging from 5.2% to 55%) consistently exhibited lower scores. A statistically significant annual decline in D1 domain (standing and transfers) was demonstrated, with greater impact in the first years of life. Patients with milder presentations (5 patients; scores ranging from 36.5% to 72.9%) also exhibited decreased scores over time in serial evaluations. Additionally, D2 and D3 domains did not form distinct clusters in this cohort, underscoring the need to select specific items within each dimension that are sensitive to clinical changes.

Conclusions: The MFM scale is an effective tool for assessing the progression of LAMA2-RD, as it is capable of detecting both changes and stability in motor function, even in the absence of therapeutic interventions. Its ability to highlight domain-specific changes, particularly in D1, provides crucial insights for refining assessment strategies. This method offers a valuable approach for evaluating the efficacy of future treatments and monitoring longitudinal changes in this patient population.

ABSTRACTS

Topic: Miscellaneous

EPNS25_889 - Hypomelanosis of Ito: beyond pigmentary mosaicism

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Hypomelanosis of Ito: beyond pigmentary mosaicism

Objectives:

To describe the cases diagnosed between 2014 and 2024 of Hypomelanosis of Ito (HI), or *incontinentia pigmenti achromians*, which is the third most common neurocutaneous disorder in pediatrics, diagnosed clinically due to the absence of a specific genetic marker. It is characterized by hypopigmented skin lesions following Blaschko's lines, often associated with neurological manifestations such as developmental delay or epilepsy, and less frequently with systemic involvement.

Methods:
Review of cases of HI diagnosed between 2014 and 2024 in a tertiary hospital's Neuropediatric Unit. Diagnostic evaluations included clinical assessment, imaging studies, and multidisciplinary follow-up.

Results:

We found three cases that met the diagnostic criteria of HI:

- **Case 1:** A 2-year-old girl with no relevant medical history presented with linear hypochromic macules on her right hemibody along Blaschko's lines. At 9 years, she experienced her first seizure in the form of temporal focal status epilepticus with secondary generalization. She continues to have nocturnal seizures under antiepileptic treatment.
- **Case 2:** A 2-year-old girl, born late preterm (34+5 weeks), presented with linear hypochromic lesions on her abdomen and right upper extremity. She exhibited multisystem involvement, including central nervous system malformations (enlarged subarachnoid space, ventriculomegaly, thin corpus callosum), congenital heart defects (right aortic arch), renal anomalies (left pyelocaliceal dilatation), and musculoskeletal malformations (absence of the first finger, duplicated and fused right hemivertebra, atlantoaxial rotatory subluxation, cleft palate). She also presented short stature and psychomotor developmental delay.
- **Case 3:** A 2-year-old boy presented with linear hypochromic streaks on his trunk, developmental delay, and epilepsy with myoclonic-atonic seizures, well controlled with sodium valproate.

Conclusions:
The presence of hypochromic macules along Blaschko's lines should raise suspicion of potential systemic and neurological involvement. These cases demonstrate the broad phenotypic variability of HI, highlighting the need for comprehensive multidisciplinary evaluations to optimize diagnosis and management.

ABSTRACTS

Topic: Neurodevelopmental Disorders / Developmental Neuroscience

EPNS25_892 - Do persistence of EEG abnormalities in children with ADHD without epilepsy comorbidity, predicts better adherence to methylphenidate at three years follow-up?

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Objectives EEG-non-epileptiform abnormalities such as slowing and/or irregularity of the background rhythm (EEG-non-epi-ab) occur often in children with ADHD. The purpose of the study was to investigate whether the persistence of EEG-ab on a control EEG in ADHD children predicts better adherence to MPH at three years follow-up.

Methods A total of 503 ADHD children (82.4% male) without previous epilepsy aged between 5-14 years were included. Baseline assessments: the occurrence of EEG ab, EEG-epi-ab, EEG non-epi-ab, and initial response to MPH. At least one control EEG was performed in all cases with EEG-epi-ab. At three years follow-up, assessments included the occurrence of EEG-ab on control EEG and adherence to MPH in children who had EEG-epi-ab on baseline EEG.

Results The EEG-ab were identified in 51,5% of ADHD children, and EEG-epi-ab in 5.3%. No statistically significant differences were observed between the groups with and without EEG-ab in terms of age, gender, initial use and positive response to MPH. Notably, EEG-non-epi-ab occurred more frequently in cases who had EEG-epi-ab on baseline EEG (81.5% vs 51.9%). At three years follow up, of the 27 children who at baseline had EEG-epi-ab, significantly higher adherence to MPH was found in cases who demonstrated EEG-non-epi-ab on last control EEG (85.7% vs 53.6%). Nobody of 27 ADHD cases developed epileptic seizures

Conclusions Children whit ADHD who had EEG-epi-ab at baseline assessment and demonstrated EEG-non-epi-ab on last control EEG had significantly higher maintenance to MPH at three years follow-up.

ABSTRACTS

Topic: Cerebrovascular Disorders

EPNS25_893 - Moyamoya Disease and Moyamoya Syndrome: A Retrospective Study of Pediatric Patients at a Tertiary Centre

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Objectives: Moyamoya vasculopathy is classified as moyamoya syndrome (MMS) and moyamoya disease (MMD), depending on the presence of an associated condition or risk factor. Our aim was to assess clinical charecteristics and outcome of MMS and MMD patients.

Methods: This is a retrospective study including 39 pediatric patients who were diagnosed with definitive moyamoya vasculopathy between January 2000-December 2024. The data regarding age at onset of symptoms and diagnosis, sex, family history, clinical course, neuroimaging findings, Suzuki grades, comorbidities, genetic analyses, medical and surgical treatment were analyzed.

Results: Thirty nine patients (25 girls, 14 boys) were included. The mean age at symptom onset and diagnosis were 67.4 (2-204 months), and 80.6 (3-204 months) months, respectively. Acute ischemic stroke (AIS) and seizures were the most common initial findings, each observed in 9 patients (23%). A concomitant genetic disorder was identified in 13 patients, most commonly neurofibromatosis type 1 (n=4). Other genetic disorders identified were microcephalic osteodysplastic primordial dwarfism type II, trisomy 21, hereditary spherocytosis, Sturge-Weber syndrome, and variants in the *ANO1*, *RNF213*, *CBL* and *CHD4*. The median age of symptom onset was 31 months (IQR: 15-67.5) in MMS, and 66 months (IQR: 18.5-120) in MMD (p=0.241). At diagnosis, 46% of patients in the MMS group were asymptomatic, while 42.3% of the MMD group presented with AIS. All patients except two received antiplatelet therapy. The mean follow-up period was 60.4 months (IQR: 20.2-110 months). During clinical follow-up, AIS recurrence rate was 38% in MMS (5/13) and 42% (11/26) in MMD, with no significant difference. None of the six patients with adolescent-onset symptoms experienced recurrence; however, there was no statistically significant difference depending on the age of symptom onset. Surgical treatment was performed in five patients (13%). Except for one patient who experienced ischemic stroke within the first 24 hours post-surgery, no stroke recurrence was observed in the remaining four patients during the postoperative period. Six patients (15%) were lost to follow-up during the study period.

Conclusions: Unlike adult series, AIS was common compared to hemorrhagic stroke in both groups. The rates of incidental diagnosis in MMS, and stroke recurrence in both groups were similar compared to the previous literature. One third of the patients were classified as MMS, and were diagnosed while asymptomatic and received therapeutic interventions. Genetic diagnosis may enable presicion treatment and help determine the prognosis in patients with MMS.

Key Words: Moyamoya vasculopathy, pediatric stroke, clinical outcomes

ABSTRACTS

Topic: Neuromuscular Disorders

EPNS25_894 - Evaluation of Clinical Features of Patients Diagnosed with Spinal Muscular Atrophy Type 1 Before and After Newborn Screening Program: A Multicenter Experience in Turkiye Objectives

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Objectives

Spinal muscular atrophy (SMA) is an autosomal recessive (AR) neuromuscular disease characterized by progressive muscle weakness. In Türkiye, nusinersen treatment has been administered since July 2017. In May 2022, SMA was included in the national newborn screening program (NSP). This study aims to evaluate the clinical outcomes of SMA Type 1 patients diagnosed before and after NSP implementation, focusing on neuromotor development, nutritional status, and respiratory support needs in a multicenter cohort of patients receiving nusinersen.

Methods

This retrospective study included data from patients who received 5 doses of nusinersen treatment diagnosed with SMA Type 1 between the ages of 3 and 96 month who were followed up in 31 pediatric neurology clinics across Türkiye from December 01 2017, to December 31 2024. Patients were divided into two groups: those diagnosed before the implementation of NSP and those diagnosed through newborn screening. The clinical characteristics, including neuromotor development, nutritional status, and respiratory support requirements, were compared between the two groups.

ABSTRACTS

Results

In the study 391 patients with SMA Type 1 were included. Of these 282 (72.1%) were diagnosed before of NSP, while 109 (27.9%) were diagnosed NSP. Among the post-NSP group, 45 patients were asymptomatic at the time of diagnosis, while the remaining patients exhibited early symptoms such as tongue fasciculations and hypotonia. The mean age of symptom onset was 2.64±2.63 months.

The mean age at treatment initiation was significantly lower in the post-NSP group (3.07±3.75 months) compared to the pre-NSP group (7.17±8.18 months).

Nutritional Status; post NSP patients 96 (88%) continued oral feeding, whereas 7 required N/G feeding and 6 required gastrostomy. In contrast, among the pre-NSP patients, 118 (41.8%) maintained oral feeding, while 62 required N/G feeding 102 required gastrostomy.

Respiratory Status; post NSP patients 93 continued to breathe spontaneously, while 16 patients ventilation with tracheostomy required. In the pre-NSP group, 114 patients maintained spontaneous respiration, while 168 patients ventilation with tracheostomy required.

Conclusions

Our findings indicate that the implementation of NSP has led to earlier diagnosis and treatment initiation in SMA Type 1 patients, resulting in improved survival, reduced need for tracheostomy and gastrostomy. The OR inheritance of SMA, we strongly recommend the inclusion of treatable AR diseases in national NSP, particularly in regions with high rates of consanguinity.

ABSTRACTS

Topic: Movement Disorders/ Cerebral Palsy

EPNS25_895 - Improvement of writing dystonia in children after chronic stimulation of globus pallidus internus

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Objectives

Action dystonia during writing is a common manifestation of children with different forms of dystonia. It may interfere with the acquisition of reading and writing abilities. Pediatric writing dystonia differs from idiopathic writer's cramp in the involvement of upper limb proximal muscles. The WCRS+S (adding shoulders score) has been recently validated by our group, rating the severity of writing dystonia in children with epsilon-sarcoglycan related myoclonic dystonia.

The objective of this study was to analyze clinical characteristics of writing dystonia in a pediatric cohort, and test clinical efficacy of globus pallidus internus (GPi) chronic deep brain stimulation (DBS) using an adapted version of the Writer's Cramp Rating Scale (WCRS).

Methods

We conducted a longitudinal study, selecting patients >5 years old, with writing dystonia of variable etiology, who possessed handwriting abilities before receiving GPi-DBS at our institution. Patients were evaluated at baseline and after GPi-DBS using WCRS+S and BFM scales. Each examination was filmed following a standardized protocol, evaluated by two movement disorders pediatric neurologists. Wilcoxon signed rank test was used to compare pre/post-DBS scale scores.

Results

Twenty patients underwent DBS surgery at a mean age of 12 years (range=7-18; 13 females, 7 males). Patients were classified into three dystonia phenotypes: isolated (n=8; etiology was TOR1A, KMT2B, IMPDH2, and idiopathic), combined myoclonus-dystonia (n=9, SGCE and DHDDS) and complex (n=3, GNAO1, GCDH, and GM type 3).
In the 20 patients, the WCRS+S median score at baseline was 16 (q1-q3:12.5-18), improving after 16.15 months of follow-up post-DBS to 6 (q1-q3: 2.25-11.5), p=0.0003). BFM scores also showed significant improvement (BFM total pre: 33 median (q1-3: 20-68.5) /post 10 median(q1-q3: 5.25-22) (p=<0.0001). WCRS+S outcomes correlated significantly with BFM outcomes. No differences in the outcome were found between dystonia groups.

Conclusions

Writing dystonia in children can be successfully treated by GPi-DBS. The WCRS+S is a useful tool to correctly evaluate writing dystonia in pediatric patients of different etiologies, and helps quantify symptom relief in patients that have undergone DBS. Future studies will be necessary to assess if this improvement has a positive impact on academic performance.

ABSTRACTS

Topic: Climate Change

EPNS25_896 - Climate Change and Neurological Disorders in Childhood: A Scoping Review

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Objectives

Climate change's impact on global health is increasingly recognized, with growing focus on its effects on the developing brain and children with neurological disorders. This scoping review aims to update evidence on climate change's effects on pediatric neurological disorders

Methods

Following the PRISMA-ScR check-list, a protocol was created. A systematic search was performed across PubMed, Scopus, WoS, ClinicalTrials.gov, euclinicaltrials.eu, and the WHO ICTRP, up to September 2024. Two independent reviewers evaluated studies according to inclusion criteria. Data extraction included study design, population, exposure/intervention and outcome variables.

ABSTRACTS

Results

Out of 482 records, 5 met the inclusion criteria. The studies, conducted in different countries (Nigeria, USA, Netherlands, 2 in China) included 23,152 children (51% male), mostly focusing on early childhood (≤8 years). Study designs were mostly observational (OCEBM 3-4 level of evidence). Epilepsy was the most frequently investigated (3/5 studies). Cold exposure delayed increased seizure risk onset (5-21 days post-exposure), while extreme heat triggered a more immediate effect (0-13 days). Greater temperature variability and exposure to air pollution (e.g., PM2.5, SO2) also increased seizure risk. Climate disasters, such as winter storms, disrupted medication access, led to more frequent seizures. Extreme temperatures exposure in pregnancy and early childhood negatively affected white matter development, with significant mean diffusivity associations ($p<0.05$). One study showed that high humidity and temperature increased neuroinfectious diseases incidence: malaria (56% of cases), followed by diarrhea, meningitis, and respiratory infections. Children in high-density, low-income areas, especially girls and those under 5 years, were the most vulnerable

Conclusions

This review resumes the limited existing evidence on climate change's impact on pediatric neurological disorders, with epilepsy and neuroinfectious diseases being the most explored. Extreme temperatures, air pollution, and climate disasters seem to increase seizure risk, impair neurodevelopment, and primarily affect young children in low-income areas. However, prospective studies on neurological conditions are lacking, highlighting the need for further high-quality research in this field.

ABSTRACTS

Topic: Fetal and Neonatal Neurology

EPNS25_897 - Long-term outcomes in children with prenatally diagnosed cortical malformations – a retrospective study

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Objectives
Malformations of cortical development (MCD) represent a complex group of congenital disorders resulting from errors in the prenatal cerebral cortex development. These malformations can manifest as developmental delay and epilepsy. The severity of symptoms ranges from mild impairments to lifelong disabilities. Approximately 40–50% of drug-resistant epilepsies in childhood are attributed to MCD. The aim of this retrospective study is to investigate the relationship between MCD types (e.g. focal cortical dysplasia, lissencephaly, hemimegalenencephaly, polymicrogyria, schizencephaly, heterotopia) and the outcome of epileptic seizures as well as neurological development.

Methods
This study is designed as a retrospective analysis focusing on pediatric patients who were diagnosed with MCD via fetal MRI between 2011-2022 and followed up postnatally. Special attention was given on the impact of different types of MCD. Data collection included clinical findings (presence/severity/treatment of seizures, supportive therapy needed), pre- and postnatal MRI results, EEG findings and neurodevelopmental diagnostics (Bayley Scales of Infant and Toddler Development (BSID-III)). Follow-up included different time points of age (4 weeks, 3 months, 6 months, 12 months, 24 months, long-term visits if available). The chi-square test was used to examine the association between MCD types and categorical variables. Mann-Whitney U tests were used to compare BSID-III scores between children within the different types of MCD.

Results
Average gestational age was 27GW (19+4 to 37+1GW) at fetal MRI. A total of 50 cases were included, which had follow-up at defined time points. We found a statistically significant difference within the subgroups of MCD regarding to presence of seizures ($p<0.01$) and of drug-resistance epilepsy ($p=0.001$), EEG-abnormalities ($p=0.001$), as well as cognitive outcome at the age of 24 months ($p<0.01$).

Conclusions
Predicting seizure and neurodevelopmental outcome in children with prenatally diagnosed MCD remains a challenge. The results of this study are intended to improve the prognosis for children with MCD applying individualized therapeutic approaches through a structured follow-up. In the long run, this study is expected to provide an evidence-based foundation for more precise prenatal counselling as well as diagnostic and therapeutic possibilities at early stage to improve neurodevelopmental outcome in affected children.

ABSTRACTS

Topic: Epilepsy: Medical and Surgical treatment

EPNS25_898 - Registered and off-label cannabidiol treatment in pediatric patients with drug-resistant epilepsy

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Objectives
The use of cannabidiol (CBD) for therapeutic purposes in recent years it has become a promising option for children with drug-resistant epilepsy**.** Highly purified cannabidiol is an approved treatment for different types of seizures in children aged at least 2 years who have Lennox-Gastaut syndrome (LGS), Dravet syndrome (DS), and tuberous sclerosis complex (TSC). The aim of this study was to compare effectiveness of cannabidiol treatment between pediatric patients with drug resistance epilepsy receiving treatment under registered and off-label indications.

Methods
The authors analysed the data of children with drug-resistant epilepsy who were treated between 2023 and 2024 with cannabidiol at the Pediatric Neurology Department. Eighteen children were enrolled. Ten children were treated according to the registered indications, while eight patients received cannabidiol for refractory epilepsy beyond the approved indications due to the lack of effectiveness of other therapies.

Results
The authors compared the effect of the cannabidiol treatment in terms of the seizures' frequency reduction and assessment of cognitive functions in relation to epileptic history, seizure types, and EEG results.

Conclusions
The data on the effectiveness of treatment with off-label medications is limited. Our analysis aims to provide information and new options for cannabidiol treatment in children refractory epilepsy.

ABSTRACTS

Topic: Miscellaneous

EPNS25_900 - Cardiac phenotype in Neurofibromatosis Type 1: A tertiary single center experience

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Objectives: The cardiovascular abnormalities in Neurofibromatosis Type 1 (NF1) is often under-estimated. Our aim was to assess cardiac abnormalities in patients with NF1.
Methods: 114 NF1 patients (65 girls, 49 boys) followed at our center between 2018 and 2024 are included. All patients underwent standard electrocardiography (ECG) and echocardiography (ECHO). Holter ECG and cardiac magnetic resonance imaging (MRI) were performed whenever clinically indicated.
Results: The mean age at NF1 diagnosis, and first ECHO study at our center was 40.9 ± 38.7 months, and 107.6 ± 54.9 months, respectively. Cardiac abnormalities were detected in 38 of 114 (33.3%) patients by ECHO. Abnormalities were identified during the first (44/114; 38.6%) second (18/30; 60%), and third (8/12; 66.7%) screenings. Holter ECG (n= 13) led to a diagnosis of atrial tachycardia in one patient. Five patients had a cardiac MRI, with three of them showing abnormalities: mitral valve prolapse (MVP) with annular disjunction and interstitial fibrosis; hypertrophic cardiomyopathy (HCM); and a neurofibroma-like lesion encasing the mid-thoracic aorta. Initial ECHO findings included mitral valve insufficiency (MVI) or MVP (n= 15), patent foramen ovale (n= 11), atrial septal defect (n= 4), tricuspid valve insufficiency (n= 3), aortic valve insufficiency (AVI) or stenosis (AVS) (n= 2), along with HCM (n= 1), and right ventricular masses or myocardial heterogeneities (n= 7). During follow-up, ECHO findings normalized in 10 patients, while new abnormalities emerged in 3. Six out of 11 patients with hypertension received antihypertensive treatment. Midaortic coarctation was identified as the cause of hypertension in one patient, who subsequently underwent aortorenal bypass surgery. Mitral valve replacement was performed in a patient with grade 2-3 MVI and MVP. A hypoperfusion challenge study was planned for a patient with HCM, AVI, AVS, dyspnea, and coexisting moyamoya syndrome. A patient with a basilar artery aneurysm had embolization. Additionally, a patient with respiratory distress at birth and café-au-lait macules with pulmonary stenosis underwent balloon angioplasty. No significant relationship was found between ECHO findings and sex, freckling, Lisch nodules, plexiform neurofibromas, optic gliomas, scoliosis, or characteristic bone lesions. Significant association was observed with hypertension (p=0.002). No differences were found between ECHO findings and the age at NF1 diagnosis or BMI.
Conclusions: This data highlights the high prevalence of cardiovascular abnormalities in NF1, including congenital heart disease, vasculopathy, hypertension, and HCM. Cardiac screening and surveillance are key for appropriate management strategies to prevent long-term hemodynamic complications.
Key-words: Neurofibromatosis type 1, cardiovascular abnormalities, screening, management

ABSTRACTS

Topic: Neuromuscular Disorders

EPNS25_901 - Modelling The benefit of Givinostat on Duchenne Muscular Dystrophy (DMD) Patients, and their Caregivers

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Objectives

Givinostat, an oral histone deacetylase inhibitor, was recently approved in the US and UK for Duchenne muscular dystrophy (DMD) treatment in patients aged ≥6 years. This study aims to evaluate the benefit of givinostat in addition to stable corticosteroids, on the disease progression of DMD patients estimated from the cost-effectiveness model. This study estimates the impact of extending patients' lives in the earlier phases of the disease on both patients and caregivers.

Methods

The EPIDYS Phase 3 trial of ambulant DMD patients aged 6 and above on stable corticosteroid treatment, and receiving givinostat in addition to stable corticosteroids, and the open-label extension study of givinostat were integrated into Project Hercules' Markov model. The relative clinical effectiveness was obtained from a published analysis of givinostat versus the CNRG-DNHS (Cooperative International Neuromuscular Research Group Duchene Natural History Study) and iDMD (imaging DMD) and compared with a base-case model comparator from the University of Leicester's natural history model. The model simulated the long-term impact of givinostat over 50 years. Health benefit was discounted at 3.5% annually. The main outcome measured was quality-adjusted life years (QALYs) gained for patients. Additional outcomes included life years (LYs) gained and health-state utility values for patients and caregivers.

Results

Givinostat, in addition to stable corticosteroids, extended the median age that patients remained in the ambulatory health states. Median utility values were over double for early and late ambulatory states (0.79 and 0.64) compared with non-ambulatory states (0.314 to 0.211). Along with the additional 2.77 LYs and patients remaining longer in the early stages of the disease with higher utility values, givinostat treatment resulted in an additional 4.55 QALYs compared with natural history. The quality of life of the caregiver was also higher for the givinostat-treated group when dependents were in early and late ambulatory states (0.86 and 0.84, respectively) than for non-ambulatory disease states (from 0.78 to 0.81).

Conclusions

Model results showed that givinostat treatment slows disease progression, improving both patient and caregiver quality of life and resulting in QALY gains.

ABSTRACTS

Topic: Epilepsy: Diagnosis and Investigations

EPNS25_902 - Risk Factors for Chronic Epilepsy Following Autoimmune Encephalitis with NORSE Presentation in Pediatric Patients

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Objectives New-onset refractory status epilepticus (NORSE) may represent the clinical presentation of autoimmune encephalitis (AE) in approximately half of cases. This study aims to evaluate risk factors associated with the development of chronic epilepsy as an outcome of definite or probable AE with NORSE presentation in a cohort of pediatric patients.

Methods This retrospective, observational, multicenter cohort study included pediatric patients diagnosed with definite or probable AE presenting with NORSE. Independent predictors for the development of chronic epilepsy were analyzed.

Results A total of 28 patients (16 males) were enrolled and followed for a median duration of 57 months (range: 12-132). At the final follow-up, epilepsy was present in 35.7% of cases, with a higher prevalence in patients with probable antibody-negative AE (p=0.04) and those experiencing a longer duration of status epilepticus (SE) (p=0.01). A younger age at NORSE onset was associated with a more favorable outcome (p=0.007), whereas a poor response to acute-phase treatment (p=0.03) correlated with the development of autoimmune-associated epilepsy.
Multivariate analysis identified probable antibody-negative AE as the key independent predictor for epilepsy development (p=0.04).

Conclusions Epilepsy is a common sequela of definite or probable AE, occurring in 43.7% of cases. Among pediatric patients presenting with NORSE, the risk of developing epilepsy is approximately one-third. Early identification of SE etiology and the timely initiation of tailored treatment are associated with improved outcomes

ABSTRACTS

Topic: Neurogenetics

EPNS25_903 - Evaluatıon Of Demographıc, Clınıcal, Electroencephalographıc, And Neuroımagıng Fındıngs In Patıents Dıagnosed Wıth Epıleptıc Encephalopathy Through Targeted Gene Panel

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Introduction: Targeted gene panels have become an important diagnostic tool in the etiological investigation of developmental epileptic encephalopathy. In this study, we aimed to contribute to the literature by presenting the demographic, clinical, electroencephalographic, and neuroimaging findings of patients who received a genetic diagnosis through targeted gene panels.

Methods: Patients diagnosed with epilepsy and identified with a genetic etiology through targeted gene panels between January 1, 2017, and August 15, 2022, in Pediatric Neurology Clinics were included in the study.

Results: Of the patients in our study, 44 (55.7%) were male and 35 (44.3%) were female. Their ages ranged from 10 to 231 months, with a median age of 107 months. The age at diagnosis ranged from 7 to 213 months, with a median age of 83 months. Seizure onset age was between 1 and 208 months, with a median seizure onset age of 39 months. The predominant seizure semiology was motor in 68 (86.1%) patients and non-motor in 11 (13.9%) patients. Among the 68 patients with motor semiology, 39 (56.5%) had tonic-clonic, 17 (24.6%) had tonic, 5 (7.2%) had myoclonic, and 5 (7.2%) had atonic seizures. Among the patients with non-motor semiology, 9 (90%) had absence seizures, and 1 (10%) had autonomic seizures. Fourteen patients (17.7%) exhibited more than one seizure type. Status epilepticus was present in 9 (11.4%) patients. All patients had concurrent EEG recordings, with 24 (30.4%) showing normal and 55 (69.6%) showing abnormal results. Genetic results showed SCN1A mutations in 21 (26.6%) patients, CACNA1A in 17 (21.5%), SCN9A in 11 (1.9%), KCNT1 in 6 (7.6%), SCN8A in 5 (6.3%), KCNQ2 in 5 (6.3%), SCN2A in 4 (5.1%), KCNMA1 in 4 (5.1%), HCN1 in 4 (5.1%), KCNA2 in 1 (1.3%), and KCNB1 in 1 (1.3%) patients. One (1.3%) patient had a homozygous mutation, while 78 (98.7%) had heterozygous mutations. The inheritance distribution was autosomal dominant (AD) in 65 (82.3%) patients, autosomal dominant/recessive (AD/AR) in 13 (16.5%), and X-linked recessive (XLR) in 1 (5.1%) patient. Variant pathogenicity distribution included 48 (60.8%) variants of uncertain significance (VUS), 11 (13.9%) likely pathogenic, 16 (20.3%) pathogenic, and 4 (5.1%) likely benign variants. Familial segregation was observed in 20 (25.3%) patients.

Conclusion: Targeted gene panels are highly beneficial in the etiological diagnosis of patients presenting with developmental epileptic encephalopathy. Due to the necessity of personalized medicine applications, all epilepsy patients with developmental delay should undergo advanced genetic evaluation.

ABSTRACTS

Topic: Neurometabolic Disorders

EPNS25_904 - Long-term survival of children with metachromatic leukodystrophy in Germany

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Objectives

Metachromatic leukodystrophy (MLD) is a life-limiting neurodegenerative disease due to pathogenic variants in *ARSA.* Patients experience severe neurological symptoms, developmental regression, and early death. Aim of the study was to analyze survival and circumstances at death in children with late infantile and juvenile MLD in Germany.

Methods

Data from 120 children with late infantile and juvenile MLD from our nationwide MLD registry was analyzed regarding natural course and survival, partly with long-term follow-ups from medical records and detailed telephone interviews.

Results

From the 63 patients known to be dead, 36 had a late-infantile form (LI), 12 an early-juvenile form (EJ), 12 a late-juvenile form (LJ) and 3 unclear. Lifespan in the LI group ranged from 2.4 to 18 years (median 6.9), in the EJ group from 12 to 22.7 years (median 15.8), and in the LJ group from 11.1 to 49.5 years (median 25.2). Disease duration after first symptoms was 0.8 to 16.6 years (median 5.6) in the LI group, 7 to 18.6 years (median 11.3) in the EJ group, and 4.7 to 39.5 years (median 15.8) in the late-juvenile group. In 27 deceased patients, where more detailed data by telephone interviews were performed, prior to death all patients exhibited complete loss of function, speech loss, dysphagia, and spasticity. From these 27 children, 25 had a gastro-tube, 23 experienced pain, 21 had epilepsy, and 16 had vegetative crises. 19 patients died at home, 2 in a hospice, 5 in a hospital, and 1 in an intensive care unit. The causes of death included disease progression in 19 patients, infections in 14, and vegetative crises in 2 (multiple answers possible). Life-sustaining measures were discontinued in 11% of patients by stopping mucus suction, 19% by discontinuing supplemental oxygen, 22% by halting daily medications, 22% by ceasing nutrition, and 41% by stopping nutrition. Additionally, 44% of patients received morphine.

Conclusions

This survey provides first insights into national long-term survival data of the natural disease course for children with MLD. Prior to death, patients had a high disease burden and were in an advanced stage of the disease. These data may serve as a reference for analyzing survival and disease burden after stem cell- or gene therapy.

ABSTRACTS

Topic: Headache / Migraine

EPNS25_905 - Extensive clinical experience with repetitive neuromuscular magnetic stimulation in pediatric headache patients

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Objectives

Primary headache disorders are frequently accompanied by myofascial symptoms in the neck muscles, particularly the upper trapezius muscle (UTM), often leading to significant limitations in daily activities and participation. Repetitive neuromuscular magnetic stimulation (rNMS) has emerged as a safe and effective intervention targeting myofascial symptoms and headaches through bottom-up neuromodulation via the trigemino-cervical complex. This observational study provides an overview of our clinical experience with rNMS, using data from a large-scale patient cohort.

Methods

Treatment consists of six sessions in three weeks, each with a net stimulation time of 30 minutes. Pediatric headache patients underwent rNMS at our pediatric headache center. A comprehensive assessment was performed, including headache questionnaires, clinical and physiotherapeutic evaluations, algometry of the UTM, and safety monitoring. Patient and parent feedback on the rNMS procedure was also collected.

Results

Data from 100 completed treatment blocks will be available at the time of the conference. Preliminary analyses (78 blocks) revealed a significant reduction in headache frequency ($p=0.016$). Pressure pain thresholds over the UTM significantly increased following rNMS, with sustained improvements observed three months after treatment ($p<0.001$). The treatment was well-tolerated (approx. 80% of patients reporting no adverse events) and adherence to the protocol was high (> 85% of sessions completed as scheduled).

Conclusions

Its high level of acceptance and sustained therapeutic effects make rNMS a promising approach for managing primary headache disorders. Further research, particularly in controlled clinical trials, is needed to validate these preliminary results and explore the full potential of rNMS. The findings suggest that rNMS is a safe and effective treatment for reducing headache symptoms and alleviating associated muscular issues.

ABSTRACTS

Topic: Headache / Migraine

EPNS25_907 - Tracking memory function in adult migraine using an adaptive computer-based tool

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Objectives

Migraine is a prevalent condition across all age groups. However, its impact on memory performance remains insufficiently explored, particularly regarding long-term memory retention and decay. Existing evidence suggests migraine-associated changes in brain networks involved in memory consolidation, but no studies to date have specifically examined these effects.

Methods

A novel computer-based tool was developed to assess memory function using an iterative, adaptive paired-associate test with verbal and non-verbal visual items. Memory consolidation strength was evaluated through the rate of forgetting (RoF) of presented items, answer accuracy, and response times. Differences in these parameters were analysed between adults with episodic migraine and healthy controls. Additionally, a longitudinal within-subject analysis of RoF in migraine patients was conducted at three time points over four months.

Results

To date, data from 21 healthy controls and 11 patients have been analysed. Although not statistically significant, there is a noticeable trend suggesting that the migraine group has a higher RoF compared to controls ($p=0.058$). This could indicate that the control group retains items in memory for a longer time or forgets them more slowly compared to the migraine group. Accuracy rates were lower in the migraine group, although the difference was not statistically significant ($p>0.05$). Response time was significantly lower in the control group compared to the migraine group ($p=0.0078$).

Conclusions

The findings of these studies could support the evaluation of the RoF as a cost-effective and sensitive behavioural marker for monitoring the memory function in migraine. These insights may also extend to other common headache disorders or neurological conditions, such as epilepsy. A non-invasive, precise, and adaptive computerized tool for cognitive assessment holds significant potential for enhancing both routine clinical care and scientific research.

ABSTRACTS

Topic: Epilepsy: Medical and Surgical treatment

EPNS25_908 - Outcomes of a Holistic Transition Management Program for Patients with Complex Epilepsy Moving from Pediatric to Adult Care in a Dedicated Transition Space: A 4-Year Experience

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Objectives

The transition from pediatric to adult care has emerged as a critical issue in pediatrics and highlighted the need for dedicated transitional care services.

Given the complex needs of the epileptic patients and the specificity of pediatric epilepsy management, the transition for adolescents and young adults with complex epilepsies is a critical challenge. It involves not only seizure management but also addressing psychosocial comorbidities and optimizing their autonomy.

La Timone Hospital in Marseille, France, opened a dedicated transition space called 'L'Appart' in 2021, designed to welcome adolescents aged 13 and older with chronic or rare conditions. Regular medical follow-up is carried out at ‘the appart’ from the age of 13, following a three-step process, integrated into the patient's regular follow-up: the re-communication of the diagnosis by the referring doctor alone with the adolescent, the holistic assessment of needs and autonomy, and finally, the transfer consultation with the adult doctor and the pediatrician present.

Methods

The medical records of epileptic adolescents followed at ‘L’Appart’ will be reviewed to evaluate the clinical characteristics of their epilepsy, with a specific focus on intellectual capacity. Patient needs were initially assessed using a self-administered questionnaire, and the responses will be analyzed and compared to their clinical characteristics. The various interventions conducted at’ L’Appart’, as well as the transfer process to adult care, will be analyzed. Finally, one-year post-transfer, we will assess patients' perceptions of their preparedness for adult care and their experiences with adult consultations through a direct patient questionnaire.

Results

From January 2021 to December 2024, 739 adolescents with neurological conditions were followed at L’Appart. Of these, 329 were diagnosed with epilepsy. The mean age at the first consultation at L’Appart was 17 years (range: 11–25 years). Among the 329 epileptic patients, 108 underwent the transfer process before December 31, 2024, with a mean age at transfer of 19 years (range: 14–23 years). Of these 108 patients, 38 participated in a comprehensive transition program, which included at least one dedicated transition appointment at L’Appart prior to transfer.

Conclusions

Our objective is to (1) describe a transition program integrated into the routine follow-up of adolescents, in a dedicated transition space, where a specialized team facilitates the transition process during each medical consultation identify the specific needs of patients with complex conditions, particularly those with intellectual disabilities, and (2) to explore strategies to address these needs effectively.

ABSTRACTS

Topic: Neurorehabiltation

EPNS25_909 - The Investigation of The Effect of VNS Efficacy on Sleep Structure and Characteristics in Pediatric Patients with Refractory Epilepsy

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Objectives

Sleep disorders are significant concern in children with resistant epilepsy, impacting quality of life and overall well-being. Studies have shown a high prevalence of various sleep disturbances,such as sleep-disordered breathing,insomnia,and excessive daytime sleepiness.The exact impact of VNS efficacy on sleep structure and characteristics in pediatric patients with refractory epilepsy is not well understood. This study aims to investigate the effects of VNS therapy on sleep structure and characteristics in children with refractory epilepsy.

Methods

Twenty-eight children diagnosed with refractory epilepsy between 2021 and 2023 who underwent VNS therapy at tertiary level pediatric neurology department were included. Those deemed suitable for VNS therapy after discussion in the epilepsy surgery council underwent polysomnography evaluation prior to VNS implantation. Polysomnography was repeated in these patients at the 12th month of VNS therapy. Additionally,the Pittsburgh Sleep Quality Index and the Epworth Sleepiness Scale were used for these patients before and after VNS therapy.

Results

Of the 28 patients hospitalized and evaluated at the epilepsy center, 60% were male.The average age of the patients was 10.5 years.The patients were using an average of 2.4 antiseizure medication.At the 12th month of VNS therapy, a statistically significant reduction in daily seizure frequency was observed in the patients.Additionally,according to the PSG results,there was a statistically significant increase in total sleep efficiency.Improvements in sleep quality were noted based on the Pittsburgh Sleep Quality Index and the Epworth Sleepiness Scale.No significant difference was observed in the frequency of apnea among the patients.Furthermore,it was noted that families reported a reduction in anxiety levels with VNS therapy.

Conclusions

This is the first study to examine the effects of VNS treatment on sleep structure and characteristics in patients with drug-resistant epilepsy in childhood.It was observed that VNS treatment reduced anxiety levels in both patients and their families,leading to a positive impact on quality of life.

ABSTRACTS

Topic: Neurodevelopmental Disorders / Developmental Neuroscience

EPNS25_910 - Evaluation of long-term clinical and cognitive functions of children with corpus callosumagenesis

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Objectives:

Corpus callosum agenesis/dysgenesis can be observed as an isolated condition or as a component of various metabolic genetic diseases that present with variable clinical features. In this study, the clinical and cognitive status of children with corpus callosum agenesis/dysgenesis was evaluated.

Methods:

Children between the ages of 6-10 years who had corpus callosum dysgenesis/agenesis on cranial MRI were included in the study. 29 children were evaluated clinically and cognitively, and the Wechsler Intelligence Scale for Children (WISC) was applied to children who were able to speak and were considered to be neurologically and cognitively adequate.

Results:

Nineteen of the children had complete corpus callosum agenesis and 10 had incomplete corpus callosum agenesis. Eighteen of the children had mental motor retardation, 11 of these had spastic tetraparesis. Five of the children with normal motor functions had autism. After the preliminary neurological and cognitive evaluation of the patients, it was planned to perform WISC on 7 of them, but 3 of them could not comply WISC. When the results of 4 patients who could undergo WISC were evaluated, 2 patients had mild mental retardation (total intelligence score levels were 55 and 60, respectively) and one of these patients also had ADHD. Two of the children had normal intelligence level total intelligence score levels were 75 and 80, respectively). Whole exome sequencing were performed on 10 of the children. As a result of genetic tests, one of them was diagnosed with Pyruvate dehydrogenase deficiency, one of them with AP4B1-associated hereditary spastic paraplegia. No genetic significant mutation was detected in the other children.

One child was clinically compatible with Aicardi syndrome. Eighteen of the children had a history of seizures, 3 of the children had microcephaly, 1 child had dilated cardiomyopathy, and 1 child had polyneuropathy, 1 child had spina bifida colpocephaly with shunt. One of the children with normal neurological examination had corpus callosum agenesis accompanied by an interhemispheric cyst.

Conclusions:

Studies evaluating the long-term follow-up and cognitive findings of corpus callosum dysgenesis are limited in the literature. The clinical outcome in children with agenesis of corpus callosum is difficult to predict. In this study, we observed that corpus callosum agenesis/dysgenesis is associated with poor cognitive prognosis.

ABSTRACTS

Topic: Neuromuscular Disorders

EPNS25_913 - Patient-Reported Outcomes From a Phase 3 Study of Givinostat in Patients With Duchenne Muscular Dystrophy

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Objectives

Givinostat, an oral histone deacetylase inhibitor, was recently approved in the US and UK for Duchenne muscular dystrophy (DMD) treatment in patients aged ≥6 years. These analyses evaluated patient-reported outcome (PRO) data from the double-blind, randomised, Phase 3 EPIDYS study, which compared the efficacy and safety of givinostat with that of placebo in ambulant boys (aged ≥6 years) with DMD (NCT02851797).

Methods

The PRO instrument in EPIDYS was the Pediatric Outcome Data Collection Instrument (PODCI), commonly used to evaluate quality of life (QoL) in patients with DMD. The PODCI comprises a global function score and five subscales: upper-extremity (UE) function, transfer and basic mobility (TBM), sports/physical function (SPF), pain/comfort (PC), and happiness (HAP). Scores range from 0 to 100, with higher scores indicating better QoL. PODCI was completed by participants or proxy in EPIDYS at baseline and months 12 and 18. Results are based on descriptive statistics only. All patients received corticosteroids during the study.

Results

The baseline mean (SD) PODCI global function scores were 77.2 (12.5) for givinostat (n=81) and 76.9 (12.9) for placebo (n=39). At month 18, mean (SD) PODCI global function scores were 72.7 (15.3) for givinostat and 69.0 (15.9) for placebo, indicating less decline for givinostat-treated patients than for the placebo group. At 18 months, mean (SD) subscale scores were higher for givinostat than placebo for UE (80.7 [14.4] vs 76.7 [15.6], respectively), TBM (80.5 [16.4] vs 76.7 [17.1]), SPF (49.9 [21.6] vs 46.1 [22.2]), PC (79.6 [19.5] vs 76.6 [20.8]), and HAP (73.4 [19.3] vs 68.8 [25.2]).

Conclusions

Patients treated with givinostat showed smaller reductions in QoL across all PODCI global scores and subscales compared with placebo. These data suggest that givinostat provides a benefit in slowing down the decline in QoL in patients with DMD.

ABSTRACTS

Topic: Neurometabolic Disorders

EPNS25_914 - Long-term outcomes after hematopoietic stem-cell transplantation (HSCT) in children with juvenile metachromatic leukodystrophy (MLD) – a single-center study

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Objectives

Metachromatic leukodystrophy (MLD) is a life-limiting neurodegenerative disease caused by pathogenic variants in *ARSA.* Patients experience regression, severe neurological symptoms and early death. Hematopoietic stem-cell transplantation (HSCT) can stabilize disease progression in pre- or early-symptomatic patients with a late-onset form of MLD. This study aims to report on the long-term outcomes following HSCT in children with early-juvenile (EJ) and late-juvenile (LJ) MLD.

Methods

Families of 15 patients were contacted for long-term follow-up after HSCT. In addition to medical records, telephone interviews were undertaken in order to acquire standardized outcome measures for MLD.

Results

Of the 15 transplanted MLD patients (5 EJ, 10 JL) 3 LJ patients were pre-symptomatically transplanted (PT). HSCT was performed at the age of 5-18 years (median 13). Two EJ patients (onset at 3.5 and 4.5 years) died aged 14.2 and 23.3 years due to disease progression. Follow-up time after HSCT was on average 12 years (range 7-24). At their last follow-up, three patients continued to walk normally (2 PT), 2 showed slight gait instability (1 PT), 2 required support while walking, and 4 experienced reduced or lost gross motor function. None had lost head control. 9 patients showed speech decline with 3 losing speech (median age 10.9 years) (no PT). 4 patients developed dysphagia (median age 15.0 years), 8 had spasticity (median age 12.8 years) and 5 showed epilepsy (median age 17.6 years) (no PT). No patient showed vegetative symptoms. No patient was under palliative care. One patient received intrathecal baclofen, 3 patients took levetiracetam, one tizanidine and one an antidepressant. Two girls needed hormone replacement therapy for primary amenorrhea. 5 patients completed regular schooling (3 PT). The 3 PT patients had regular jobs, while the others worked in a sheltered employment.

Conclusions

This study provides single-centre data on long-term outcomes after HSCT in children with EJ and LJ MLD. The data reflect the burden of MLD after HSCT but also show differences compared to the natural course, where disease burden concerning neurological symptoms, drug use, and socio-medical- and daily-life aspects is clearly higher. Pre-symptomatically transplanted patients with LJ MLD showed best outcome, with regular schooling and jobs and independent walking and preserved speech. Careful patient selection for HSCT appears critical to optimize long-term outcomes.

ABSTRACTS

Topic: Headache / Migraine

EPNS25_915 - Multimodal examination of neck muscles in children and adolescents with headache disorders: palpation, algometry, infrared thermography, and ultrasound

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Objectives

Headache disorders in children and adolescents are often associated with complaints or symptoms in the neck muscles, which play a significant pathophysiological role due to the convergence of afferents via the trigemino-cervical complex. Currently, the muscular component is assessed using a time- and resource-intensive physiotherapeutic manual diagnostic approach that is partially painful for the children and insufficiently objective and reproducible. Therefore, infrared thermography (IRT) and ultrasound diagnostics, as non-invasive, point-of-care imaging techniques, are to be investigated for diagnosing and monitoring muscular symptoms.

Methods

The study includes three cohorts: 1) children and adolescents without headache disorders and without traumatic brain injury (TBI) in the past 24 months, 2) children and adolescents with headache disorders, and 3) children and adolescents who are being treated following a TBI. Study visits comprise: symptom-oriented medical history, neck disability index manual examination of the neck muscles, pressure pain thresholds by algometry, IRT and ultrasound.

Results

Preliminary data analysis showed that children with primary headache disorders have a lower pressure pain threshold, i.e. higher muscular sensitivity, and higher temperatures of the trapezius muscle than the healthy control group, suggesting a possible inflammatory state in the trapezius muscle. More comprehensive analyses will be available at the time of the conference.

Conclusions

The diagnostic methods of physiotherapy, algometry, IRT, and ultrasound diagnostics will be compared in terms of their ability to detect headache-associated muscular changes. Furthermore, the potential of IRT and ultrasound diagnostics to differentiate between children and adolescents with and without headache disorders will be evaluated.

ABSTRACTS

Topic: Neuromuscular Disorders

EPNS25_916 - Givinostat in DMD: results of the EPIDYS (study) with particular attention to MR measures of muscle fat fraction

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Objectives

Givinostat, a histone deacetylase (HDAC) inhibitor, is approved in the USA and UK for the treatment of Duchenne muscular dystrophy (DMD) in patients aged ≥6 years. This analysis sought to evaluate the efficacy of givinostat measured by muscle fat fraction in five key muscle groups required for ambulation at Week 72 vs placebo compared with baseline.

Methods

EPIDYS was a multicentre, double-blind, parallel-group, 72-week Phase 3 study of ambulatory males with genetically confirmed DMD (aged ≥6 years, on stable corticosteroids), randomised 2:1 to oral givinostat or placebo (NCT02851797). Two participant groups were stratified by baseline vastus lateralis fat fraction (VLFF): Group A ("target group") VLFF >5% to <30%, and Group B ("off-target group") VLFF either <5% or >30%. A flexible weight-based dosing regimen for givinostat was used, with a high starting dose (20–70 mg twice daily [b.i.d.]) to maximise efficacy, reduced as prespecified to 13–47 mg b.i.d., and then 10.6–37.4 mg b.i.d., to manage adverse events (AEs). The primary endpoint was mean change from baseline to Week 72 in 4SC time. A key secondary endpoint was mean change in VLFF by magnetic resonance spectroscopy (MRS). Fat fraction of VL and other thigh muscles were investigated as a exploratory endpoint using quantitative MRI imaging of water and fat (Dixon imaging).

Results

179 patients were enrolled, 59 in the off-target group (37 givinostat/22 placebo), and 120 in the target group (81 givinostat/39 placebo). Magnetic resonance cohort: >5 to <30% VLFF n=114 (77 in givinostat group and 37 in placebo group). There was significant less MRS VL fat infiltration in givinostat-treated subjects over 18 months compared to placebo (difference in least squares means [givinostat-placebo]: 2.92%; nominal *P*=0.0354). MRS VLFF fraction results were confirmed using quantitative imaging MRI (Dixon Imaging). The treatment effect of givinostat was demonstrated in each of the selected 5 key thigh muscles/muscle groups required for ambulation at Week 72 vs placebo (VL, nominal *P*=0.0033; biceps femoris long head, nominal *P*=0.0235; semitendinosus and quadriceps, nominal *P*=0.0009 each; and hamstrings, nominal *P*=0.0026).

Conclusions

Quantitative MR measures of muscle fat infiltration showed that givinostat ameliorates muscle deterioration in patients with DMD. These results also support the use of quantitative MR, a noninvasive biomarker to assess disease progression.

ABSTRACTS

Topic: Neurorehabiltation

EPNS25_919 - Study of corticokimatic coherence and desynchronization of mu rhythms in children with cerebral palsy undergoing intensive rehabilitation intervention

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Objectives

Intensive rehabilitation interventions are increasingly proposed in children with cerebral palsy (CP), arguing that they are more clinically efficient than classical rehabilitation. However, this is still debated. Therefore, biomarkers of brain plasticity are of interest to support this hypothesis. In this study we used high density EEG to measure neurophysiological markers of proprioceptive and motor pathways in a randomized controlled study assessing the efficacy of early hand and arm bimanual intensive therapy including lower extremities (eHABIT-ILE) against standard care in a cohort of children with CP.

Methods

29 children aged 1 to 5 years with bilateral spastic CP were included in 2 centers participating in this multicentric trial (CHU Angers and CHU Brest). Spino-cortical proprioceptive processing was assessed through the measure of corticokinematic coherence (CKC) in the somato-sensory area contralateral to passive rhythmic finger movements. We also studied the strength of the event-related desynchronization (ERD) of the mu rhythm in the alpha and beta frequency bands to passive rhythmic finger movements. 26 children were studied 2 times, at baseline and 3 months after either standard care or an eHABIT-ILE two weeks session that occurred after the baseline session.

Results

Data were analyzed in the sensors space at the group level only. The strengths of the coherence peaks as well as those of the mu rhythm ERD did not significantly between both sessions in both groups of patients.

Conclusions

This first analysis does not support EEG as a valuable tool to assess brain plasticity at short term after an intensive rehabilitation intervention through the analysis of CKC and desynchronization of mu rhythms. Further analyses in the sources space, taking into account individual responses to the therapy and types of brain lesion are needed to draw definitive conclusions.

ABSTRACTS

Topic: Movement Disorders/ Cerebral Palsy

EPNS25_920 - Proposed Algorithm for the Differential Diagnosis of Diseases with Bilateral Basal Ganglia involvement: Pictorial Presentation of a Single-Center Experience

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Objectives: The basal ganglia are paired deep gray matter structures primarily involved in motor control and initiation, as well as non-motor functions such as emotional behaviors and cognitive functions. Ailments affecting these structures result in characteristic disturbances of movement and muscle tone. The basal ganglia can be affected by a broad spectrum of diseases with varying etiologies, making the diagnosis of these conditions often challenging. The aim of our study is to provide an algorithm based on neuroimaging clues to aid in the differential diagnosis of conditions with bilateral basal ganglia lesions.

Methods: This retrospective, single-center observational study included all patients with bilateral basal ganglia involvement referred to our clinic over the past five years. We selected cases with MRI-confirmed bilateral basal ganglia lesions and performed a detailed review of their neuroimaging data, correlating these findings with clinical presentations and paraclinical results.

Results: We selected representative cases to highlight the most common causes of bilateral basal ganglia injury in pediatric patients. The cohort was initially divided into two main categories: acute and chronic conditions. Within each category, we further classified the cases based on the underlying etiology. The primary etiological groups included metabolic disorders such as mitochondrial diseases, Wilson disease, leukodystrophies, and lysosomal storage disorders; degenerative diseases including Huntington's disease and neurodegeneration with brain iron accumulation; neurocutaneous disorders for example neurofibromatosis; genetic disorders including tubulinopathies; infectious and inflammatory conditions; toxic causes such as carbon monoxide poisoning and vascular diseases. We analyzed common neuroimaging findings across these groups, which were then organized into a pictorial algorithm designed to facilitate diagnostic reference.

Conclusions: Certain basal ganglia changes on MRI examination can be highly suggestive of a specific condition or etiology. Quick recognition of these changes and their correlation with clinical and paraclinical findings allows for faster, more accurate diagnosis, thereby enabling more targeted and effective treatment strategies.

ABSTRACTS

Topic: Neurogenetics

EPNS25_922 - Ion Channelopathies in Familial Episodic Pain Syndromes: Insights from SCN10A and TRPA1 Variants

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Objectives

Familial Episodic Pain Syndromes (FEPS) are a group of rare inherited disorders characterized by recurrent pain episodes without identifiable structural abnormalities. These syndromes are primarily associated with mutations in *SCN10A* and *TRPA1*, genes encoding ion channel subunits involved in nociception. We aim to describe two cases of FEPS—one caused by a mutation in *SCN10A* and the other in *TRPA1*—to highlight their distinct phenotypic presentations, diagnostic challenges, and the importance of genetic testing in differential diagnosis.

Methods

Two patients with recurrent pain episodes of unknown etiology underwent comprehensive evaluation. Genetic analysis was performed using Whole Exome Sequencing (WES). The first patient, a 13-year-old male, experienced recurrent, severe burning pain in the penis and testicles, lasting one week per episode, occurring every one to three months, and associated with burning pain during urination. His history included methylphenidate-induced arrhythmia, leading to discontinuation, but cardiac evaluations found no pathology.He also reported flushing erythematous lesions on the trunk. Examination revealed no genital swelling or erythema, and the neurological assessment was normal. Urinalysis, Doppler ultrasound, pelvic MRI, and renal ultrasound were unremarkable.

The second patient, a 26-year-old female with a history of Sjögren's syndrome and fibromyalgia, presented with generalized burning and tingling pain, predominantly in the hands and feet, sometimes accompanied by macular-type rashes. She reported redness, itching, and pain following topical cream application, hypersensitivity to bed sheets, and muscle cramps. During pain episodes, she experienced shortness of breath, and palpitations. Additionally, she had dysuria, though urinalysis and imaging failed to identify an etiology. GLA testing for Fabry disease was normal.

Results

WES revealed a heterozygous c.1523G>A (p.Arg508Gln) variant in *SCN10A* in the male patient, supporting FEPS Type 2. *SCN10A* encodes NaV1.8, a voltage-gated sodium channel highly expressed in the testis, correlating with the patient's localized genital pain. The female patient carried a *TRPA1* c.2987G>A (p.Arg996His) variant, previously reported in a patient with painful neuropathy (PMID: 37079850), suggested a diagnosis of FEPS Type 1. *TRPA1* is highly expressed in the bladder, potentially explaining her dysuria and pain sensitivity.

Conclusions

These cases highlight the heterogeneity of FEPS and the value of genetic testing in unexplained pain syndromes. The distinct pain localizations align with the tissue-specific expression of *SCN10A* and *TRPA1*, emphasizing their roles in sensory processing. Early genetic screening is crucial for timely diagnosis and personalized management in recurrent, idiopathic pain cases.

ABSTRACTS

Topic: Miscellaneous

EPNS25_924 - Volumetric MRI study of brain alterations in glutamatergic disorders: GRIN, STXBP1, and SYNGAP

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Objectives

The aim of this work is to explore possible common and specific volumetric features that could be identified in conventional brain MRI of patients with three different glutamatergic synapse disorders: *SYNGAP1*, *GRIN*, and *STXBP1.* This information may enhance diagnostic accuracy and provide a more nuanced understanding of these conditions.

Methods

Structural MRI data were obtained from patients diagnosed with *SYNGAP1* (n=17), *GRIN* (n=20), and *STXBP1* (n=11) mutations. Automated segmentation tools were used to extract regional brain volumes, including cortical, subcortical, ventricular, cerebellar and white matter volumes. Independent t-tests Mann–Whitney U test were performed to compare the regional brain volumes between patients and an age-matched control. An ANCOVA approach was used to adjust for covariates such as age, sex and disease. Statistical significance was set at $p<0.05$.

Results

The analysis revealed significant volumetric differences between patients and controls. Shared patterns included larger volume of the basal ganglia (putamen, Cohen's d = 2.32, accumbens, Rank-biserial correlation coefficient r = 0.26), thalamus (d = 1.28), and cortical gray matter across parietal ($p < 0.00001$, d= 2.7), frontal ($p < 0.00001$, d=2.49), temporal ($p < 0.00001$, d=1.64), and occipital lobes ($p < 0.00001$, d=1.49). Higher ventricular volume (r = 0.39) and bilateral white matter volume deficit (d = 1.38) were also observed. Limbic structures, such as the amygdala (d = 2) and the parahippocampal region (d = 1.28), showed volume deficits, while regions like the cingulate gyrus (r = 0.9) and insula (d = 0.7) presented higher volumes. Cerebellar volume was significantly smaller overall (d = 0.72), with specific regions of the vermis showing larger volumes.
Disease-specific findings included significant cerebellar atrophy and bilateral enlargement of the supplementary motor cortex in *STXBP1* patients, suggesting compensatory mechanisms for severe motor impairments. *SYNGAP1* patients exhibited anterior body enlargement of the corpus callosum, while *GRIN* patients showed milder structural abnormalities.

Conclusions

This study highlights significant structural brain differences between patients with *SYNGAP1*, *GRIN*, and *STXBP1* mutations and healthy controls. Shared patterns, such as augmented ventricular volumes and limbic system volume deficits, suggest common neurodevelopmental disruptions, while disease-specific alterations, including smaller cerebellar volume and higher volume of the corpus callosum, reflect the unique clinical profiles of each disorder. These findings underscore the utility of volumetric measures of conventional MRI for identifying potential biomarkers for diagnosis and monitoring in rare neurodevelopmental conditions.

ABSTRACTS

Topic: Cerebrovascular Disorders

EPNS25_926 - Impairment of executive functions as a long-term outcome in children with early onset arterial ischemic stroke

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Objectives

Relatively few studies of cognitive sphere in children with stroke are devoted to the investigation of executive functions such as cognitive control and working memory. However, these executive functions have a significant impact on a child's academic performance and socialization.
The **aim** was to investigate the features of cognitive control and working memory at primary school age in children who suffered pediatric arterial ischemic stroke (PedAIS) under 24 months of life.
Methods

Cohort study, prospective design. Clinical group: 57 children (38 boys), PedAIS onset under 2 y.o., brain MRI confirmation. There were perinatal (n=12, 21%) and pediatric (n=45, 79%) types of ischemic stroke onset. Cognitive tests have been performed at the stage of long-term consequences when they started primary school at 7.8±1.3 y.o.
Control group: 47 children (21 boys) with no neurological disorders in medical history. Cognitive tests have been performed at the age they started primary school at 7.8±1.2 y.o.
Go/No-Go task (*cognitive inhibition*), The Corsi block-tapping test (*working memory capacity*) have been conducted for the cognitive assessment.
Statistical analysis: RStudio software, descriptive statistics, Kruskal–Wallis and Dunn's tests with Benjamini–Hochberg procedure.
Results

Subcortical stroke type (n=38, 67%), parity of left (n=23, 40%) and right-sided (n=21, 37%) were found in clinical cohort in general. There were no significant differences in the cognitive control and working memory within the clinical group depending on the hemispheric localization (left- or right-sided, bilateral). Children with combined infarct localization (simultaneous involvement of the cortical and subcortical area in the focus of the infarction) showed lower results in working memory than children with subcortical types of stroke (p=0.0496).
Significant differences were found between PedAIS and control group participants in the working memory task (p=0.044). The clinical group and the control group had significant differences in the results of Go/No-Go task (p=0.005).
Conclusions

Children with PedAIS early onset demonstrated lower results in cognitive control and working memory tasks at the primary school age compared to the healthy controls. Infarct localization both in cortical and subcortical areas had a more pronounced negative impact, while left/right hemispheric localization didn't show any obvious effect on executive functions in those patients.

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ABSTRACTS

Topic: Movement Disorders/ Cerebral Palsy

EPNS25_927 - When Movement Becomes Awry: Unraveling Phenotype-Genotype Corelates of Paroxysmal Dyskinesias In Omani Population

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Objectives To unravel the phenotypic variability of patients harboring the genetic mutation for Paroxysmal Dyskinesias and to delineate the comorbidities, management response and effect on activities of daily living to establish phenotype-genotype correlates.

Methods It was a retrospective review of genetically confirmed cases of paroxysmal dyskinesia meanwhile we picked up novel pathogenic mutation for paroxysmal kinesogenic dyskinesia and it was performed according to local regulations and was approved by the institutional ethical committee.

Results We identified 12 affected members with paroxysmal dyskinesias from 5 different families;10 cases had paroxysmal kinesogenic dyskinesias (PKD) and two members had non kinisogenic dyskinesia (PNKD). Family 2 had maximum affected cases i-e 4, two of which are siblings though all 4 are of same tribe with double consanguinity. All of them harbored pathogenic homozygous variant c.799del (p.Asp267*46) of PRRT2 gene and have kinisogenic dyskinesia (pharmacosensitive) but have different cognitive abilities.We didn't find strong association between frequency of dyskinesias and cognitive impairment as they were independently related. Family 3 had three siblings; two of which harbor pathogenic heterozygous c.649del (p.Arg217Glufs*12) variant of PRRT2 gene with infantile onset seizures and no evolution of PKD but one of them is severely autistic and their one sib harbor different mutation like rest of the Omani families with infantile onset seizures and early onset dyskinesias warranting therapeutic intervention. PNKD is identified in single family; mum had onset at 9 years with less frequent episodes and severe exacerbation during her two pregnancies followed by secondary infertility (mosaic Turner) but our patient is 8 years old with onset at 4 months of age having daily episode of dystonia which starts in the upper limbs then spread to involve whole body with lower limb scissoring, orofacial dyskinesia exacerbated with stress and partial response to clonazepam. We identified pathogenic PDE2A mutation in one child with background speech delay and evolved to paroxysmal hyperkinetic movements at 3 years of age with daily multiple episodes and refractory to clonazepam as well as carbamezapine, the variant has been segregated in parents and one sib harbored homozygous variant with delay till date.

Conclusions Paroxysmal Dyskinesias are phenotypically variable in terms of age of onset, movement phenomenology and comorbidities especially the seizure occurrence and cognitive impairment. Overall genetic testing helps identifying the exact etiology, the variable nature of paroxysmal dyskinesias make genotype-phenotype correlation challenging in face of unique clinical profile; posing the therapeutic implications.

ABSTRACTS

Topic: Epilepsy: Diagnosis and Investigations

EPNS25_928 - Frontal Onset Absence Epilepsy in Children: A Single Center Experience

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Objectives

Childhood absence epilepsy is a common paediatric epilepsy syndrome with specific seizure semiology, electroencephalographic features and treatment. A careful anamnesis, physical examination including hyperventilation and EEG are usually sufficient for the diagnosis. Childhood absence epilepsy usually responds well to treatment and patients can discontinue antiepileptic drugs at a later age. Studies have found that frontal-onset absence, which is considered as a subgroup of childhood absence epilepsy, is generally more resistant to treatment. We aimed to compare our patients with frontal onset absence epilepsy with the literature.

Methods

Patients who were followed up in the pediatric neurology clinic with the diagnosis of absence epilepsy were retrospectively examined. Among the patients with childhood and juvenile absence epilepsy; patients with frontal-onset spike waves followed by typical generalized 3 Hz waves in EEG findings were included in the study. Demographic data, clinical, laboratory and imaging findings of the patients were recorded.

Results

10 patients were identified, 6 female and 4 male. The mean age of seizure onset was 7 (3-12). Apart from absence seizures, 3 patients had seizures with generalized tonic-clonic semiology. Bilateral EEG was detected in 5 patients and unilateral frontal onset in the other 5 patients. Cranial MRI was performed in 8 patients and was found to be normal. 2 patients were not using antiepileptic drugs. 3 patients were using monotherapy and 5 patients were using polytherapy. 3 patients had learning or behavioral problems.

Conclusions

The seizure onset age and normal cranial imaging of the patients in our study were consistent with the literature. While the bilateral frontal onset rate (12/7) was found to be higher in the literature, it was found to be equal in our patients (5/5). Learning and behavioral problems were also seen in our patients, consistent with the literature. The rate of patients using polytherapy in our study was found to be higher than in the literature.

We support the idea that frontal onset absence epilepsies may be more resistant as a subtype of childhood absence epilepsies and that behavioral and learning problems may be seen. However, we believe that studies with a larger number of patients are needed.

ABSTRACTS

Topic: Infectious and Inflammatory Diseases/ Neuroimmunology

EPNS25_929 - Six Faces of Autoimmune Encephalitis: A Case Series

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Objectives: Autoimmune encephalitis (AE) is a non-infectious, immune-mediated disorder affecting the cortical and white matter of the brain. It typically presents with seizures, movement disorders, and/or psychiatric symptoms in the acute or subacute phase. This study presents six pediatric cases with varying clinical manifestations, diagnosed as seronegative or seropositive autoimmune encephalitis.

Methods: Patients diagnosed with autoimmune encephalitis based on clinical and laboratory findings at our pediatric neurology clinic between 2023 and 2024 were included in this case series.

Results: The study included six patients (three males, three females) aged 7–17 years (median age: 11 years). Clinical presentations included status epilepticus (n=2), encephalopathy (n=1), psychiatric symptoms (n=1), ophthalmoplegia (n=1), and hemiplegia (n=1). Cerebrospinal fluid (CSF) analysis revealed oligoclonal band positivity and/or pleocytosis in five of six patients. Brain magnetic resonance imaging (MRI) findings varied among cases: two patients had normal MRI scans, while others exhibited distinct abnormalities. The patient with ophthalmoplegia demonstrated T2/FLAIR hyperintensity in the left cerebellar pedicle. The patient with hemiplegia presented with an extensive lesion involving the left frontal lobe and corpus striatum. Two patients had limbic region involvement. One patient developed AE secondary to herpes simplex virus (HSV) encephalitis, with no detectable antibodies in CSF or serum; however, Purkinje cells exhibited immunoreactivity to an unidentified antibody. Another patient with hemiplegia tested positive for CV2/CRMP5 (Collapsin Response Mediator Protein 5) antibody. Two patients were positive for LGI1 (Anti-leucine-rich glioma-inactivated-1) antibodies in CSF/serum—one presenting with ophthalmoplegia and the other with status epilepticus, later developing faciobrachial dystonia and hyponatremia, consistent with LGI1-associated AE. The remaining two patients had normal MRI findings and no detectable autoantibodies; however, their clinical presentation—new-onset seizures, psychiatric symptoms, and characteristic EEG findings (delta brush and periodic lateralized epileptiform discharges [PLEDs])—supported an AE diagnosis. All patients were screened for paraneoplastic syndromes, but no underlying malignancy was identified. All patients responded to immunomodulatory therapy, with no recurrence except for one seronegative AE patient who experienced a second attack. Despite re-evaluation, no causative antibodies were identified in this case.

Conclusions: This case series highlights unusual clinical presentations of autoimmune encephalitis, contributing to an expanded understanding of its phenotypic spectrum. Increased awareness of these diverse manifestations is essential for timely diagnosis and management.

ABSTRACTS

Topic: Movement Disorders/ Cerebral Palsy

EPNS25_930 - Paroxysmal Dyskinesia in Children : Back to the Basics after Genetic Studies ?

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Objectives

Paroxysmal dyskinesias (PxD) are recurring episodes of chorea, dystonia, ballism, or any combination of the above, of abrupt onset and offset, without loss of consciousness. Recognising these conditions is important, as treatments are available. These rare movement disorders are typically categorised into four main phenotypes by Demirkiran and Jankovic's clinical classification based on triggers and duration : kinesigenic PxD (PKD), non-kinesigenic PxD (PNKD), PxD induced by prolonged exercise (PED) and hypnogenic PxD (PHD), although this final group is no longer technically part of the PxDs. The main genes for each category were discovered between 2004 and 2012, respectively *PRRT2, PNKD* (previously *MR-1*), *SLC2A1* and *ADCY5.*

Today, with the development of genetic techniques, over 35 genes are associated with PxDs, with significant phenotypic heterogeneity and genetic pleiotropy. The main objective of this study is to describe a cohort of paediatric paroxysmal dyskinesias by describing the frequency of different PxD phenotypes and the various genes involved.

Methods

This retrospective study involves 72 paediatric patients presenting with PxD and having undergone the "paroxysmal movement disorder" gene panel (Dr Riant, AP-HP). All patients had their medical follow-up within the Paris public hospital system (AP-HP). Clinical, biological, radiological and genetic data was collected from electronic medical records via Orbis software.

Results

The cohort consists of 64% predominant PKD, 24% predominant PNKD, 19.4% PED, and 19.4% PHD. The gene panel led to genetic diagnosis for 50% of patients, and the main genes involved were *PRRT2* (28.4%), *ADCY5* (9.5%) and *ATP1A3* (6.8%). Further genetic analyses in 21/36 patients with a negative panel brought to light pathogenic variants in four genes previously not associated with PxDs : *KMT2B, CHD8, SLC6A19* and *KCNJ10*.

We found notable clinical features associated with the most frequent genes, namely a history of epilepsy and an onset of PxD after 3 years of age for *PRRT2*, and nocturnal episodes for *ADCY5*. Baseline neurological examination is typically normal for *PRRT2*, abnormal for *ATP1A3* and variable for *ADCY5*.

Conclusions

This study is the first description of a paediatric PxD cohort with wider genetic analyses, evaluating proportions of each gene involved and bringing to light new genes associated with PxDs. We find Demirkiran and Jankovic's classification still relevant in 2025. Moreover, associated with the analysis of certain notable clinical features, it can help with diagnosis and therefore treatment prior to a genetic diagnosis. We bring forward an algorithm which summarises the diagnostic approach for paediatric PxDs.

ABSTRACTS

Topic: Infectious and Inflammatory Diseases/ Neuroimmunology

EPNS25_931 - Intrathecal continuous Interferon A admission via pump in children with subacute sclerosing panencephalitis - A multicenter experience

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Objectives Subacute sclerosing panencephalitis (SSPE) is a long-term consequence of measles infection in infancy. It causes neurodegeneration with symptoms such as behavioral change, massive decline in cognitive and motor function and epilepsy.

The course of the disease is progressive with early death within a few years of diagnosis. Sporadic remission has only been reported in 5% of the cases.

There is no causal treatment until now. Immunomodulant therapy with Interferon A (IFN A) and Isoprinosine can expand the life expectancy of affected children, but no data concerning continuous intrathecal infusion of IFN A in children and adolescents is available.

The first objective was to evaluate safety and then also efficacy of this treatment option.

Methods In this retrospective study we included 14 patients from 9 pediatric centers that have been treated with continuous application of intrathecal interferon alpha (mostly Roferon alpha) via a subcutaneous reservoir and Isoprinosine orally.

Patients were monitored on a regular basis, as the reservoirs need to be refilled every 3 weeks. Clinical staging was done using the criteria of Jabbour et al., 1975.

Data analysis was performed using SSPS Version 28.

Results Patients were followed up for an average of 4.4 years (25th-75th percentile 2,03-7,3 years). Mean survival was 10,37 years. Duration of intrathecal IFN-admission ranged from 28 days to 5408 days (mean 1581,36 days). Revision of the reservoir was necessary 16 times in 8 patients mostly due to catheter dislocation (n=5) ,malfunctioning (n=3) and battery exchange (n=2) due to long runtime.

In four patients, progression was not only slowed down, but they improved clinically after IFN A admission.

Conclusions Intrathecal interferon A admission can be considered as a treatment option in children and adolescents with SSPE that also receive Isoprinosine treatment. As Roferon alpha is no longer available, alternative drugs and application regimen should be developed.

ABSTRACTS

Topic: Neuromuscular Disorders

EPNS25_932 - Disease progression modeling in Duchenne muscular dystrophy: delayed decay in 4-stair climb with givinostat compared with standard of care

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Objectives

Givinostat, an oral histone deacetylase inhibitor, was recently approved in the US and UK for Duchenne muscular dystrophy (DMD) treatment in patients aged ≥6 years, based on findings from the Phase 3 EPIDYS study. To explore its potential impact on disease progression, the DMD Clinical Trial Simulation tool, developed by C-Path's Duchenne Regulatory Science Consortium (D-RSC), was updated with data from EPIDYS and the ongoing long-term safety and tolerability study (LTSE) to simulate the 4-stair climb (4SC) endpoint and assess differences in the time course of DMD progression between patients receiving givinostat and standard of care (SoC).

Methods

The analysis used nonlinear mixed-effects modelling. To align with the D-RSC model, 4SC was transformed into climb velocity (1/s). The published DMD disease progression model of 4SC was validated with baseline demographic data from patients in the EPIDYS study receiving SoC. The model was then re-estimated using only data from givinostat-treated patients. The model performance was assessed using visual predictive check (VPC) diagnostics. Simulations were then conducted in 1000 virtual patients using baseline demographic data from the available studies, comparing the updated (givinostat) and published (SoC) models; 100 replicates were simulated, accounting for interindividual variability. Virtual patients were followed for 5 years, and the effects of givinostat and SoC were compared using the median curve with 95% CI.

Results

Baseline data from a total of 357 patients were included in the model, with 296 receiving givinostat and 61 receiving SoC. Patients with missing baseline age, baseline 4SC scores or observations, or those who became non-ambulant and unable to perform the 4SC were excluded. VPC diagnostics showed good agreement between model predictions and observed data for both SoC-treated patients from EPIDYS and givinostat-treated patients from EPIDYS and the LTSE. Results of the 5-year simulations showed that givinostat was associated with a delay of approximately 2 years in the DMD progression curve for 4SC starting at 9 years of age. At 14 years of age, the model showed that patients treated with givinostat were able to climb 4 stairs faster (approximately 0.1 1/s) than those receiving SoC.

Conclusions

Using the D-RSC disease progression model, this analysis demonstrated a delay in DMD progression, as measured by decline in 4SC, in patients treated with givinostat compared with SoC.

ABSTRACTS

Topic: Neurodevelopmental Disorders / Developmental Neuroscience

EPNS25_934 - Towards the Description of a Common Clinical Phenotype for KLF7 Variants: a Case Series of Eight Patients

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Objectives The Krüppel-like factor (KLF) family includes zinc finger-containing transcription factors that play a critical role in neural development. Among them, KLF7 is essential for nervous system development. Recent evidence links variants in the *KLF7* gene with hypotonia, dysmorphic features, psychomotor delay, and autism, with haploinsufficiency of *KLF7* potentially causing a distinct neurodevelopmental phenotype. Our study aims to collect data from patients with *KLF7* variants to better define the associated clinical phenotype and contribute to understanding the impact of these variants on neurodevelopment.

Methods In this study, we retrospectively enrolled eight patients with KLF7 variants, identified through GeneMatcher, from six different medical centers around the world. Patient data were collected in a dedicated database and analyzed qualitatively.

Results The cohort consists of five males and three females, with unremarkable family and perinatal histories. Six patients had global developmental delay, while one patient had motor delay only. Four patients had their first neurological examination before the age of one year. One of them had generalized hypertonia and later developed dystonia, one had axial hypotonia and progressed to parkinsonism, while the other two had generalized hypotonia that eventually resolved. One patient presented with a broad-based gait in the second year of life and later developed ataxia. Another patient presented with a clinical picture of parkinsonism at the age of 12 years. In terms of cognitive development, six patients have mild to severe intellectual disability. Six patients show autistic features and one of them also attention deficit and hyperactivity disorder. Only three patients exhibit dysmorphic features. Seven patients underwent brain magnetic resonance imaging; a common feature of reduced trophism at the supra- and/or subtentorial level was found in three of them; four patients had white matter abnormalities. Genetically, all patients carry de novo heterozygous *KLF7* variants.

Conclusions This case series describes eight previously unreported patients with *KLF7* variants. Consistent with previous studies, all patients exhibit at least one neurodevelopmental feature, with four patients have both intellectual disability and autistic features; four others present a movement disorder that has never been associated with *KLF7* variants before. Therefore, our case series expands the known phenotype of the KLF7 gene and supports its inclusion in the search for the genetic basis of neurodevelopmental and movement disorders. These findings further reinforce the growing evidence of a shared genetic basis between these conditions.

ABSTRACTS

Topic: Epilepsy: Medical and Surgical treatment

EPNS25_937 - Fenfluramine in non-Dravet SCN1A patients

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Objectives SCN1A mutations are associated with a highly heterogeneous epileptic spectrum, encompassing severe forms such as Dravet syndrome and milder epileptic phenotypes. Fenfluramine (FFA), a serotonergic modulator, has demonstrated efficacy in Dravet syndrome and yielded positive outcomes in other DEE such as Lennox-Gastaut syndrome and CDKL5 deficiency disorder. However, its effects in non-DEE epilepsies remain unexplored. This study aims to assess the efficacy of FFA in patients with SCN1A-related non-Dravet, non-DEE epilepsy.

Methods We retrospectively analyzed data from 12 patients (8 females, 4 males) followed at seven epilepsy centers, including GEFS+ (n=7), Severe Myoclonic Epilepsy Borderland (n=2), myoclonic-atonic epilepsy (n=1), and 2 patients with unclassified epilepsy presenting predominantly with focal febrile and afebrile seizures. All patients were resistant to previous anti-seizure medications (ASM). FFA was added to their ongoing ASM regimen at a mean dose of 0.37 mg/kg/day (range: 0.1–0.7 mg/kg/day).

Results Seizure frequency prior to FFA ranged from one every two months to multiple seizures per day. As add-on therapy, FFA resulted in a mean seizure reduction of 91%, with complete seizure resolution in over half of the patients. Notably, patients with GEFS+ achieved a >90% seizure reduction, with 5/7 cases seizure-free. The 2 patients with unclassified epilepsy reached 90% seizure reduction. The 2 SMEB patients experienced an 87.5% reduction, while the patient with myoclonic-atonic epilepsy became seizure-free but discontinued FFA due to psychomotor agitation, likely triggered by seizure cessation. Currently, 11 of 12 patients continue FFA treatment without major adverse effects; two reported transient mild appetite reduction and mild sleep disturbances. The mean treatment duration is 16.8 months (range: 3 months–4.5 years). Three patients exhibited positive behavioural and cognitive changes. Six patients demonstrated significant improvement or complete normalization of EEG abnormalities.

Conclusions This case series represents the first description of FFA use in patients with non-Dravet SCN1A-related pharmacoresistant epilepsy. Our findings suggest that SCN1A pathogenic variants may play a role in mediating FFA's therapeutic response and support its consideration as an add-on treatment option in this patient population.

ABSTRACTS

Topic: Neuromuscular Disorders

EPNS25_939 - Givinostat Effect on Respiratory Function in Duchenne Muscular Dystrophy Before and After Ambulation Loss: Results from EPIDYS, OLE, and PRO-DMD-01

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Objectives

Givinostat, an oral histone deacetylase inhibitor, was recently approved in the US and UK for Duchenne muscular dystrophy (DMD) treatment in patients aged ≥6 years. This study evaluated the effect of givinostat on the pulmonary function of patients who experienced loss of ambulation (LoA) during follow-up.

Methods

Data from the double-blind, randomised, phase 3 EPIDYS study in ambulant boys (aged ≥6 years) with DMD (NCT02851797) and its ongoing open-label extension (NCT03373968) were indirectly compared with results from PRO-DMD-01 (NCT01753804), a natural history study of disease progression among boys with genetically confirmed DMD. The comparison was balanced using the matching-adjusted indirect comparison method, adjusting for patient characteristics at LoA. Forced vital capacity (FVC) %-predicted mean trajectories before and after LoA were estimated using longitudinal mixed effects models to account for repeated measures and fitted to data over all available assessments during the pre- and post-LoA periods.

Results

This analysis included 56 patients treated with givinostat and steroids compared with published data on 51 patients from the PRO-DMD-01 study who received steroids only. Among weighted givinostat-treated patients, 2 years before LoA, the weighted least-squares mean (standard error [SE]) FVC %-predicted was 91.3% (2.2%), decreasing to 83.0% (2.3%) at LoA and 74.4% (2.4%) 2 years post-LoA. The mean (SE) annual decline in FVC %-predicted was 3.6% (1.2%) before LoA and 3.9% (1.3%) after LoA. In the PRO-DMD-01 study, the mean (SE) annual decline in FVC %-predicted was 5.6% (2.1%) before LoA; this increased to 10.1% (2.2%) after LoA.

Conclusions

FVC% trajectories showed a slower and less pronounced decline in patients treated with givinostat in addition to steroids than in those treated with steroids only, with no difference observed before and after LoA in the givinostat group. These findings suggest improved stabilisation of pulmonary function with givinostat treatment.

ABSTRACTS

Topic: Cerebrovascular Disorders

EPNS25_940 - Natural history of Schimke immunoosseous dysplasia with a focus on cerebrovascular events

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Objectives: Schimke Immunoosseous Dysplasia (SIOD) is a rare autosomal recessive multisystem disorder characterized by spondyloepiphyseal dysplasia, progressive renal disease, immunodeficiency, and an increased risk of vascular complications. This study investigates the incidence, clinical features, and mechanisms of cerebrovascular events in SIOD patients, aiming to enhance diagnostic and management approaches.
Methods: Six patients diagnosed with SIOD and followed between 1995 and 2024 were included in the study.
Results: All patients (5 boys, 1 girl) had homozygous variants in *SMARCAL1***.** The median age of symptom onset and diagnosis were 32.5 (12-84) months, and 58.5 (18-84) months, respectively. The median follow-up was 40 (3-86) months. All patients had growth retardation, in combination with generalized or eyelid edema (n= 2), global developmental delay (n= 2), and dysmorphic findings (n= 1) as the initial symptoms. Four patients developed nephrotic syndrome; one requiring peritoneal dialysis and another undergoing renal transplantation. Three patients received intravenous immunoglobulin therapy for immunodeficiency. The median age of onset for nephrotic syndrome and immunodeficiency were 5 (3-7) years, and 7 (3-8) years, respectively.
One patient deceased at another center and two were lost to follow-up. All three patients who remained under our care had cerebrovascular events. The median age of onset of cerebrovascular attacks was 5 (3-20) years, with a median attack frequency of 9 (1-15). Cerebrovascular attack load varied among patients, with two patients who experienced 15 and 9 cerebrovascular attacks characterized by unilateral headache, aphasia, and contralateral extremity numbness and weakness. A single attack in one patient manifested as sudden-onset blurred vision, speech impairment, and numbness. The attacks typically lasted 5-15 minutes. Patients with diffusion restrictions and stenosis on imaging studies were treated with acetylsalicylic acid and enoxaparin. The patient who experienced 15 cerebrovascular attacks had a diagnosis of moyamoya syndrome, and was receiving cholestyramine for hyperlipidemia and antihypertensive therapy. At the last follow-up, one patient deceased from respiratory distress, one patient with pancytopenia deceased from lung hemorrhage, and one patient was successfully transferred to the adult clinic.
Conclusions: Progressive renal disease, hypertension, arteriosclerosis due to hyperlipidemia and immune dysfunction, along with inflammation, vascular reactivity, and reduced elastin in vascular tissues due to *SMARCAL1* variants, may contribute to cerebrovascular pathology in SIOD patients. Management of cerebrovascular events, which are a major cause of morbidity and mortality, plays a critical role and highlights the importance of teamwork in management.

ABSTRACTS

Topic: Neurogenetics

EPNS25_941 - Linking Molecular Findings to Patient Priorities: Uncovering Overlooked Phenotypes in Pitt-Hopkins Syndrome

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Pitt-Hopkins syndrome (PHS), due to TCF4 variants, present with intellectual disability, seizures, respiratory abnormalities, and severe language impairment. Despite the high prevalence, dysautonomic symptoms remain poorly described. Behavioural and cognitive phenotyping is also underexplored. However, assessing behavioural and functional phenotypes is a priority in clinical trials for genetic neurodevelopmental disorders.

Objectives: To perform precision phenotyping in a large cohort to 1) refine genotype-phenotype correlations, 2) identify overlooked symptoms, 3) validate behavioural and cognitive assessment tools, 4) evaluate patients' and caregivers' quality of life (QoL) and parental stress.

Methods: We conducted an ambispective observational multicenter study of confirmed PHS patients. Molecular data, clinical exams, neurological findings, and adaptive skills were studied. Parental stress was assessed. Applying international diagnostic criteria, we evaluated individuals' clinical profiles and correlated with variant localization, reported as a predictor of phenotype.

Results: Thirty patients (11 months to24 years, fifteen females) presented 20 different single nucleotide variants and ten total or partial gene deletions. Psychomotor and language delays were constant. Among those older than 3 years, 70% achieved independent gait. Epilepsy affected 20%, requiring polytherapy in five; three had infantile spasms. Altered breathing patterns occurred in over half of patients over the age of six, with variable response to drugs. Neuroimaging findings were frequent but mostly non-specific. Constipation, aerophagia and abdominal distension were very common. Dysautonomic symptoms were seen in over one-third of individuals. These symptoms significantly limit QoL. About adaptive profile, daily living and expressive communication skills were most impaired. Behaviour and sleep was generally not a problem.

Conclusions: PHS is a well-recognized condition, but many QoL-impacting symptoms remain underreported. Our study broadens the clinical perspective and shares our follow-up experience. We provide validated clinical scales that identified key disabilities, enabling prioritization of symptoms for future trials, and could be integrated into research. Precision phenotyping enhances the characterization of ultra-rare conditions like PHS, also enabling individualized assessments and symptom monitoring both in natural progression and treatment evaluation.

ABSTRACTS

Topic: Movement Disorders/ Cerebral Palsy

EPNS25_942 - DIP2B CGG repeat expansion in siblings with neurodevelopmental disability and progressive movement disorder

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Objectives Trinucleotide repeat expansions are an emerging class of genetic variants associated with many movement disorders. Unbiased genome-wide analyses can reveal novel genotype-phenotype associations and provide a diagnosis for patients and families.

To identify the genetic cause of a severe progressive movement disorder in two affected brothers.

Methods A family of two affected brothers and unaffected parents had extensive phenotyping and natural history followed since birth. Whole-genome and long-read sequencing methods were used to characterize genetic variants and methylation status.

Results We describe a CGG repeat expansion in the 5'-untranslated region (UTR) of DIP2B in two affected male siblings presenting with a novel DIP2B phenotype including neurodevelopmental disability, dysmorphic traits, and a severe progressive movement disorder (prominent chorea, dystonia, and ataxia).

We leveraged the genome sequence data in the rare disease cohort from the 100,000 Genomes project (Genomics England) Data Release v19 dated 31st October 2024. We identified unrelated probands that had been diagnosed with ataxia, excluding those that were listed in 'Submitted diagnostic discovery' and those that had known pathogenic or likely pathogenic variants and were flagged as 'Case solved' in the 'GMC exit questionnaire' (n=788). We used ExpansionHunter to estimate the repeat number in DIP2B with the following coordinates: chr12:50505004-50505024 for GRCh38 genomes (n=721) and chr12:50898787- 50898807 for GRCh37 genomes (n=67). For the five probands with repeat numbers >60, we obtained information of their sex, ethnicity, age of disease onset, family history and symptoms. Fisher's exact test was used to compare the frequency of individuals with >60 repeat units in this ataxia cohort to the general population frequency in the gnomAD database. There is a significantly higher proportion of individuals with large CGG repeats in the DIP2B 5'UTR in the ataxia cohort (5/788 from the 100,000 Genomes Project) than the general population (43/19,240 from the gnomAD database8) (odds ratio = 2.8, p = 0.04).
We have described a pair of male siblings with a severe, early onset prominent hyperkinetic and ataxic phenotype inherited from an apparently asymptomatic father. Our data suggest that a CGG repeat expansion in the DIP2B 5'-UTR is associated with these phenotypes. We have further identified five more individuals with similar phenotypes with > 60 CGG repeats in DIP2B in the ataxia cohort from the 100,000 Genomes Project that support this association.
Conclusions

This is the first report of a severe progressive movement disorder phenotype associated with a CGG repeat expansion in the 5'-UTR.

ABSTRACTS

Topic: Fetal and Neonatal Neurology

EPNS25_943 - Post-neonatal epilepsy following symptomatic neonatal arterial ischemic stroke: predictor variables and safety of early discontinuation of anti-seizure medications

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Objectives

Few studies on epilepsy following neonatal acute ischemic stroke (NAIS) focused on seizure burden using video-EEG monitoring during acute phase. Recently, early discontinuation of ASMs in neonates with acute provoked seizures has been recommended. We aimed to investigate the predicted value of EEG and MRI findings in the acute phase, and evaluate the role of ASMs discontinuation before discharge in this population

Methods

We prospectively evaluated 10 neonates (≥36 weeks gestational age) admitted to the Neuro-NICU from 2018 to 2023, with symptomatic seizures due to MRI-confirmed NAIS. All neonates were continuously monitored with video-EEG. We defined the cumulative seizure burden as the sum of both clinical and EEG-recorded seizures. Early MRI DWI sequences were used to determine stroke location.

Results

All neonates presented with unilateral clonic seizures, in one infant apneic seizures were also seen. Mean video-EEG monitoring was 43 hours (SD=15). Phenytoin was effective for seizure control as first-line (6 cases), second-line (2 cases), third-line (1 case), and fourth-line (1 case) treatment. MRI was performed 3 days (SD=1.9) after symptom onset and showed involvement of the middle cerebral in 9/10, associated in two with injury in the thalamus and basal ganglia, and in one in the thalamus only. One infant had a stroke in the posterior cerebral artery territory. All patients were discharged seizure-free and off ASMs. During follow-up, 3 patients experienced later-onset seizures: one had infantile spasms (IS) at 7 months, one had a focal seizure at 2.5 years, and one had a convulsive status epilepticus at 4.2 years. IS resolved with prednisone, while others remained seizure-free on levetiracetam. Cumulative seizure burden was significantly higher ($t(8)=3.2$, $p=0.011$), and DWI MRI showed basal nuclei injury in only in those infants who developed epilepsy later in life.

Conclusions

In neonates with NAIS, involvement of deep brain structures and cumulative seizure burden appear predictive factors for the development of post-neonatal epilepsy. Discontinuing ASMs before discharge is justified: ASMs used in the acute phase are ineffective in IS, and epilepsy may emerge after two years of age. Larger studies are needed to validate our findings. Videos will be presented.

ABSTRACTS

Topic: Neuromuscular Disorders

EPNS25_945 - Givinostat efficacy in Duchenne muscular dystrophy: natural history comparison applying propensity score matching

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Objectives

The efficacy and safety of givinostat, an oral histone deacetylase inhibitor approved in the USA and UK for the treatment of Duchenne muscular dystrophy (DMD) in patients aged ≥6 years, have been assessed in the Phase 3 EPIDYS study in ambulant boys with DMD (NCT02851797). DSC/14/2357/51 (NCT03373968) is an ongoing open-label, long-term safety, tolerability and efficacy study of givinostat in boys aged ≥6 years.

Methods

Using propensity score matching based on baseline functional test results and type of steroid, 142 patients from EPIDYS and DSC/14/2357/51 treated with givinostat were matched with 142 patients from ImagingDMD (NCT01484678) and CINRG (NCT00468832) DMD natural history studies (control group). Kaplan–Meier survival analyses were used to determine the median age at which DMD progression milestones, as measured by persistent loss to perform a 4-stair climb (Lo4SC), loss of rise from floor (LoR) and loss of ambulation (LoA), occurred. Hazard ratios (HRs) and 95% confidence intervals (CIs) comparing the givinostat and control groups were calculated using Cox proportional hazards models.

Results

Twenty-one (14.8%) patients exhibited Lo4SC in the givinostat group vs 52 (36.6%) in the control group (HR=0.39 [0.24, 0.65], p<0.001). The median (95% CI) age at Lo4SC was 17.9 (15.65, NE) years in the givinostat group vs 13.9 (13.50, 14.88) years in the control group. LoR occurred in 45 (31.7%) givinostat-treated patients compared with 61 (43.0%) controls (HR=0.66 [0.45, 0.96], p=0.028) at a median (95% CI) age of 14.9 (13.60, 15.97) vs 12.9 (12.20, 14.33) years, respectively. LoA occurred in 14 (9.9%) patients receiving givinostat compared with 39 (27.5%) in the control group (HR=0.42 [0.23, 0.76], p=0.004) at a median (95% CI) age of 18.1 (18.09, NE) vs 15.2 (14.70, 18.31) years, respectively.

Conclusions

Compared with matched, steroid-treated controls, patients treated with givinostat experienced delayed disease progression. These results confirm the efficacy of givinostat, as demonstrated in the EPIDYS study, with longer-term treatment.

ABSTRACTS

Topic: Neuromuscular Disorders

EPNS25_946 - Long-Term Safety of Givinostat in Patients With Duchenne Muscular Dystrophy: Results From an Open-Label Extension Study

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Objectives

Givinostat, an oral histone deacetylase inhibitor, was recently approved in the US and UK for Duchenne muscular dystrophy (DMD) treatment in patients aged ≥6 years. This study evaluated safety data from the ongoing open-label, long-term safety, tolerability and efficacy study of givinostat in boys (NCT03373968) who completed or were screened but not randomised in previous DMD givinostat studies and agreed to enter this study.

Methods

As of the 31 December 2021 data cutoff, 194 patients have enrolled: givinostat (n=110), prior placebo (n=54) and not included in prior study (n=30) groups. All patients received givinostat and corticosteroids during this study. Safety data were evaluated for patients who received ³1 givinostat administration.

Results

The mean duration of givinostat exposure was 616, 506 and 451 days in the givinostat, prior placebo and not-included groups, respectively. Overall, 87.1% of patients reported ³1 treatment-emergent adverse event (TEAE), with a similar incidence among all groups. Most TEAEs were mild to moderate in severity. Among the most frequently reported TEAEs (³10% of the overall population), diarrhoea was reported more frequently by the prior placebo (27.8%) and not-included (36.7%) groups than by the givinostat group (18.2%). More falls were reported by the givinostat group (20.0%) than by the prior placebo (9.3%) and not-included (13.3%) groups. More reports of thrombocytopenia were observed in the prior placebo group (20.4%) than in the givinostat (9.1%) and not-included (10.0%) groups. The givinostat group reported pyrexia (17.3%), increased blood triglycerides (12.7%) and decreased platelet count (9.1%); in comparison, the incidence of these TEAEs in the prior placebo group was 13.0%, 16.7% and 14.8%, respectively, and 6.7% for each TEAE in the not-included group. Decreased platelets and increased triglycerides followed by stabilisation are consistent with givinostat treatment initiation.

Conclusions

These results are consistent with the known safety profile of givinostat. No new safety signals were observed in patients continuing givinostat.

ABSTRACTS

Topic: Epilepsy: Diagnosis and Investigations

EPNS25_947 - Volumetric MRI differences in pediatric idiopathic generalized epilepsy and frontal lobe epilepsy

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Objectives: In this study, we investigated the brain volume differences between frontal lobe epilepsy (FLE), idiopathic generalized epilepsy (IGE) and healthy controls.

Methods: T1-weighted brain magnetic resonance imaging scans of 19 children diagnosed with IGE (mean age: 10.47 ± 4.15 years),14 children with FLE (mean age: 10.43 ± 4.15 years), and 18 age- and sex-matched healthy controls (mean age: 12,06 ± 3,73 years) were analyzed using SPM12 (Statistical Parametric Mapping) and CAT12 (Computational Anatomy Toolbox) software. Differences in regional gray matter volume were tested with the full factorial model with age, sex, and total intracranial volume as covariates ($p<0.001$, uncorrected for multiple comparisons).

Results: The FLE group had significantly smaller gray matter volumes of the left inferior temporal gyrus, bilateral medial frontal cortex, left middle frontal gyrus, bilateral frontal pole, right supramarginal gyrus, left postcentral gyrus, and right cerebellum exterior compared to controls. The IGE group had greater volume in the bilateral angular gyrus, left lingual gyrus, left supramarginal gyrus compared to controls. The FLE group had significantly smaller gray matter volumes of the right superior frontal gyrus, left orbital part of the inferior frontal gyrus, left inferior temporal gyrus, left superior parietal lobule, and right cerebellum exterior compared to IGE.

Conclusions: This study shows that FLE and IGE affect brain areas. These findings highlight that children diagnosed with FLE have smaller gray matter volumes in the frontal cortex and extra-frontal regions compared to IGE.

ABSTRACTS

Topic: Epilepsy: Diagnosis and Investigations

EPNS25_948 - Vigabatrin Toxicity in a Child with Infantile Epileptic Encephalopathy Syndrome Due to PIGA Gene Mutation

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Objectives

Infantile epileptic spasm syndrome (IESS) is one of the most common developmental and epileptic encephalopathies (DEE) in infancy and childhood. In this syndrome, epileptic spasms, hypsarrhythmia pattern on electroencephalography and psychomotor developmental delay may be observed. In this study, we report vigabatrin toxicity in an IESS patient with a pathogenic mutation in the PIGA gene.

Methods

This presentation is organized as a case report.

Results

A 1-month-old male who was born at term with a birth weight of 3360 grams presented with hypotonia, feeding difficulties and seizures in the form of flexor spasms in clusters. His two siblings had a history of intrauterine death. Physical examination revealed microcephaly, high palate, micrognathia, dysmorphic facial appearance and central hypotonia. The patient had no head control, no object tracking and was unable to make eye contact. Electroencephalography revealed findings of modified hypsarrhythmia. Brain MRI showed mild bilateral ventricular enlargement and thin corpus callosum. During vigabatrin treatment (70 mg/kg/day), diffusion restriction at the bilateral globus pallidus and central tegmental tract was found on brain MRI performed when the patient developed encephalopathy at the age of 3 months and was evaluated as compatible with vigabatrin toxicity. Genetic analysis revealed a c.356G>A (p.Arg119Gln) hemizygous missense variant in the exon 2 of the PIGA gene, which was classified as pathogenic according to the ACMG 2015 variant classification guidelines. After discontinuing vigabatrin, the patient's clinical findings improved significantly.

Conclusions

The development of vigabatrin toxicity in a patient with PIGA gene mutation-associated infantile epileptic encephalopathy syndrome (IESS) is important because it is reported for the first time in the literature. Further case reports are needed to understand the relationship between genetic causes and vigabatrin toxicity in IESS

ABSTRACTS

Topic: Neurometabolic Disorders

EPNS25_951 - Beta-propeller protein associated neurodegeneration (bpan): electroencephalographic characterization of a cohort of 16 patients

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Objectives BPAN is the most common neurodegenerative brain iron accumulation disorder (NBIA), caused by de novo mutations in the *WDR45* gene, which plays an important role in autophagy and frequently presents as a developmental and epileptic encephalopathy. We aimed to describe the electroencephalographic findings of BPAN in a cohort of 16 patients.

Methods: A retrospective qualitative analysis of electroencephalographic recordings (EEGs) was performed during follow-up of individuals with pathogenic variants in *WDR45*.

Results: Twenty electroencephalographic (EEG) recordings of 16 individuals (13F/3M) between 1 and 17 years of age were obtained. Basal brain activity in wakefulness was poorly organized according to age in 15/16 of the recordings. Sleep phase recordings were available for 14 out of 16 subjects, and all displayed a lack of well-organized physiological grapho-elements. Beta rhythms of variable amplitude according to age and diffuse distribution in both wakefulness and sleep were identified in 90% of the recordings. Intercritical epileptiform findings (present in all but one register) showed: (1) bilateral and/or generalized epileptiform discharges (70%); (2) focal epileptiform activity (15%) and; (3) multifocal epileptiform activity (10%). The distribution of these alterations was predominantly in anterior and/or posterior areas. In 2 patients, with a severe neurological phenotype, findings of status epilepticus were identified during sleep. Critical episodes were recorded in only one patient, in the form of epileptic spasms followed by generalized non-motor seizures, absence type, associated. One patient had “atypical” EEG findings, with dominant posterior rhythm and sleep structuring appropriate for the patient's age at the time of recording and absence of diffusely distributed fast rhythms.

Conclusions: In this cohort of BPAN patients, EEG findings showed a combination with: poorly organized brain activity, absence of adequate NREM sleep phase structuring, fast rhythms of diffuse distribution and bilateral and/or generalized intercritical disturbances from early ages. The finding of status epilepticus during sleep, in patients with similar features, is remarkable and useful for the clinical setting, with treatment consequences. We postulate the EEG as a potential biomarker for BPAN patients.

ABSTRACTS

Topic: Cerebrovascular Disorders

EPNS25_952 - A Clinical Analysis of 51 Deep Supratentorial Pediatric Arteriovenous Malformations Treated with Gamma Knife Radiosurgery

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Objectives
Gamma Knife (GK) radiosurgery has emerged as a crucial non-invasive treatment modality for pediatric arteriovenous malformations (AVMs), particularly in deep supratentorial regions. Pediatric patients benefit from the precision of GK, which delivers highly focused radiation while minimizing damage to surrounding healthy tissue. Compared to traditional surgical approaches, GK radiosurgery offers reduced hospitalization time, lower procedural morbidity, and preservation of vital brain structures. This study presents our institutional experience with GK radiosurgery for deep supratentorial pediatric AVMs, emphasizing its safety, efficacy, and role in protecting the developing brain.

Methods
We conducted a retrospective analysis of pediatric patients (<18 years) treated with GK radiosurgery for deep supratentorial AVMs at our institution between February 2009 and June 2024. Patient demographics, AVM characteristics, treatment parameters, and clinical and radiological outcomes were analyzed. The inclusion criteria were deep supratentorial AVMs confirmed by angiography.

Results
A total of 51 pediatric patients (mean age: 11.7 years, range: 4–18 years, 54.9% male) underwent GK radiosurgery. Among them, 31 patients had a minimum of 6 months of follow-up, with the longest follow-up extending to 156 months. The mean AVM volume was 2.5 cm^3, treated with a median marginal dose of 18 Gy (mean 18.43 Gy). Headache was the most common symptom (24/51 patients, 47.1%), followed by seizures (8/51 patients, 15.7%). Intracerebral hemorrhage was the initial presentation in 31 patients (60.8%). The mean Spetzler-Martin score was 3.09. Among the 31 patients with at least 6 months of follow-up, obliteration was confirmed in 29 (93.5%). The mean obliteration time was 25.5 months (range: 6–76 months). Post-GK complications were minimal.

Conclusions
This study demonstrates that deep supratentorial AVMs represent a distinct clinical entity, with headache and seizures being the most common presentations and a high proportion of patients presenting with hemorrhage. GK radiosurgery provides an effective and safe treatment option for these deep-seated pediatric AVMs, offering high obliteration rates with minimal complications. The ability to preserve brain function, minimize hospital stays, and protect developing neural structures underscores its importance in pediatric AVM management. Further research with larger cohorts and extended follow-up is necessary to confirm these findings and refine treatment strategies for this challenging AVM subgroup.

ABSTRACTS

Topic: Neuromuscular Disorders

EPNS25_953 - Efficacy of givinostat in the off-target population of EPIDYS: a subgroup analysis

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Objectives

Givinostat, an oral histone deacetylase inhibitor, was recently approved in the US and UK for Duchenne muscular dystrophy (DMD) treatment in patients aged ≥6 years.

Methods

The efficacy of givinostat was evaluated in the double-blind, randomised, Phase 3 EPIDYS study in ambulant boys (aged ≥6 years) with DMD having baseline vastus lateralis fat fraction (VLFF) >5% but ≤30% (primary analysis/target population) (NCT02851797). The objective of this analysis was to evaluate givinostat efficacy, as measured by the change in a 4-stair climb (4SC) time (seconds) from baseline to Month 18, in a subgroup of patients who did not meet the VLFF criterion (off-target population), defined by VLFF £5% or >30%.

Results

Of 179 patients enrolled in EPIDYS, 59 were in the off-target group (37 givinostat/22 placebo), and 120 were in the target group (81 givinostat/39 placebo). The givinostat dose was weight-based and flexible; all patients received chronic corticosteroids. The baseline 4SC mean (standard deviation [SD]) time was 3.9 (1.4) and 3.7 (1.6) s in the off-target givinostat and placebo groups, respectively, and 3.4 (1.1) and 3.5 (1.3) s in the target groups. The nominally higher baseline 4SC time in the off-target groups suggests a more advanced disease. At Month 18, the 4SC mean (SD) time was 6.6 (7.9) and 9.8 (13.3) s in the off-target givinostat and placebo groups, respectively, and 4.7 (3.2) and 6.4 (7.7) s in the target groups. Although the off-target subgroup was not powered to detect a statistically significant difference, the least-squares mean difference relative to placebo indicated a 2.78 s smaller decline with givinostat. In the target group, a 1.78 s smaller decline was observed for givinostat relative to placebo (p=0.037).

Conclusions

These findings suggest that givinostat efficacy is consistent in a relatively more advanced disease population. All patients with DMD, including those not meeting the target population criteria, could have the potential for treatment benefits with givinostat.

ABSTRACTS

Topic: Neuromuscular Disorders

EPNS25_954 - Thorough QT study on the effect of therapeutic and supratherapeutic dosing of givinostat in healthy volunteers

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Objectives

To evaluate the effect of givinostat on cardiac repolarisation, an assessment was performed on of the impact of therapeutic and supratherapeutic doses on the QT/QTc interval.

Methods

This single-centre, randomised, partially double-blinded, placebo-corrected, Phase 1 crossover study evaluated the effect of a therapeutic dose and a supratherapeutic dose of givinostat on the QT/QTc interval. Healthy volunteers received each treatment, givinostat hydrochloride monohydrate oral suspension as a therapeutic dose (100 mg) or supratherapeutic dose (300 mg), placebo oral suspension, or moxifloxacin oral tablet (positive control, 400 mg), according to a 4-period, 12-sequence, block randomisation scheme. Cardiodynamic assessments were performed via continuous recordings collected from supine 12-lead ECG, from 1 h pre-dosing to 36 h post-dose, paired with PK samples.

Results

Baseline ECG parameters were within expectations for healthy adults. Givinostat 100 mg had no clinically relevant effect on heart rate or cardiac conduction (i.e. PR and QRS intervals). A non-clinically relevant prolongation of 5.5 ms for 100 mg (therapeutic dose) and a clinically relevant increase of 13.6 ms for 300 mg (supratherapeutic dose) were observed. Givinostat 100 mg (therapeutic dose) had no clinically relevant effect on the QTc interval >10 ms at any post-dose time point. Based on an E_{max} model used to predict the effect of givinostat on the QTc interval at supratherapeutic doses, a QT effect >10 ms can be excluded for all plasma concentrations of givinostat observed in this study (i.e. up to ~745 ng/mL).

Conclusions

Givinostat at a therapeutic dose (up to 53.2 mg twice daily for Duchenne muscular dystrophy) is not expected to pose a risk of QT prolongation.

ABSTRACTS

Topic: Infectious and Inflammatory Diseases/ Neuroimmunology

EPNS25_956 - Brain volumes in seronegative autoimmune encephalitis

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Objectives

Seronegative autoimmune encephalitis (SAE) is characterized by the absence of identifiable pathogenic autoantibodies in serum or cerebrospinal fluid (CSF). In this study, we aimed to perform volumetric brain measurements in patients with SAE using VolBrain to find out if there are structural changes associated with this condition.

Methods

Diagnosis of SAE was based on clinical criteria including neurological symptoms, compatible brain magnetic resonance imaging (MRI) findings, and an inflammatory CSF profile without identifiable pathogenic autoantibodies. Healthy control participants were selected from individuals matched with the patient group based on age and sex. We used VolBrain software to assess volumes (cm3) and asymmetry indexes for different levels of atrophy of total intracranial (IC), total brain, gray matter, white matter, limbic cortex, cerebellum and subcortical regions.

Results

The study included fifteen patients (9 (60%) males) with a mean age of 11.9 years and fifteen healthy control participants with a mean age of 13.9 years. Regarding the asymmetry of the abnormal appearing white matter (AAWM), the median value for the patient group was 3.809 cm^3, while that of the control group was 1.383 cm^3, with a statistically significant difference observed ($p = 0.019$). The median intracranial (IC) volume for the patient group was 1302 cm^3, compared to 1425 cm^3 for the control group, which was also statistically significant ($p = 0.011$). The median amygdala volume for the patient group was 2.020 cm^3, whereas for the control group it was 2.120 cm^3, demonstrating a statistically significant difference ($p = 0.04$). For pallidum volume, the patient group median was 2.523 cm^3, while the control group had 2.860 cm^3 ($p = 0.038$). The median thalamus volume for the patient group was 10.98 cm^3, while that of the control group was 12.25 cm^3, also exhibiting a statistically significant difference ($p = 0.04$). Brain volume alterations in SAE cases could not be compared with the seropositive group due to the limited number of cases.

Conclusions

This study is the first to demonstrate volumetric changes in the brains of children with SAE. Our findings indicate significant differences in various brain structure volumes between patients and healthy controls, suggesting that structural alterations are associated with the pathophysiology of SAE. Our results underscore the importance of volumetric measurements in understanding the neurological impact of SAE and highlight the need for further research to explore the underlying mechanisms and potential therapeutic interventions.

ABSTRACTS

Topic: Infectious and Inflammatory Diseases/ Neuroimmunology

EPNS25_957 - Can We Avoid Lumbar Puncture in the Diagnosis of Peripheral Facial Palsy in Children: A Retrospective Study from North-Eastern Slovenia

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Objectives

Peripheral facial palsy (PFP) is the most common cranial nerve disorder in children. Our aim was to show that neuroborreliosis-related PFP can only be diagnosed on the basis of epidemiological and clinical features in combination with specific antibodies for Borrelia spp. in serum.

Methods

A retrospective study was conducted including 133 patients diagnosed with PFP between 2017 and 2024 in northeastern Slovenia.

Results

The group consisted of 69 boys (51.9%) and 64 girls (48.1%), median age was 11 years. 44 (33.1%) patients were diagnosed with neuroborreliosis and 77 (57.9%) with Bell's palsy, 12 (9.0%) patients had other causes. Most cases were treated in the warmer season. The distribution of PFP according to the affected side was almost equal (46.6% left and 49.6% right), two patients had bilateral PFP. We observed positive meningeal signs in only 6 patients (4.5%). A history of tics bite in the last 6 months was not significantly associated with the cause of PFP ($X2 = 2.033$, $p = 0.362$). In 44 (33.1%) patients, specific antibodies for Borrelia spp. were detected in serum at the time of diagnosis. In 93 cases (69.9%) we successfully performed a lumbar puncture (LP). Children diagnosed with neuroborreliosis-related PFP were statistically significantly more likely to have CSF pleocytosis than children with Bell's palsy and other causes ($X2 = 51.815$, $p < 0.001$). 24 (18.0%) patients had specific antibody for Borrelia spp. detected in the cerebrospinal fluid (CSF). In 24 (18.0%) patients, specific antibodies for Borrelia spp. were detected in the CSF. In one patient, Borrelia was successfully cultured from the CSF. All 44 patients (33.1%) diagnosed with neuroborreliosis-related PFP received antibiotic treatment. 47 (35.3%) patients received treatment with corticosteroids. There were no cases of late seroconversion to specific antibodies for Borrelia spp. at follow-up.

Conclusions

When we compare our results with a prospective clinical study conducted in Slovenian children in 2010, we find that the percentage of children with neuroborreliosis-related PFP is lower in our study. There is a statistically significant association between CSF pleocytosis and neuroborreliosis-related PFP. Since all the children with positive intrathecal synthesis for specific antibody to Borrelia spp. also had specific antibody present in the serum at diagnosis, we propose that these children be treated with antibiotics even if lumbar puncture is not performed.

ABSTRACTS

Topic: Miscellaneous

EPNS25_958 - Neurological symptoms among pediatric patients after COVID-19: long COVID and post-COVID-19 experience

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Objectives

Neurological manifestations of SARS-CoV-2 Infection (although primary affects the respiratory system) occur in acute or post-acute stages and may persist as long-lasting symptoms known as “long COVID“or post-COVID-19. Professional organizations recognized these symptoms as important issues among young patients. We aimed to investigate the clinical profile, outcomes, and management of neurological manifestations after COVID-19 infection in children.

Methods

A retrospective chart review of all pediatric patients admitted to our tertiary pediatric center due to neurological symptoms after COVID-19 from December 2020 to June 2022 was performed followed by 1-year follow-up period.

Results

A total of 84 patients were included, median age 12.7 years (range 0.5-18 years). Girls were significantly more affected than the boys (female n = 51; 60.7%.; $\chi 2=3,86$; p=0,049) The most common neurological manifestation in our patients was headache (n = 47; 55.95%), dizziness (n = 19; 22.6%), visual disturbances (n=9; 10.7%), afebrile seizures (n = 6; 7.1%), anosmia/hyposmia (n = 4; 4.7%). Fatigue and sleep disorders occurred in 13.7% (11/84) of our patients. Four out of six patients with afebrile convulsions manifested another seizure during follow-up; therefore, antiseizure medication was introduced. Psychological consultation and/or psychotherapy was required in 22.6% (19/84), out of which four patients required psychiatric consultation. The largest number of patients with neurological symptoms after COVID-19 infection presented between October 2020 and March 2021 (n = 44; 52%), before the Omicron outbreak.

Conclusions

Long-lasting neurologic symptoms have contributed to the daily limitations as well as morbidity in pediatric patients and are more frequent in school-age children, predominantly in girls. Symptoms were reported more in patients infected with pre-Omicron variants. Available vaccination may represent a possible preventive measure, especially in school-age children where these severe conditions seem more frequent. Neurological symptoms after COVID-19 infection require medical attention and proper management, with the purpose of exclusion of more severe conditions. In most patients, post-COVID-19 clinical symptoms have resolved. This pandemic additional indicated the need for better understanding and support for mental disorders in children.

ABSTRACTS

Topic: Neurogenetics

EPNS25_959 - "Early-Onset Spastic Paraplegia Due to TFG Mutation: Clinical and Genetic Insights"

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Introduction

The TFG gene (Trafficking from ER To Golgi Regulator) is essential for the transport of proteins from the endoplasmic reticulum (ER) to the Golgi apparatus. That is crucial in maintaining the dynamic function of the ER and its associated microtubules. Mutations in the TFG gene are linked to several hereditary disorders, including autosomal recessive spastic paraplegia 57 and hereditary motor and sensory neuropathy, Okinawa type. These mutations can lead to neurological manifestations due to ER dysfunction.

Aim

This abstract aims to present a case of a paediatric patient with a homozygous TFG mutation, inherited from heterozygous parents. The objective is to add clinical phenotype data for this TFG variant of uncertain significance.

Case Summary

A paediatric patient presented with progressive lower limb spasticity, gait disturbances, and developmental delays. Genetic testing revealed a homozygous c820+5G>A mutation in the TFG gene, inherited from both heterozygous parents. This mutation is associated with a severe form of hereditary spastic paraplegia (HSP), leading to significant neurodegenerative changes.

The genomic report suggests that this variant is classified as uncertain based on current evidence but is considered potentially compatible with the clinical presentation. The parents, both heterozygous carriers, exhibit no symptoms, consistent with an autosomal recessive inheritance pattern. The child, however, displays a full spectrum of symptoms, including spasticity, muscle weakness, and optic atrophy.

Discussion

TFG mutations are a significant cause of early-onset HSP. Recent studies have expanded our understanding of TFG-related neurologic disorders, highlighting the gene's critical functions in neurons and its involvement in diseases like Charcot-Marie-Tooth disease type 2 and hereditary spastic paraplegia.

Conclusion

This case highlights the importance of genetic testing and counselling in paediatric neurology. Identifying heterozygous carriers and homozygous affected individuals provides valuable insights into inheritance patterns and potential risks for future offspring. We are not aware of published cases with a similar variant; thus, we aim to contribute to the understanding of this variant

ABSTRACTS

Topic: Infectious and Inflammatory Diseases/ Neuroimmunology

EPNS25_960 - Ocrelizumab Experience in Pediatric and Adult Relapsing Remitting Multiple Sclerosis Patients

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Objectives

Ocrelizumab, a recombinant humanized anti-CD20 monoclonal antibody, demonstrates safety and efficacy in adults with multiple sclerosis (MS). However, data on its use in pediatric-onset MS (POMS) and comparative data between POMS and adults remain limited.

Methods

This retrospective study evaluated relapsing-remitting POMS patients from four pediatric neurology clinics and adult relapsing-remitting MS (RRMS) patients from an adult neurology clinic treated with ocrelizumab between January 2020 and January 2025. Patients receiving ocrelizumab for at least 12 months were included. Data collected included gender, age, ocrelizumab treatment duration, line of therapy at ocrelizumab initiation, pre- and post-treatment relapse rates, EDSS scores, imaging findings before and after treatment and treatment-related adverse events.

Results

The study included 26 POMS (F/M=16/10) and 73 adult RRMS patients (F/M=50/23) with mean ages of 16.9 and 38 years, respectively. Mean ocrelizumab treatment duration was 23 months (range: 12–48 months) for POMS and 28.5 months (range: 15–40 months) for adults. Ocrelizumab was initiated as first-line therapy in 7 out of 26 pediatric and 3 out of 73 adult patients (p=0.0029). The mean number of relapses in the year prior to ocrelizumab treatment were 1.2 in POMS and 0.68 in adults (p=0.0003). The mean pre- and post-treatment EDSS scores were 2 and 1 in pediatric patients, respectively, and 2.28 and 2.65 in adult patients, respectively. After a minimum 12 months of ocrelizumab treatment, relapse occurred in 1 pediatric and 4 adult patients, with no statistically significant difference between the groups. Ocrelizumab treatment was discontinued in 1 child due to disease progression and in 4 adults due to disease progression and pregnancy. There were no treatment discontinuations due to side effects in either group.

Conclusions

Ocrelizumab is safe and effective in both POMS and adult RRMS. POMS is characterized by higher neuroinflammation and disease activity, leading to earlier ocrelizumab initiation compared to adult RRMS. Our findings provide support for the recommendation to initiate high-efficacy therapies early in the course of POMS. This study represents the largest series comparing ocrelizumab use in POMS and adult RRMS.

ABSTRACTS

Topic: Movement Disorders/ Cerebral Palsy

EPNS25_961 - Emotional profile in pediatric subjects with cerebral palsy

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Objectives

The presence of psychopathological difficulties in young subjects with cerebral palsy (CP) and their caregivers is well-documented in the literature; however, these results have mainly been investigated through questionnaires filled out by the caregivers. This study is an observational, prospective, monocentric research aimed of analyzing, through neuropsychological assessments completed by individual pediatric subjects with CP and their caregivers, the presence of specific emotional patterns and psychopathological profiles.

Methods

Subjects with CP in the hemiplegic or diplegic form, aged between 8 and 16 years, with an Intelligence Quotient (IQ) above 70, and without active epilepsy or genetic syndromes, were included in the study. The sample currently being analyzed consists of 27 patients; however, the study is ongoing and expanding, both in terms of the number of patients and the questionnaires used. They were assessed using motor function scales: the Gross Motor Function Measure and the Manual Ability Classification System. Regarding the evaluation of the emotional profile, they were assessed with the Child Behavior Checklist, Pediatric Quality of Life Inventory, Children's Depression Inventory and the Multidimensional Anxiety Scale for Children. A correlation analysis has been carried out between motor function and emotional aspects.

Results

The results obtained from this preliminary study confirm the data in the literature, as there is a prevalence of internalizing disorders, such as social withdrawal, depression and, in particular, anxiety that is uniformly perceived both by the affected individuals and by the caregivers. These results were reported despite the severity of motor impairment involved. Overall life is experienced as disabling, particularly regarding self-perception of health, but also in relation to emotional aspects. The latter is only partially shared by caregivers; while mothers strongly perceive the impact on health due to motor impairment, fathers perceive it more in relation to academic performance.

Conclusions

The immaturity of the emotional aspect in these subjects, who experience changes in their bodies due to motor impairment, considering also the major vulnerability related to the adolescence period, represents a destabilizing factor for personality development, leading to a risk trajectory towards the evolution of an anxiety disorder. Therefore, the early identification of emotional difficulties together with an individual emotional rehabilitation and interventions for the parental couple could help reduce the growing presence of psychiatric comorbidities in these subjects.

ABSTRACTS

Topic: Infectious and Inflammatory Diseases/ Neuroimmunology

EPNS25_963 - Pediatric autoimmune-associated epilepsy – Phenotyping, therapeutic options and long-term outcome

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Objectives

Epileptic seizures are a common acute symptom of autoimmune encephalitis (AIE) and epilepsy is sometimes the result of AIE even if inflammatory activity is no longer detectable, categorized as “autoimmune-associated epilepsy (AAE)”. There is a growing spectrum of antibody(ab)-mediated central nervous system (CNS) autoimmune disease, including rare and overlapping phenotypes, such as autoimmune glial fibrillary acidic protein-ab associated astrocytopathy (GFAP-A), AIE with co-existing ab against anti-myelin oligodendrocyte glycoprotein (MOG) and N-methyl-D-aspartate receptor (NMDAR) or MOG-ab-associated disease (MOGAD) with cortical lesions and seizures, termed fluid attenuated inversion recovery (**FLA**IR) imaging showing hyperintense cortical lesions in **M**OG associated **E**ncephalitis with **S**eizures (FLAMES).
While it is difficult to determine if seizures occur in the context of the acute phase or AAE, we want to know more about the clinical phenotypes of AAE, identify risk factors and/or biomarkers for AAE as well as the most effective treatment regime for the acute and chronic phase of the diseases.

Methods

By adapting a project from another group, which evaluates an AIE-cohort with predominantly adult patients of the GENERATE registry, we exclusively focus on a pediatric cohort. We collect retrospective and prospective clinical data from pediatric patients with epileptic seizures in the disease course of AIE, GFAP-A and/or MOGAD recorded in the GENERATE or GENERATE junior registry. Follow-up data 12 ± 3 months after disease onset or 6 months after resolution of any inflammatory activity should be available.

Results

As preliminary results to date we identified 61 patients (47/68 NMDAR-ab positive AIE [NMDARE], 14/21 MOGAD, GFAP-A data not yet available) with seizures in the acute phase of the disease fulfilling the inclusion criteria. 16/58 patients with sufficient follow up data and either MOGAD (5/21) or NMDARE (11/37) continued with antiseizure medication (ASM) including levetiracetam, valproic acid or lamotrigine. 3/21 patients with MOGAD developed further seizures after the initial episode of encephalitis and were diagnosed with AAE, all sufficient treated with levetiracetam.

Conclusions

Despite seizures at disease onset are common in ab-mediated CNS autoimmune diseases the risk for AAE seems to be moderate according to our data. Risk factors could be the type of the detected ab, the frequence of seizures in the acute phase and the time of immune therapy. Levetiracetam was effective in controlling seizures in the acute and chronic phase. But the cohort was too small to compare efficacy of other ASM.

ABSTRACTS

Topic: Epilepsy: Diagnosis and Investigations

EPNS25_964 - The Applicability of the ILAE 2022 Childhood Epileptic Syndrome Classification Diagnostic Criteria: A Retrospective Study of 1000 Children Diagnosed with Epilepsy

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Objectives: In 2022, the International League Against Epilepsy (ILAE) reviewed epileptic syndromes and published new nomenclature and diagnostic criteria. Data on the practical use of the new classification and nomenclature of childhood epileptic syndromes, as well as the changes it has caused, are insufficient. Our aim was to identify the epileptic syndrome spectrum and specific epileptic syndromes observed in our population using the ILAE 2022 epileptic syndrome classification.

Methods: The medical records of all children diagnosed with epilepsy at the Gazi University Pediatric Neurology Clinic, a tertiary-level University Hospital, between 2019 and 2024 were retrospectively reviewed for age at seizure onset, seizure type, comorbidities, electroencephalography (EEG), magnetic resonance imaging (MRI), and genetic testing results. Epileptic syndrome classification according to the ILAE 2022 criteria was performed for all patients and compared with the previous syndrome diagnosis based on medical records.

Results: Data obtained from 1000 children with epilepsy (66% male) were analyzed, and epileptic syndrome classification based on the ILAE 2022 diagnostic criteria was possible in 43% of cases. According to the ILAE 2022 classification, 270 children (27%) had only a change in the nomenclature of their epileptic syndrome. 163 children (16%) who could not be classified with previous classifications were classified using the ILAE 2022 criteria. 281 children (28%) who had been classified with previous systems could not be classified with the ILAE 2022 criteria. 245 children (24%) were categorized into a new category for epileptic syndrome. No change in classification was made for 41 children (4.1%).

Conclusions: The ILAE 2022 diagnostic criteria resulted in a change of diagnosis in 67% of children with epilepsy. The ILAE 2022 criteria will enable standardization in the classification of childhood epileptic syndromes.

ABSTRACTS

Topic: Neuro-Oncology

EPNS25_966 - Non-Invasive Approaches for Peripheral Neuropathy in Pediatric Oncohaematology: Diagnostic Performance of Inertial Measurement Unit (IMU)-Based Gait Analysis and Pediatric-Modified Total Neuropathy Score

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Objectives

Peripheral neuropathy is a common yet often under-recognised complication in children with oncohaematological conditions, contributing to morbidity and adversely affecting quality of life. Standard diagnostic tools, such as electroneurography (ENG), are effective but invasive and challenging in paediatric populations. This study explores the potential of gait analysis using IMU sensors as a non-invasive approach to detect peripheral neuropathy in children undergoing chemotherapy and compares its performance with the Paediatric-Modified Total Neuropathy Score (ped-modTNS).

Methods

This prospective observational study included children and young adults (0–23 years) with oncohaematological conditions and suspected neuropathy after chemotherapy or stem cell transplantation. Data collection covered clinical and demographic details, chemotherapy regimens, neuropathic symptoms (ped-modTNS), age-adjusted ENG results, and gait analysis recorded within ±24 hours. Gait analysis assessed temporal-spatial and nonlinear variability measures, comparing participants to 112 healthy individuals (6–25 years). Statistical analyses included Kruskal-Wallis tests and diagnostic accuracy (AUC, sensitivity, specificity, PPV, and NPV), using ENG as the reference standard.

Results

"We conducted 34 recordings on 25 patients (median age 14 years, IQR 6). The most common diagnoses were acute lymphoblastic and acute myeloid leukaemia. ENG identified abnormalities in 21/34 recordings (11 sensorimotor, 8 motor, and 2 sensory neuropathies). Ped-modTNS was positive (>0) in 29 cases, with 20 scoring ≥3. Individual gait metrics showed no significant differences based on symptoms, ped-modTNS, or ENG results, but composite nonlinear metrics were promising. Tandem walking frontal plane variability (TW-NL frontal) had 98% sensitivity and 100% NPV for ENG-confirmed neuropathy, though specificity was low (40%). Ped-modTNS had slightly lower sensitivity (91%) and NPV (83%) but higher specificity (71%)

Conclusions

Preliminary IMU-based gait analysis suggests that composite scoring of tandem walking nonlinear metrics shows high sensitivity and NPV, supporting their potential as a screening tool. Integrating this method with clinical scales like ped-modTNS may improve early neuropathy detection in children with oncohaematological conditions. Further research should expand sample size and assess composite scoring approaches.

ABSTRACTS

Topic: Neurogenetics

EPNS25_967 - Exome sequencing facilitates personalized treatment in developmental and epileptic encephalopathy patients in LMIC

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Objectives

Developmental epilepsy and encephalopathy (DEE) are severe epileptic syndromes with onset in neonates and infants. Up to 50% of DEEs have underlying genetic causes. DEE in low-middle income countries (LMIC) is mostly treated with empiric therapy of epilepsy, which may contradict the underlying mechanism of the disease. The use of genetic testing is still very limited in clinical settings in LMIC. This study aims to look at the genetic profile of DEE patients which may influence management and genetic counseling.

Methods

DEE patients were identified by pediatric neurologists and patients with obvious perinatal insults were excluded. Genomic DNA was extracted from each patient's blood samples and variant interpretation was performed.

Results

We identified pathogenic or likely pathogenic variants in 20 out of 60 (33.3%) individuals, and variants of unknown significance (VUS) in 9 out of 60 (15.0%). Of the 29 out of 60 patients with an identified possible genetic etiology, eight diagnoses carried management implications, including treatment of the underlying biochemical abnormality, treatment change of antiseizure medication, and screening for disease-related complications.

Conclusions

Our study shows that implementing exome sequencing in clinical practice is feasible and worthwhile in LMIC. Early genetic diagnosis informs targeted management, both with available anti-seizure managements, dietary modification, and molecular and gene therapies.

ABSTRACTS

Topic: Infectious and Inflammatory Diseases/ Neuroimmunology

EPNS25_968 - Neuropsychiatric Lupus in Children: Insights from a Large Single-Center Cohort

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Objectives

Neuropsychiatric systemic lupus erythematosus (NPSLE) represents one of the most serious SLE manifestations involving the central and peripheral nervous system with a wide neuropsychiatric presentation. Early diagnosis and treatment in particular are challenging in pediatric patients due to the heterogeneity of clinical features. Childhood-onset SLE is also associated with a more aggressive disease course than adult-onset SLE, with higher risk for major organ involvement including the nervous system. However, major neuropsychiatric manifestations despite significant morbidity and impact on quality of life continue to be infrequently reported in pediatric NPSLE. This study describes the demographic, clinical, and neuropsychiatric features of pediatric-onset NPSLE patients. From the analysis of this well-defined cohort, we seek to contribute to a profound understanding of this complex condition by estimating the prevalence and spectrum of major NPSLE manifestations.

Methods

A retrospective study of pediatric-onset NPSLE patients followed in pediatric rheumatology and neurology clinics was done to capture comprehensive data on demographic characteristics, clinical presentations, neuropsychiatric manifestations, and laboratory findings. Only patients with major NPSLE manifestations were included. Data from electronic medical records, archived patient files, and laboratory test results were collected to assess disease characteristics and outcomes.

Results

The age at diagnosis of NPSLE ranged from 5.5 to 17.5 years, with a mean of 13.11 years SD 2.79 years among the 22 patients. Of these, 27.27% were males (n = 6) and 72.73% females, n=16. Seizure disorder was the most common CNS manifestation, observed in 9 patients. Other neurological findings included movement disorder (chorea) in 7 patients, acute confusional state in 5 patients, psychosis in 3 patients, major depression in 3 patients, cerebrovascular disease in 2 patients, mononeuropathy in 1 patient, cranial neuropathy (facial paralysis) in 1 patient, delirium in 1 patient, and posterior reversible encephalopathy syndrome (PRES) in 1 patient. Among 158 pediatric-onset lupus patients, 22 (13.9%) were diagnosed with NPSLE. Of these, 12 patients (54.5%) initially presented with acute confusional state (n=4), chorea (n=5), facial paralysis (n=1), psychosis (n=1), and seizures (n=3).

Conclusions

A large single-center cohort of pediatric-onset lupus patients (n=158) revealed that 13.9% (n=22) had major NPSLE manifestations, with seizures and movement disorders being the most common CNS findings, emphasizing the importance of early recognition and targeted management in affected patients.

ABSTRACTS

Topic: Epilepsy: Diagnosis and Investigations

EPNS25_969 - HCN gene-related diseases in childhood: a neurological perspective

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Objectives

Hyperpolarization-activated cyclic nucleotide-gated (HCN) channels play a crucial role in the regulation of neuronal excitability and rhythmic activity in the central and peripheral nervous systems. HCN channels contribute to the generation of the hyperpolarization-activated cation current , which influences synaptic integration, pacemaker activity, and neuronal oscillations. Dysfunctional HCN channels can lead to altered neuronal excitability, aberrant network synchronization, and susceptibility to seizures. Mutations in HCN genes, particularly HCN1, HCN2, and HCN4, have been implicated in a spectrum of neurological disorders, including epilepsy, developmental delay, and movement disorders. Recent studies have identified both gain-of-function and loss-of-function HCN mutations associated with epileptic encephalopathies, idiopathic generalized epilepsy, and familial febrile seizures.

Methods

Clinical findings and EEG of two consecutive patients with HCN2 and HCN1 mutations respectively were evaluated.

Results

A 6.5-year-old girl patient was admitted due to epileptic seizure. Her medical history remarcable with 4 seizures with firs seizure at age of 2, and that she was started on LEV and then sodium valproate. Her electroencephalography (EEG) consisted with belateral centro-parieto-temporal epileptic activity. Brain MRI was normal. She Had mild developmental delay. Genetic analysis revealed a de novo pathogenic heterozygous mutation of HCN2 gene as NM_001194.4 c.1717C>A p. (Arg573Ser). Şhe was seizure free with LEV and clobozam. On the other hand, the other child was admitted at 5.5 year with a history of autism spectrum disorders , intellectual disability and epilepsy. Seizures were started at 3 years old and sodium valproate was given. Her EEG, brain MRI was normal. She was put on sodium valproate and clobozam treatment. Genetic analysis revealed a novel maternally inherited heterozygous pathogenic mutation NM_021072.4 c.406C>T (p. His136TYR) in *HCN1* gene.

Conclusions

The HCN channel has been identified as a new and interesting channelopathy candidate in epilepsy. Here in, we describe two new patients with rare HCN2 and HCN1 gene mutations. The mutation in the HCN1 gene is a novel mutation which expanded the genotype of the disease.

ABSTRACTS

Topic: Neuromuscular Disorders

EPNS25_970 - Cardiac safety data for givinostat in ambulant patients with Duchenne muscular dystrophy: results from EPIDYS study

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Objectives

MD is associated with dilated cardiomyopathy and clinical trials of different HDAC inhibitors have observed electrocardiogram (ECG) changes. Accordingly, a thorough evaluation of the potential effect of givinostat on ECG and echocardiogram (ECHO) parameters was performed in the EPIDYS study.

Methods

EPIDYS (Epigenetic Rescue of Dystrophin Dysfunction) was a multicentre, randomised, double-blind, placebo-controlled, Phase 3 trial to evaluate the safety and efficacy of givinostat in 179 ambulatory boys aged ≥6 years with genetically confirmed DMD. A weight-based flexible dosing approach was used. The starting dose was 20–70 mg oral givinostat twice daily (b.i.d.), reduced to 13–47 mg and then 10.6–37.4 mg in case of predefined adverse events (AEs). All subjects who were on stable corticosteroids and received ≥1 dose of study drug, givinostat (n=118) and control who received placebo (n=61), were assessed throughout the 72-week trial for AEs, blood chemistry, vital signs, ECG and pulmonary function.

Results

The mean (standard deviation [SD]) Fridericia-corrected QT interval (QTcF) change from baseline at end of study (EOS) was −6.35 ms (16.872) for the givinostat group and −1.32 ms (12.834) for the placebo group. No QTcF prolongation of >450 msec was recorded in either group. A QTcF change from baseline of >30 ms and <60 ms was seen in 10 (5.6%) subjects in the givinostat group; however, no subject had a change from baseline of >60 ms at any visit. Other ECG parameters remained stable throughout the study. The mean (SD) left ventricular ejection fraction (echo-LVEF) decline from baseline at EOS had a numerically smaller trend for the givinostat group (−1.161 [6.8055]) than the placebo group (−3.358 [7.5704]).

Conclusions

No QTc prolongation was recorded with givinostat or placebo, and other ECG parameters remained stable. A beneficial trend change in LVEF from baseline to EOS was observed suggesting that givinostat helped preserve LV-function vs placebo.

ABSTRACTS

Topic: Headache / Migraine

EPNS25_971 - Apelin 13 and 36 levels: Biomarker for Pseudotumor Cerebri in children?

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Objectives

Previous studies mentioned about Apelin 13 and its neuroprotective effects.We would like to demonstrate apelin 13 and 36 biomarker of pseudotumor cerebri disease (PTCD) in pediatric population. Herein, we assessed Apelin 13 and 36 level with oxidant capacity (TOS) and antioxidant capacity (TAS) in serum of pediatric PTCD and healty controls.

Methods

Individuals consisted of 33 children with pseudotumor cerebri and 44 controls. Gender, age, radiologic MRI findings, grade of papillodema and treatments of patients were recorded in SPSS packet programme. We evaluated serum apelin 13, 36, TOS and TAS levels with Enzyme Linked Immunosorbent Assay (ELISA) method. Normal distrubuted parameters were compared with student T test and One Way ANOVO tests. Non-normally distributed parameters were analyzed by Kruskall Wallis and/ or Mann Whitney U test. Chi-square test and Fisher exact test were used to compare categorical variables. Statistical significance value was accepted as $p<0.05$.

Results

The patient group had pathological MRI findings and a higher rate of papillodema. When MRI findings were compared with apelin 13 levels, a statistically significance difference was found (p=0,022). The mean apelin 13 level of patients with radiologic signs was found to be increased. We showed a statistical significant difference between TOS level and papillodeme (p=0.006). Our study recommened that patients with grade 3 papillodeme had a lower TOS level than other patients group. A significant statistical difference was found in Apelin 36 level and treatment of patients (p=0,022). Serum Apelin 36 levels increased in patient group. It was determined that Apelin 36 level was an important predictor of PTCD (p=0,012). If a one- unıt standard deviation increase in apelin 36 level, the risk of PTCD enhanced 1.035 times.

Conclusions

In our study, we found that Apelin 36 levels were lower on average in patient groups, and also apelin 13 levels were not a predictive biomarker for PTCD. The major limitation was the low number of individuals. Since our study is cross-sectional, we do not have information about the apelin levels of the patients before treatment. However, we have shown the correlation between apelin 36 levels and PTCD.

ABSTRACTS

Topic: Epilepsy: Diagnosis and Investigations

EPNS25_972 - Cardiac Effects of Levetiracetam in Children with Genetic Generalized Epilepsy: A Follow-up Study

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Objectives
Epilepsy is a disorder characterized by seizures that affect the central nervous system, often accompanied by autonomic dysfunction. This autonomic dysfunction can lead to cardiac arrhythmias and sudden death. Some antiepileptic drugs used in the treatment of epilepsy are known to cause cardiac arrhythmias, conduction blocks, and increased excitability. However, significant cardiac side effects associated with levetiracetam use are rarely reported in the literature. The aim of this study is to investigate the cardiac side effects of levetiracetam in newly diagnosed patients with genetic generalized epilepsy.

Methods
The study population included 52 pediatric patients with newly diagnosed genetic generalized epilepsy who were prescribed levetiracetam between 2020 and 2023. All patients were followed for at least 1 year. The initial and maintenance doses of levetiracetam were recorded, and cardiac examination, electrocardiogram (ECG), and echocardiography (ECHO) were performed before treatment and after 1 year of levetiracetam therapy.

Results
The study included 52 patients diagnosed with genetic generalized epilepsy, of whom 22 were female (42.3%) and 30 were male (57.7%). The mean age was 9.31 ± 4.49 (range 3–17) years. No statistically significant differences were observed before and after the first year of levetiracetam treatment in terms of PR intervals (p=0.725), QRS complexes (p=0.4), QT interval (p=0.124), QTc (p=0.4), TP-e interval (p=0.485), Tp-e/QT (p=0.709), and Tp-e/QTc (p=0.49). Additionally, no statistically significant differences were observed in the ECHO parameters: Z-scores of AAD (p=0.626), PAD (p=0.712), EF (p=0.666), LVEDD (p=0.535), IVSd (p=0.099), and LVPWd (p=0.104) when comparing pre-levetiracetam and first-year measurements.

Conclusions
In this study, no cardiac side effects of levetiracetam were observed. While some studies have reported potential effects on repolarization, we did not observe such effects in our cohort. We believe this may be due to the fact that our study was a follow-up conducted on the same patient cohort. This study demonstrates that levetiracetam can be safely used from a cardiac perspective in pediatric patients diagnosed with genetic generalized epilepsy.

ABSTRACTS

Topic: Miscellaneous

EPNS25_974 - Spectral Dynamics of Non-Rapid Eye Movement Sleep Parasomnias in Children

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Objectives

Disorders of arousal (DOA), including sleepwalking, sleep terrors, and confusional arousals, are non-rapid eye movement (NREM) parasomnias characterized by complex behaviors emerging from slow-wave sleep (SWS). These episodes reflect a dissociated sleep-wake state, with electroencephalographic (EEG) patterns showing coexisting sleep-like and wake-like activity. While DOA are more common in childhood, most neurophysiological studies focus on adults, leaving uncertainty about whether observed EEG abnormalities are specific to severe, persistent cases or generalizable to pediatric DOA. Using high-density EEG, we aimed to characterize the spectral dynamics preceding and during DOA episodes in children, identifying features unique to pediatric cases.

Methods

Children aged 5–17 with a diagnosis of DOA, based on the International Classification of Sleep Disorders (ICSD-3), were recruited from a sleep medicine center and the general population. Participants underwent one or two overnight video-polysomnography sessions with high-density EEG (256 channels, 500 Hz sampling rate). Sleep staging and event scoring followed American Academy of Sleep Medicine criteria. DOA episodes were defined by sudden behaviors and distinguished from physiological motor arousals. EEG analysis involved artifact removal using artifact subspace reconstruction and wavelet-enhanced independent component analysis. Power spectral density was computed at scalp and source levels, focusing on slow-wave activity (0.5–4 Hz) and additional frequency bands (theta, alpha, sigma, beta, and low gamma). Topographic and source-space analyses were conducted using standardized low-resolution brain electromagnetic tomography estimates.

Results

EEG spectral analysis revealed distinct frequency-specific changes during DOA episodes. Delta power (1–4 Hz) increased in the 5 seconds preceding an episode but showed a regional decrease in central areas after motor onset. Beta power (11–16 Hz) remained stable both before and during episodes, with no localized increases. Sigma power (11–16 Hz), associated with sleep spindles, exhibited a transient suppression in central regions prior to motor onset. These spectral changes distinguished DOA episodes from baseline sleep, highlighting regional cortical activity differences before and after movement onset.

Conclusions

Our findings support the hypothesis that DOA represents a dissociated sleep-wake state rather than a simple transition to wakefulness. The observed EEG patterns suggest that DOA episodes are not purely unconscious states but exist on a continuum where varying degrees of awareness may re-emerge. These insights refine our understanding of NREM parasomnias and their neurophysiological underpinnings in children.

ABSTRACTS

Topic: Epilepsy: Diagnosis and Investigations

EPNS25_975 - Epilepsy Services Improvement Programme (ESIP) across North East North Cumbria (NENC) region: A collaborative initiative by engagement and peer reviews for incremental improvement with the delivery of National Epilepsy Care Standards for children and young people with epilepsy

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Objectives: To collaborate with a range of partners to evaluate local compliance with National Epilepsy Care Bundle (NECB) and develop Service Improvement Plans to respond to the requirements of the Bundle. The NENC Epilepsy Leadership Group supported the delivery framework and the identification of tangible local actions, timescales and measures of performance.

Methods: Available information was collated, reviewed and updated in discussions, including current insights of clinical and non-clinical teams regarding the 4 areas of care of NECB: variation in care, Mental Health, access to tertiary care and epilepsy surgery, and healthcare transition for Children and Young People with Epilepsy.

A bespoke template 'SIP' form, with baseline information from existing sources via desktop data-gathering, was shared with Clinical Teams and Trust colleagues within 4 weeks prior to scheduled meetings. We ensured pre-meeting engagement with services with pre-populated questionnaires and by outlining the meetings. Interactivity enabled detailed discussion and proposals on reducing service gaps incrementally over 12 months; follow-up meeting(s) was planned to enhance the process iteratively. Information was formalized and recorded digitally during the meeting, by the project team, and sent to the epilepsy team for comments post-meeting.

Results: Data was collected from 8/8 services, with 8/8 SIP meetings completed, showing 100% process engagement. All SIP meetings were attended by the project team, Service Clinical Lead, Epilepsy Specialist Nurse (ESN) and Trust General Manager, and most meetings included Trust Clinical Directors and LDT Place based Commissioning Leads.

ESIP has achieved its aim of providing a platform for clinical and non-clinical teams collaboration to improve epilepsy care across the region. This programme has provided useful information about enablers and barriers within services that are shared with service managers and commissioners. It has identified areas of challenges needing improvement in areas of NECB such as provision for two weeks assessment by paediatrician with expertise of new suspected epilepsy, full patient access to children's epilepsy specialist nurses, timely investigation provision and tertiary pathways. Significant gaps in transition care and Mental Health screening/intervention provision. Feedback about the ESIP process and meeting was received from most of the services and was unanimously positive.

Conclusions: ESIP aims to provide an engaging platform for clinical and non-clinical teams, reduce service gaps and improve epilepsy care regionally. Our findings provide insight into the efficient use of resources to improve patient-centred care and satisfaction. This project highlights the validity of replicating similar projects for epilepsy services across the UK.

ABSTRACTS

Topic: Neurodevelopmental Disorders / Developmental Neuroscience

EPNS25_976 - Risk of epilepsy associated with sleep disorders and language regression in early childhood in autistic patients

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Objectives

Since sleep disorders (SD) and language disorders (LD) in early childhood have been invoked as early indicators of the risk of developing autism spectrum disorder (ASD), we considered the possibility that they may be significantly associated with the development of comorbidities such as epilepsy (EPIL).

Methods

A cohort of 32,221 patients under 15 years of age from a health area was retrospectively studied. Between 2018-2024, 174 children were referred to a multidisciplinary unit specialising in the diagnosis of ASD. A history of sleep disorders during infancy (SDI) was recorded at the first visit form as well as its presence at the time of the first visit (SDFV). Three language development groups were described as: Normal language (NL), language delay (LDY) and language regression (LRG). Its presence was also recoded at the first visit form. During follow-up, the diagnosis of epilepsy was made based on clinical symptoms and EEG. A stratified association and percentages study was performed and analysed with the Epi.Info 7.2.4.0 and Excel 2018.

Results

The percentage of boys (n=131; 75.3%) was significantly higher (p=0.0000) than that of girls in all the strata, and their age (5.25 ±3.06 years) did not differ significantly between groups, so neither of the two variables, age or gender, could act as a confounding factor. SDI was recorded at the first visit form and in 142 cases its presence was confirmed at the time of the first visit (SDFV).

In 29 cases of the SDL group (30.2%) EPIL was confirmed, while only 6 were detected in those with normal sleep (6.25%) (OR=2.9(95% CI=1.1-8.1) P=0.003). In 36 cases of the SDL group (30.3%) EPIL was confirmed, while it was present in only 10 cases with normal sleep (8.4%)(OR:3.9(95 CI=1.7-9) p=0.001). In the LRG group, 19 (82.6%) out of 23 patients presented EPIL, this percentage was significantly higher than those who did not present EPIL 4 (17.4%)(p=0.0000). Neither in the LD group (EPIL= 41 cases (61.2%)) nor in the NL group (EPIL=10 cases (71.4%)) the percentages showed significant differences.

Conclusions

1) Patients with SDI have a risk almost three times higher of being diagnosed with epilepsy at later ages than those who had normal sleep. 2) Patients with SDFV presented almost four times more risk of being diagnosed of EPIL than those who had normal sleep. 3) Autistic patients with EPIL presented a significantly higher proportion of LRG than those who had LD or NL.

ABSTRACTS

Topic: Epilepsy: Diagnosis and Investigations

EPNS25_977 - Understanding practice and confidence in discussing Sudden Unexpected Death in Epilepsy in children

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Objectives

Sudden unexpected death in Epilepsy (SUDEP) is a significant cause of death in children and young people (CYP) with the condition, affecting 1.2 per 1000 per year – similar to adult figures. For this reason, a national bundle of care for children and young people (CYP) with epilepsy states all CYP should receive appropriate and tailored information on risks of SUDEP, and ensuring this is reviewed annually and documented. The charity SUDEP Action has been developing a paediatric-specific tool to augment these discussions; however, little is known about the baseline practice of clinical staff. We sought to gather data across a region from epilepsy care professionals.

Methods

(Retrospective method) Questions were developed by team members, and reviewed by wider stakeholders, after which a survey was created on Google Forms. This was shared with all epilepsy professionals across the region via email and WhatsApp, running over a two-month period (July and August 2024).

Results

20 responses were received from professionals across the region, involving Epilepsy Specialist Nurses, Advanced Clinical Practitioners, and Consultants, representing 12 services in total. 17 respondents (85%) did not use a protocol to help in structuring their SUDEP discussions. Regarding confidence levels, 14 respondents (70%) replied they were ‘not confident’ or ‘somewhat confident’ in having SUDEP discussions. There was wide variability in the numbers of CYP (within each professional’s clinical caseload) that professionals felt were appropriate for a SUDEP discussion.

Conclusions

The results show there is wide variation in confidence and practice around SUDEP discussions across the region. There is little in the way of standardisation (e.g. frequency of discussion), coupled with limited confidence. Moreover, there is currently inequity regarding whether CYP are even given the opportunity to have these discussions, and hence be fully informed of this important topic. SUDEP Action’s paediatric checklist represents an opportunity to drive improvement. We plan to implement this tool later this year and re-evaluate changes in practice across the region.

ABSTRACTS

Topic: Infectious and Inflammatory Diseases/ Neuroimmunology

EPNS25_978 - Autoimmune Basal Ganglia Encephalitis: Clinicopathological and radiological features

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Objectives Autoimmune basal ganglia encephalitis (BGE) is a rare form of autoimmune encephalitis characterised by basal ganglia (BG) inflammation and movement disorders. This study aims to identify the clinicopathological and radiological features, and clinical outcomes of paediatric patients with BGE.

Methods A retrospective single centre cohort study with patients identified from a database comprising all patients diagnosed with autoimmune encephalitis (AE) from 2006-2022. Inclusion criteria comprised fulfilment of criteria for probable or definite AE by the Cellucci criteria, with evidence of basal ganglia inflammation on MRI. Imaging was reviewed and scored on a standardised proforma by one radiologist. Clinical and paraclinical data was extracted from clinical records. The Paediatric Autoimmune Encephalitis Score (PASS) and Modified Rankin Scale (MRS) were used to assess disability and recovery.

Results Nine patients (4 female, 5 male, mean age 6.4 yrs) were included. NMDAR antibodies were isolated in 2/9. 8/9 patients presented with seizures, 4 requiring ICU admission for seizure management. 8/9 developed movement disorders including myoclonus, choreoathethosis, dystonia, tremor, and tics. Speech pathology was seen in 6/9 and sleep dysregulation in 4/9. 6/9 displayed psychiatric features, including emotional lability, anxiety, low mood and agitation. BG abnormalities on T2/FLAIR were symmetrical in 6 and asymmetric in 3. Unilateral BG encephalitis was not seen. Abnormalities were observed in the caudate in 8/9, putamen in 8/9 and globus pallidus in 6/9. Abnormalities were observed in the cortical grey matter in 4/9. Infrequently limbic changes (1/9), brainstem (1/9) and cerebellar (1/9) abnormalities were seen. Changes in white matter were not observed. Resolution of changes occurred in the majority (8/9) of patients. Four patients received no immunotherapy, 4 a combination of steroids and intravenous immunoglobulin (IVIG), and 1 patient received steroids, plasma exchange and IVIG. The mean PASS score at nadir was 11 (range 2-30), improving to a mean of 1 (range 0-4) at follow-up. The mean MRS decreased from 4 at the illness nadir to 1 at two-year follow-up.

Conclusions

Autoimmune BGE is a rare, but distinct, form of autoimmune encephalitis that presents with a combination of seizure activity, movement disorders, speech and cognitive deficits, sleep disturbances, and psychiatric symptoms. Children with BGE mostly demonstrated positive clinical and radiological outcomes.

ABSTRACTS

Topic: Epilepsy: Diagnosis and Investigations

EPNS25_979 - Focal interictal EEG abnormalities in patients with juvenile myoclonic epilepsy

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Objectives
This study aimed to assess focal EEG abnormalities in juvenile myoclonic epilepsy (JME) patients.

Methods
The clinical characteristics of 81 newly diagnosed JME patients with available follow-up data of more than 12 months and a total of 205 EEG recordings from these patients were retrospectively evaluated for focal abnormalities. First seizure type and age at onset, family history of epilepsy, and history of febrile convulsion and absence seizures were evaluated. Focal EEG findings were evaluated under four categories: isolated unilateral or bilateral focal discharges, diffuse unilateral discharges, asymmetric generalized discharges, focal abnormalities preceding/following generalized discharges.

Results
Out of 81 patients 54 (66.7%) were females and 27 (33.3%) were males. Mean age at the onset of seizures 154 months ± 30 months. Myoclonic jerks (MJ) were present in all patients, generalized tonic–clonic seizure in 62 (82.7%) and absence seizures in 22 (27%) of them. Sixty one (75.3%) of the patients had focal EEG abnormalities. The following frequencies were observed among patients isolated unilateral focal discharges 48.1%, bilateral focal discharges 44.4%, unilateral diffuse discharges 39.5%, asymmetric generalized discharges 40.7%, focal abnormalities preceding/following generalized discharges 23.5%.

Conclusions

Focal electroencephalographic abnormalities are more frequent than expected in patients with JME. These features should not be misinterpreted as being focal epilepsy.

ABSTRACTS

Topic: Neuro-Oncology

EPNS25_981 - Association of clinical characteristics and outcome in pLGG

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Objectives Pediatric low-grade glioma (pLGG) are nowdays considered as neurodevelopmental disease. They encompass tumors of heterogenous histology. Activation of RAS/MAPK pathway represents the key molecular features in tumorigenesis of pLGG. Recent studies implicate risk association of molecular and clinical characteristics of pLGG in order of proper management. We describe the association between the pLGG features and patient outcome.

Methods For purpose of this retrospective study, the medical records of pLGG patients in period 2010-2020 were evaluated. Patients, with genetic tests performed on tumor tissue, were included in the study. Data on tumor histology, molecular genetics, location, treatment and patient outcome (the presence/absence of neurological sequelae) were collected, using descriptive statistics.

Results 38 patients were included in the study. The most favourable outcome had all of 12 patients with pilocytic astrocytoma of cerebellum, with KIAA-BRAF fusion. All other 9 patients with KIAA-BRAF fusion, with non-cerebellum location, had also astrocytoma. In these, outcome depended on location and less on genetic features. 8 patients had BRAF mutation (V600E), where half of them had ganglioglioma. In those with residual tumour, the progression was often. In 2 patients with astrocytoma and FGFR1 mutation, outcome was favourable in one with total resection. In 2 patients with NF1 gene mutation, outcome depended on location. In last 5 patients we couldn't identify the driver mutation, but most of these patients had favourable outcome associated with total tumor resection.

Conclusions We pointed out the association between pLGG characteristics and patient outcome and found tumor location plays the most important role.

ABSTRACTS

Topic: Fetal and Neonatal Neurology

EPNS25_982 - Fetal neurological malformations in the prenatal counseling committee: the experience of a tertiary care hospital

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Objectives

Prenatal counseling committees are essential for advising families facing complex malformations from a multidisciplinary approach. The involvement of pediatric neurologists specialized in fetal pathology is crucial for providing guidance on the prognosis of these neurological malformations.

To describe the cases presented in the prenatal counseling committee with neurological malformations in 2024.

Methods

A retrospective longitudinal descriptive study, reviewing cases of neurological malformation pathology presented in the prenatal counseling committee of a tertiary care hospital.

Results

18 cases with brain malformations confirmed by neurosonography or fetal MRI were analyzed. The most frequent conditions were bilateral ventriculomegaly (6), cerebellar/vermian hypoplasia (6), agenesis of the corpus callosum (2), megacisterna magna (2), holoprosencephaly (2), and neural tube defects (2). Most cases presented multiple brain malformations, and 50% had associated anomalies in other organs. Diagnosis was primarily made between weeks 12 and 23, confirmed by neurosonography, while MRI detailed lesions in 12 cases. Genetic alterations were identified in 8 cases, and one case involved parvovirus infection. 60% of pregnant women chose to terminate the pregnancy.

Conclusions

This study highlights the value of prenatal counseling committees in the evaluation and guidance of cases of fetal neurological malformations and the need to consolidate this model in tertiary care hospitals.

ABSTRACTS

Topic: Infectious and Inflammatory Diseases/ Neuroimmunology

EPNS25_983 - Sspe-the monster behind measles

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Objectives: Subacute sclerosing panencephalitis (SSPE) is a serious complication of measles. Its incidence is rare, and it has a long latency period, around 2-10 years. The onset of the disease is either with psychiatric or neurological symptoms, but the evolution is invariably towards dementia, mutism, spastic tetraplegia, vegetative state and death. The EEG trace and the neuroimaging aspects are specific for the disease, however serology from CSF is necessary to make the diagnosis. The treatment of the disease is with nonselective antiviral drugs such as Isoprinosine and Interferon, as well as symptomatic treatment of the epileptic seizures and spasticity. The prognosis remains very poor. The aim of the study is evaluation of the patients with SSPE referred in our clinic in the last 10 years, in association with epidemiological data on measles epidemics in Romania and vaccination trends in the same period.

Methods: The study is retrospective, with a cohort of 6 patients, 3 girls and 3 boys. The inclusion criteria in the study are the definite diagnosis of SSPE according to Dyken criteria. The data was extracted from patients` medical files.

Results: Four out of 6 patients have a history of measles, all in infancy, prior to the first dose of vaccine. Currently, 2 children are in a vegetative state and 2 have died. Correlations were made between the moment of the infection, the place of residency and the virus strain which was endemic. The strains identified are known for the association with SSPE.

Conclusions: Our cases follow the natural history of the disease. Vaccination status or lack of a measles history are not reasons to exclude the diagnosis of SSPE. The onset of the disease was in the majority of cases with discrete symptoms like lack of focus, forgetfulness, school problems and subtle myoclonus. All children were infected in infancy, during the spikes of the epidemic waves, and the infection could have been prevented by herd immunity.

ABSTRACTS

Topic: Neurogenetics

EPNS25_984 - A case of linear sebaceous nevus syndrome treated with alpelisib

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Objectives

Linear sebaceous nevus syndrome (SLNS) or Schimmelpenning-Feuerstein-Mims syndrome is a mosaic RASopathy characterized by the association of craniofacial sebaceous nevus with variable multisystem alterations, being one of the main ones hemimegalencephaly, which usually causes refractory epilepsy.

In many cases, this RASopathy results from a somatic variant in PIK3CA gene.

Alpelisib is a PI3K protein inhibitor approved by the FDA for the treatment of patients with PROS (PIK3CA-related overgrowth spectrum) and has shown promising results in pediatric patients, especially with regard to the improvement of neurological symptoms and control of overgrowth.

Methods

Retrospective review of a SLNS case with refractory epilepsy secondary to hemimegalencephaly.

Results

We present the case of a 10-month-old girl with hyperkeratosis and discrete congenital hypertrophy of the left lip. At 4 months, he developed marked hypertrophy of the left upper and lower lip, associated with hypertrophy of the gums, tongue, and palate. In addition, she presents a well-defined, yellowish-orange left hemifacial plaque, along with strabismus and seizures consistent in generalized hypertonia or only disconnections.

With the suspected diagnosis of SNSL we performed a magnetic resonance imaging (it showed left hemimegalencephaly with diffuse polymicrogyria), an electroencephalogram (compatible with focal epilepsy), biopsy of the skin lesion (compatible with sebaceous nevus) and genetic study in tissue (pathogenic variant in PIK3C).

Anticonvulsant treatment (levetiracetam, oxcarbazepine and vigabatrin) was started, with poor seizure control, pending finally surgical evaluation (first one was made with the result of the MRI).

In this context we begin treatment with alpesilib, prior obtaining compassionate use (it is only approved in children over two years of age) and in this moment we are waiting for the first results.

Conclusions

We want to highlight the importance of the multidisciplinary management (neuropediatricians, dermatologists and anatomopathologists).

Furthermore, we conclude that in refractory epilepsies it is important to use drugs directed to the gene variant found.

ABSTRACTS

Topic: Epilepsy: Diagnosis and Investigations

EPNS25_985 - Heart rate variability changes over time: longitudinal observation in Dravet Syndrome to track SUDEP risk trajectories

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Objectives: Heart rate variability (HRV) changes is a promising biomarker of SUDEP (Sudden Unexpected Death in Epilepsy) risk in Dravet syndrome (DS). Longitudinal data is lacking, hampering its use as outcome measure in clinical trials aiming at reducing SUDEP risk. The aim of our study is to describe the natural history of SUDEP change over time, accounting for age, antiseizure medications and seizure burden.

Methods: We extracted from nap EEGs of subjects with Dravet Syndrome EKG data in wake and sleep between 2004 and 2024. We included only subjects with at least two recordings in wake or in sleep. As HRV parameter we choose high-frequency (HF) power estimated with autoregressive models and normalized over total power. We analyzed HRV change over time, accounting for the effect of possible confounders (age, antiseizure medications) and risk factors for SUDEP (frequency of generalized tonic-clonic seizures, history of status epilepticus) using multiple linear regression.

Results: 42 subjects had at least two recordings in wake or sleep (40 wake, 21 sleep, 19 both). The first recording was recorded at a mean age of 5.52 +/- 6.46 sd, the second followed after 17.7 +/- 7.6 sd years. Mean change in HF between first and second recording was 4.057 n.u. +/- 20.03 sd in wake and 12.95 n.u. +/- 24.17 sd in sleep. In 13/42 (31%) subjects HRV increased in sleep. Younger patients and patients with higher seizure burden tended to have lower increases in HRV.

Conclusions: This pilot study points towards a global increase of HRV over time in DS, in contrast with the physiogical decline with ageing. This could be explained by protective effects of novel ASMs, by reduction of seizure burden or both. This will be clarified by prospective studies.

Bibliography

1. Perulli M, Battista A, Sivo S, et al. Heart rate variability alterations in Dravet Syndrome: The role of status epilepticus and a possible association with mortality risk. Seizure Eur J Epilepsy. 2022;94:129-135. doi:10.1016/j.seizure.2021.11.023
2. Delogu AB, Spinelli A, Battaglia D, et al. Electrical and autonomic cardiac function in patients with Dravet syndrome. Epilepsia.2011;52(SUPPL. 2):55-58. doi:10.1111/j.1528-1167.2011.03003.x
3. Perulli 1, Scala I , VenditiR, Amadio A, Gambardella ML, Quintiliani M, Contaldo I, Veredice C, Della MArca G, Brunetti V, Battaglia DI Short- vs long-term assessment of heart rate variability: Clinical significance in Dravet Syndrome Elsevier 2023 Sep:146:109357. doi: 10.1016/j.yebeh.2023.109357.

ABSTRACTS

Topic: Movement Disorders/ Cerebral Palsy

EPNS25_986 - CODY-SAMP: Combined Dystonia Scale for Assessment of Motor Phenotype, validation study of a composite tool based on clinical and deep learning assessment of combined movement disorders.

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Objectives The heterogeneity of hyperkinetic movement disorders syndromic associations, physiological background and etiology make it difficult their recognition, monitoring and measurement disease progression or under therapeutical interventions. Combined phenotypes represent the majority of genetic dystonias of pediatric onset. Their classification and follow-up are challenging due to phenotype complexity; and multiplication of tools increases difficulty of administration and reproducibility between assessors. A composite clinical scale with characteristics that allow follow-up over transition from pediatric to adult care is needed. The objective of the current work is the development and validation of a clinical scale combined with a numerical tool allowing assessment of these complex phenotypes.

Methods We designed a clinical scale named CODY-SAMP (Combined Dystonia-Scale for Assessment of the Motor Phenotype) with 3 sections i) dystonia, ii) associated hyperkinetic movement disorders and iii) associated neurological features and a corresponding 16-minute standardized video protocol for assessment of patients with combined movement disorders including dystonia. The severity and frequency of hyperkinetic movements are measured and associated neurological features listed. Video recordings from two groups of 25 pediatric and 25 adult patients, from Montpellier Beau Soleil Clinic and BC Children's Hospital, Vancouver, were assessed for inter-rater reliability by 5 raters (neurologists and pediatric neurologists) and intra-rater reliability by assessment of 25 video recordings twice, at a minimum of two months interval by two of the raters. Construct validity was studied by comparison of the outcomes from CODY-SAMP for dystonia with BFMDRS scores and for tremor with kinematic motion trackers. We trained a convolutional neural network combined with supervised machine learning algorithms for movement detection and classification on the standardized recorded data. The model training was performed on videos assessed and labeled by two movement disorders specialists, on snippets of 10 seconds

Results Using the clinical scale we developed, applied to pediatric and adults's patients with combined movement disorders, we identified the distinct hyperkinetic movement disorders (dystonia, tremor, myoclonus chorea, tics, stereotypies) and associated neurological motor features with a good inter- and intra-rater reliability. Machine-learning models trained recognized the distinct patterns of hyperkinetic movement disorders and permit distinguishing more common syndromic associations.

Conclusions We developed CODY-SAMP, a composite scale that allows assessment of combined movement disorders in both, pediatric and adult populations. It allows us to discriminate between different syndromic associations, suggesting possible etiologies.

ABSTRACTS

Topic: Epilepsy: Diagnosis and Investigations

EPNS25_988 - Clinical and genetic spectrum of NEXMIF pathogenic variants: a single center experience

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Objectives

NEXMIF (Neurite Extension and Migration Factor), formerly known as KIAA2022, is an X-linked gene implicated in a spectrum of childhood neurological disorders, primarily intellectual disability (ID), epilepsy, and autism spectrum disorder (ASD). Pathogenic variants in *NEXMIF* have been associated with a range of neurodevelopmental phenotypes, with affected males exhibiting severe symptoms due to hemizygosity, while often the carrier females show wide phenotypic diversity ranging from completely asymptomatic to severe intellectual disability and drug-resistant epilepsy. Recent studies highlight the role of *NEXMIF* in synaptic function and neuronal development, where loss-of-function mutations disrupt dendritic morphology and *synaptic* plasticity, contributing to cognitive and behavioral deficits.*NEXMIF*-related epilepsy presents with diverse seizure types, including focal and generalized epilepsy, often with early onset and pharmacoresistance.

Methods

We retrospectively evaluated 4 consecutive children (1 male) with pathogenic NEXMIF mutation.

Results

Age of onset of symptoms ranged from 1 month to 2 years-old. The follow-up period was 2-9 years. None of them were consanguineous. All patients were admitted with suspected seizures of varying semiologies; one patient had developmental delay, and the other had a neuropsychiatric disorder and neuroregression. All patients had normal metabolic investigations and normal brain neuroimaging. Electroencephalography (EEG) shows active epileptic abnormalities in the whole group, and 3 patients were taking at least 2 antiseizure drugs, and two of them had drug-resistant epilepsy. Three of the patients had de novo heterozygous pathogenic mutations in *NEXMIF* gene as de novo heterozygous NM_001008537.3 c.3218del (p.Pro1073HisfsTer17), de novo heterozygous NM_001008537.3: C.680T>A; p.(Leu227Ter), de novo, heterozygous c.1954C>T (p.Q652*) (p.Gln652Ter) mutations and hemizygous NM_001008537.3 c.406G>A p.G136R mutation. Male patient had maternaly inherited hemizygous VUS variant as NEXMIF gene. Although the maternaly inherited patients is male, he is seizure free with centrotemporal spikes.

Conclusions

We defined our patients diagnosed with neurological diseases associated with NEXMIF gene mutation by genotype-phenotype relationship. Contrary to expectations, we observed that our male patient had a more benign course.

ABSTRACTS

Topic: Neuromuscular Disorders

EPNS25_989 - Viral myositis with significant hyperCKemia in young females –management of an acute complication or underlying condition

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Objectives

Benign acute inflammatory myositis in children is a rare, self-limiting complication of a viral infection that occurs in school-age children, mostly in males, and rarely in a severe form (with a risk of rhabdomyolysis/kidney damage). Differential diagnosis includes numerous inflammatory and non-inflammatory myopathies. Myositis due to influenza is more often described with influenza type B virus infection, while rhabdomyolysis in girls with influenza type A virus infection. The early appearance of myositis during the disease in females is also suggestive of an immune-mediated mechanism.

Methods

We present two pediatric female patients with significant hyperCKemia due to viral myositis.

Results

Case report 1: A nine-year-old girl, a previously healthy athlete, was hospitalized for limping, myalgia due to an acute febrile respiratory illness. Initially, elevated values of creatine kinase (CK) - 23498U/L were found along with elevated liver transaminases. Microbiologically, she was influenza B positive. Nephrological and cardiological examinations were normal. Additional neurological (screening for neuromuscular diseases) and metabolic evaluation arrived normal. Supportive treatment was followed by a gradual recovery. Case report 2: A thirteen-year-old girl was hospitalized due to pain in the lower extremities and symptoms of febrile respiratory infection. Initially, elevated values of CK - 60153U/L were found along with elevated liver transaminases. Microbiologically, she was influenza A positive. She was treated with oseltamivir and increased parenteral hydration with calcium supplementation due to hypocalcemia. Close monitoring by a nephrologist and cardiologist was performed. Additional neurological and metabolic workup arrived normal. Formerly, she developed hyperCKemia after an influenza infection. Electromyoneurography and metabolic evaluation were normal at that time. The father, three of his father's sisters, and an uncle also manifested rhabdomyolysis due to an infection. Further diagnostic processing was not possible due to a lack of parent cooperation.

Conclusions

Severe forms of inflammatory viral myositis in children are rare. The pathophysiological mechanism is unclear. The laboratory limit of CK level suggestive of additional evaluation for inflammatory and non-inflammatory myopathies is unknown, and a rational treatment algorithm is insufficient. Significantly elevated CK values suggest an additional pathology. In muscle diseases with rhabdomyolysis, rare metabolic myopathies, dystrophinopathies, rheumatological diseases come into consideration; therefore, neuropediatric and interdisciplinary treatment is important.

ABSTRACTS

Topic: Neuromuscular Disorders

EPNS25_991 - Pattern of muscle ultrasound abnormalities in merosin-deficient muscular dystrophy

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Objectives

To characterize the muscle involvement pattern in merosin-deficient muscular dystrophy related to LAMA2 (LAMA2RD) using ultrasound and compared with the previously described findings on MRI.

Methods

A total of 22 patients with a confirmed diagnosis of LAMA2RD were studied using a specifically designed protocol that assessed 28 different muscles distributed across the head, neck, upper limb, trunk, and lower limb. Symmetric involvement was verified through bilateral assessment. Muscle echogenicity was evaluated semi-quantitatively using the Heckmatt scale. The involvement pattern was analyzed using hierarchical clustering and visualized through heatmaps. Additionally, specific intramuscular hyper-echogenicity distribution patterns were examined in the medial and lateral gastrocnemius and deltoid muscles. Ultrasound-based comparative distribution rules between muscles were also investigated. The results were compared with the MRI-based pattern described by Quijano-Roy et al.

Results

Most muscles exhibited a dystrophic echogenicity pattern, with Heckmatt grades of 3 or 4. There was relative preservation of the soleus muscle (especially in comparison to the gastrocnemii) and the oblique and transverse abdominal muscles (especially in comparison to the rectus abdominis). The tibialis anterior muscle tended to have greater echogenicity than the gastrocnemii, while the biceps brachii showed higher echogenicity than the triceps brachii. The medial gastrocnemius often displayed a predominance of superficial hyper-echogenicity, whereas the deltoid exhibited a "tiger-stripe" pattern of involvement. Muscles that do not show fat replacement on MRI, such as the sternocleidomastoids or masseters, frequently demonstrated marked involvement on ultrasound.

Conclusions

A standardized ultrasound protocol for the assessment of LAMA2RD is presented, which could be extended to other muscular dystrophies. LAMA2RD is characterized by a marked increase in echogenicity in affected muscles, with relative preservation of the soleus and lateral abdominal muscles. Increased echogenicity appears to precede fat replacement. Further studies involving radiomics and muscle size analysis will be conducted through international collaborations within the framework of natural history studies.

ABSTRACTS

Topic: Epilepsy: Diagnosis and Investigations

EPNS25_992 - Evaluating the Use of Cannabidiol (CBD) in Children with Epilepsy: How well do we review effectiveness and adverse events?

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Objectives

Highly purified cannabidiol has been approved by NICE for Dravet syndrome, Lennox-Gastaut syndrome and tuberous sclerosis with the requirement that frequency of convulsive seizures is checked every 6 months, and CBD is stopped if the frequency has not fallen by 30% compared with the 6 months before starting treatment. Real-world data on effectiveness, duration of use and reasons for discontinuation remain limited. We audited the review of CBD effectiveness and adverse events in children with epilepsy.

Methods

A retrospective analysis was conducted. All children with epilepsy who are currently prescribed highly purified CBD and have been followed for at least 6 months at a tertiary centre were included (44 patients). Data were collected on seizure frequency and category, changes in concomitant anti-epileptic drugs (AEDs), quality of life measures and parental/guardian feedback, adverse effects, and discontinuation rates. Seizure types including drop seizures were defined according to the NICE guidelines. Treatment response was categorized as significant improvement (>30% seizure reduction), or non-significant improvement (<30% reduction) or worsening seizures. Reasons for discontinuation were recorded.

Results

A total of 44 children were included in the analysis. After six months, significant reduction of total seizures was seen in 62%, non-significant response in 17% and worsening in 21% of patients. Of the 44 patients, 21 (n=21/44) provided information about changes in GTCS and 10 patients (n=10/44) documented changes in drop seizures. The data revealed 67% experiencing a reduction in GTCS whereas 33% observed no change or worsening of their condition. Furthermore, 70% of patients reported a decrease in drop seizures. Improvements in sleep, behaviour, and overall well-being were reported in 12% of total cases. Adverse effects were observed in 17% patients (most commonly drowsiness, appetite changes, and gastrointestinal discomfort) at 6 months and 10% (most commonly liver dysfunction) at 12 months. All 44 children continued CBD after 6 months; 10% children were discontinued at 12 months – all for liver dysfunction.

Conclusions

In this audit all children were reviewed at 6 months, but documentation and use of seizure diaries was noted to be inconsistent. CBD was not discontinued in the 38% of children who did not fulfil NICE criteria for continuation. Overprescribing is well-known to be a problem in people with epilepsy and may be under recognised but even more problematic in children with pharmaco-resistant epilepsy and may affect medications other than CBD. Clinician education and re-audit will be required to improve effective prescribing and deprescribing.

ABSTRACTS

Topic: Epilepsy: Medical and Surgical treatment

EPNS25_993 - VNS Therapy™ for rare drug-resistant epilepsies and developmental epileptic encephalopathies: a single center experience

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Objectives

Rare Epilepsies and developmental epileptic encephalopathies (DEEs) that do not include channelopathies and brain malformation are often resistant to antiseizure medications (ASMs), and their management can be challenging. Moreover, specific tailored treatments for these conditions are not available, thus VNS Therapy™ may result in an early option after the failure of 2 ASMs. We investigate here the use of VNS in these groups.

Methods

First, we investigated the presence of published articles on the use of VNS Therapy™ in Rare Drug Resistant Epilepsies (DRE) and DEEs with a review of the literature. Then, among 68 patients receiving VNS Therapy at our center, we included those with rare DRE or DEE without major brain malformations or channelopathies having a follow-up > 1 year. For each patient we prospectively collected: age at the onset of seizures, age at the implant, length of the follow-up, seizure types (generalized, focal, both, spasms), results of the genetic tests, seizure outcomes with the McHugh scoring, number and type of concomitant ASMs and VNS stimulation parameters.

Results

The literature search identified a limited number of articles with low number of patients involved, highlighting a need for these data. In our study, 16 pediatric patients (9 with DRE and 6 with DEEs) implanted at a mean age of 8.3 years (±4.6 years), were included in the study. The mean age at seizure onset was 2.8 years (median 1 year). For the 9 patients with DRE the average epilepsy duration before implantation was of 5.6 years, and a mean follow-up (FU) of 7.67 years. All the patients reached the VNS target dose of 1.75 within 10 weeks of titration. The DEEs group presented a mean age at implant of 8.7 years, with previous mean duration of epilepsy of 7.8 years. The mean follow-up period was 6.9 years. At last follow-up, 9 patients were classified as McHugh scale IA (3 were seizure-free, 20%), 5 as McHugh class IIA, 1 as class IIIA, and 1 as class V. Two patients were without concomitant ASMs at last follow up.

Conclusions

Seizures outcomes after VNS Therapy™ in patients with DRE or DEE in the context of rare diseases, without major brain malformations or channelopathies, are limited in the literature and our study shows promising results. These insights suggest that VNS Therapy™ might be a good early option for these kind of patients for which a specific treatment is not yet available.

ABSTRACTS

Topic: Epilepsy: Diagnosis and Investigations

EPNS25_994 - Language Model Applications for Early Diagnosis of Childhood Epilepsy

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Objectives: Accurate and timely epilepsy diagnosis is crucial to reduce delayed or unnecessary treatment. While language serves as an indispensable source of information for diagnosing epilepsy, its computational analysis remains relatively unexplored. This study assessed – and compared – the diagnostic value of different language model applications in extracting information and identifying overlooked language patterns from first-visit documentation to improve the early diagnosis of childhood epilepsy.

Methods: We analyzed 1,561 patient letters from two independent first seizure clinics. The dataset was divided into training and test sets to evaluate performance and generalizability. We employed two approaches: an established Naïve Bayes model as a natural language processing technique, and a sentence-embedding model based on the Bidirectional Encoder Representations from Transformers (BERT)-architecture. Both models analyzed anamnesis data only. Within the training sets we identified predictive features, consisting of keywords indicative of ‘epilepsy’ or ‘no epilepsy’. Model outputs were compared to the clinician’s final diagnosis (gold standard) after follow-up. We computed accuracy, sensitivity, and specificity for both models.

Results: The Naïve Bayes model achieved an accuracy of 0.73 (95% CI: 0.68-0.78), with a sensitivity of 0.79 (95% CI: 0.74-0.85) and a specificity of 0.62 (95% CI: 0.52-0.72). The sentence-embedding model demonstrated comparable performance with an accuracy of 0.74 (95% CI: 0.68-0.79), sensitivity of 0.74 (95% CI: 0.68-0.80), and specificity of 0.73 (95% CI: 0.61-0.84).

Conclusions: Both models demonstrated relatively good performance in diagnosing childhood epilepsy solely based on first-visit patient anamnesis text. Notably, the more advanced sentence-embedding model showed no significant improvement over the computationally simpler Naïve Bayes model. This suggests that modeling of anamnesis data does depend on word order for this particular classification task. Further refinement and exploration of language models and computational linguistic approaches are necessary to enhance diagnostic accuracy in clinical practice.

ABSTRACTS

Topic: Neuromuscular Disorders

EPNS25_995 - Expert opinion about neurodevelopment abnormalities in SMA type 1 and presymptomatics. An ENMC survey.

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Objectives

Spinal muscular atrophy (SMA) is a complex neuromuscular, multisystemic disorder with a central nervous system component. This study aimed to assess current practices, knowledge gaps, and expert perspectives on key aspects of SMA management, including intervention assessments, neurodevelopmental evaluation, and biomarker development.

Methods

A survey was distributed via REDCap to a panel of SMA experts in Europe, America and Australia. The questionnaire covered several topics related to SMA cognition and neurodevelopmental phenotype such as frequency of problems at different cognitive domains in SMA type 1 and presymptomatically treated patients, the role of different factors in the neurodevelopmental phenotype, the methods for evaluation of neurodevelopmental issues, the screening and diagnostic approach and the detection of gaps. Quantitative data were analyzed descriptively, while open-ended responses were thematically analyzed to identify key themes and priorities.

Results

A total of 16 centers completed the survey. Language expression problems, restricted social interest and intelectual problems were described as common in SMA type 1 patients and more rare in presymptomatic patients. SMN2 copy number and motor severity was considered as important factors in the emergence of neurodevelopmental problems. Evaluation was performed using multiple and variable scales and approaches. Unmets needs were identified by the experts as lack of valid epidemiology of neurodevelopmental abnormalities and their pattern in SMA, the improvement of assessment scales, and the development of biomarkers. Qualitative analysis revealed key concerns, including the need for standardized neurodevelopmental evaluation protocols and enhanced multidisciplinary collaboration. Experts highlighted challenges in assessing long-term neurocognitive outcomes and emphasized the importance of systematic follow-up strategies.

Conclusions

The results of this expert survey highlight current practices and unmet needs in SMA management. The findings underscore the importance of standardized approaches for neurodevelopmental assessment and call for greater collaboration in multicenter research initiatives. These insights provide a foundation for refining clinical guidelines, improving patient outcomes, developing preventive strategies and advancing research and treatments for SMA neurodevelopment issues.

ABSTRACTS

Topic: Fetal and Neonatal Neurology

EPNS25_996 - Trio Study in Fetuses with Central Nervous System Malformations (CNS-TRIO Project)

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Objectives

Central nervous system (CNS) malformations are a major cause of late pregnancy termination, often due to diagnostic uncertainty. This study aims to assess the added value of a TRIO approach, combining fetal and parental magnetic resonance imaging (MRI) and exome sequencing (ES), to refine diagnosis and prognosis based on our previous experience.

Methods

This single-center observational study will include pregnant women whose fetuses have been diagnosed with a CNS malformation via neurosonography and confirmed by MRI. Fetuses with a known poor prognosis or pathogenic genetic array findings will be excluded. MRI will be performed on both parents, and TRIO exome sequencing will be conducted on fetal and parental DNA. Findings will be analyzed by fetal sex and type of CNS malformation. Diagnosis precision and the likelihood of parental MRI findings will be subjectively evaluated by the pediatric neurologist and the radiologist. Prognosis will be assessed using risk assessment methods for gross motor and cognition domains using single- and trio-data. Anxiety and stress levels will be measured before and after testing using the State-Trait Anxiety Inventory (STAI) and Perceived Stress Scale (PSS-10). Pregnancy outcomes, including requests for termination, neonatal survival, and neurological development using a developmental inventory will be recorded.

Results

This study anticipates an improved diagnostic yield by integrating parental MRI and TRIO sequencing, allowing for a more accurate prognosis of fetal brain anomalies of uncertain significance.

Previous pilot findings suggest that detecting similar structural or genetic patterns in parents can help reclassify variants of uncertain significance, aiding clinical decision-making. We expect more diagnostic certainty and an improvement in prognosis confidence as well as a reduction in parental anxiety due to clearer prognosis and better counseling.

Conclusions

Incorporating parental imaging and genetic studies into prenatal CNS anomaly diagnosis has the potential to enhance clinical decision-making, reduce diagnostic and prognosis uncertainty, and improve parental psychological well-being.

ABSTRACTS

Topic: Infectious and Inflammatory Diseases/ Neuroimmunology

EPNS25_998 - Acute disseminated encephalomyelitis (ADEM): differential diagnosis and effectiveness of plasma exchange in a 1 year-7 months-old patient after SARS Cov-2 infection

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Objectives. Acute disseminated encephalomyelitis (ADEM) is an autoimmune demyelinating lesion of the central nervous system (CNS), which requires differential diagnosis with a group of other demyelinating diseases and occurs after infection. **Goal.** To present the clinical and paraclinical features of the course of ADEM in a patient for 1 year and 8 months, as well as the effectiveness of the therapy, including plasmaphoresis.

Methods. Neurological assessment of the patient's status, magnetic resonance imaging (MRI), virological and immunological examination of blood serum and cerebrospinal fluid.

Results. At the age of 1 year and 7 months, the patient became acutely ill with the development of ophthalmoplegia, limb paresis, and coordination disorders after a viral infection. An examination of the cerebrospinal fluid was conducted to rule out infectious meningitis. Negative results were obtained when examining blood serum for antibodies to MOG, antibodies to NMDA receptors and aquaporin-4. Neuroborreliosis is also excluded Antibodies Ig G SARS Cov-2 7.88 (normal to 1) were detected. The patient was treated with methylprednisolone 20 mg/kg/course and human immunoglobulin 2 grams per kilogram per course, oral prednisone was continued, but the neurologic deficit worsened after a slight improvement. A decision was made to perform plasmaphoresis, after which the degree of paresis decreased and the gait improved. MRI after plasmaphoresis: MRI picture of multifocal demyelinating process (ADEM) at the stages of treatment. In the dynamics of reduction of previously detected areas of damage, minimal reduction of the volume of parenchyma from the previous study, ventriculodilatation, changes in the subependymal signal, as a consequence of steroid therapy.

Conclusions. ADEM is a difficult to diagnose autoimmune disease that also requires the exclusion of other demyelinating lesions of the CNS and occurs after viral infections, including those associated with SARS Cov-2. Timely clarification of the diagnosis allows you to use all possible treatment methods. The use of plasmaphoresis in the case of insufficient effectiveness of the previous stages of treatment allows to significantly improve the patient's neurological status.

ABSTRACTS

Topic: Neurogenetics

EPNS25_1000 - Sturge Weber Syndrom - Skin biopsy in common pathogenic somatic GNAQ variant

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Objectives

Sturge Weber Syndrome (SWS) is a rare genetic neurocutaneous syndrome characterized by vascular anomalies, leptomeningeal angiomatosis, and glaucoma. About 75-100 % of SWS patients develop early-onset refractory epilepsies and neurocognitive/neuropsychiatric deficits. In up to 80 %, classical SWS is caused by tissue-specific somatic mosaicism of a recurrent missense variant in the *GNAQ* gene.

Methods

Thirteen SWS patients, who underwent skin biopsy and/or brain surgery, were enrolled in this study. All patients were clinically followed up over years (glaucoma, seizure and neurocognitive outcome, medication, MRI findings, brain surgery).
We investigated either skin (n=12) or brain tissue resected during epilepsy surgery (n=1) within DNA extraction from tissue samples and blood, exome sequencing and cancer gene panel next-generation sequencing, Sanger Sequencing of GNAQ hotspot variant and High-Resolution Melt (HRM) analysis of qPCR for detection of the GNAQ hotspot variant.

Results

In contrast to peripheral blood samples, tissue samples from all patients were found to harbor the hotspot *GNAQ* c.548G>A p.(Arg183Gln) variant at fractions ranging from 0.65 % to 8.2 %. We also established and validated a high-resolution melt analysis quantitative PCR (HRM-qPCR) assay for reliable and cost-effective confirmation, showing that this method is sensitive enough to detect variants at a fraction as low as 0.3 %.

Conclusions

Our results highlight the importance of tissue specific analysis with a highly augmented coverage for deep sequencing and suggest that HRM-qPCR is a powerful and inexpensive tool for the detection of low-level somatic variants. Data from our case series strongly suggest that testing skin biopsies is pivotal in the genetic diagnostic of SWS as testing blood samples leads to negative results.

ABSTRACTS

Topic: Epilepsy: Medical and Surgical treatment

EPNS25_1001 - Evaluation of the treatment approaches of pediatricians and pediatric neurologists to febrile seizures

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Objectives

The aim of this study is to evaluate the treatment approaches of pediatricians and pediatric neurologists toward febrile seizures.

Methods

The study was conducted online using Google Forms between June 1, 2024, and December 31, 2024, among physicians working in Türkiye. A 34-question survey was developed to assess physicians' treatment approaches to patients under and over one year of age presenting with simple febrile seizures, complex febrile seizures, and febrile status epilepticus, as well as the factors influencing their treatment choices. The study data were analyzed using SPSS Statistics Software. A p-value of <0.05 was considered statistically significant.

Results

A total of 97 pediatric neurologists and 87 pediatricians were included in the study. While 77 (89%) of pediatricians reported seeing 10 or fewer patients with febrile seizures per month, 68 (70%) of pediatric neurologists reported seeing more than 10 such patients per month (p<0.001).

Among infants under one year of age with complicated febrile seizures, 49 (51%) of pediatric neurologists initiated continuous antiseizure treatment, while 48 (49%) opted for intermittent prophylaxis. In contrast, 66 (76%) of pediatricians initiated continuous treatment, whereas 21 (24%) preferred intermittent prophylaxis (p<0.001).

For patients over one year of age with complicated febrile seizures, 45 (46%) of pediatric neurologists prescribed continuous treatment, while 52 (54%) used intermittent prophylaxis. Among pediatricians, 70 (80%) initiated continuous treatment, whereas 17 (20%) opted for intermittent prophylaxis (p<0.001).

When asked about the most effective treatment for febrile seizures, 39 pediatric neurologists (40.2%) preferred oral intermittent prophylaxis, whereas only 12 pediatricians (13.8%) opted for oral prophylaxis (p<0.001).

Conclusions

This study reveals significant differences in the treatment approaches of pediatricians and pediatric neurologists toward febrile seizures. Pediatric neurologists prefer intermittent prophylaxis more frequently than pediatricians. These findings suggest that clinical experience and training, depending on the specialty, influence treatment preferences. Future training programs and standardized guidelines may help bridge these differences and optimize febrile seizure management across specialties.

ABSTRACTS

Topic: Epilepsy: Medical and Surgical treatment

EPNS25_1002 - STIRIPENTOL AS AND ADJUNCTIVE THERAPY FOR REFRACTORY EPILEPSY IN SLC6A1-NDD

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Objectives

SLC6A1-related neurodevelopmental disorder (*SLC6A1*-NDD) is a rare disease characterized by intellectual disability, epileptic encephalopathy, neurobehavioral and/or psychiatric manifestations. In many cases the epilepsy is refractory.

SLC61A encodes a GABA transporter, GAT1, which reuptakes GABA into presynaptic neurons and glia. One of the mechanisms of action of Stiripentol is the enhancement of GABAergic transmission by inhibiting GABA transaminase (GABA-T), blocking the GABA transporter (GAT) and acting as a positive allosteric modulator of GABA A receptors.

We aimed to investigate Stiripentol as an adjunctive therapy in these cases.

Methods

Retrospective review of two patients with SLC6A1-NDD with refractory epilepsy treated with Stiripentol as adjunctive therapy, one from Milan (Italy) and the other one from Basel (Switzerland).

Information on family and personal history, psychomotor development, behavioral manifestations, epilepsy, genetic studies, EEG and previous anticonvulsive medications were collected.

In the Italian case, the Stiripentol was introduced together with sodium valproate, ethosuximide and clobazam. In the Swiss case, it was added to sodium valproate, cannabidiol and clobazam.

Results

In the Italian case, the introduction of Stiripentol led to a freedom of seizures. In the Swiss case, a very significant reduction in the number of seizures was achieved.

In both cases, an improvement in cognitive and behavior was showed.

No important side effects were reported.

Conclusions

Given these promising results, we can conclude that Stiripentol in adjunctive therapy can be an effective alternative in cases of SL6CA1-NDD with refractory epilepsy.

ABSTRACTS

Topic: Epilepsy: Medical and Surgical treatment

EPNS25_1003 - Cannabidiol and Cognitive-Behavioral Comorbidities in Epileptic Encephalopathies

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Objectives: Developmental epileptic encephalopathies are marked by refractory epilepsy during childhood along with neurodevelopmental comorbidities. Addressing these comorbidities presents challenges due to the lack of diagnostic tools. This study aimed to replicate the BECOME questionnaire for caregivers of pediatric patients with refractory epilepsies who have been treated with cannabidiol (CBD) for at least one month from 2022 to 2024, and to independently analyze the results in cognitive, behavioral, and quality of life areas, regardless of its anti-seizure effects.

Methods: A retrospective analysis was carried out using clinical history and telephone interviews with family members to collect data related to cognition, language and communication, emotional and behavioral aspects, physical condition, sleep, and quality of life. Results were categorized into two groups based on whether seizures had been reduced by more than 50% or if the reduction was less than 50% or nonexistent.

Results: We gathered data from 16 patients who had received CBD since 2022. In terms of etiology, 2 had Dravet syndrome, 5 had Lennox-Gastaut syndrome, 1 had tuberous sclerosis, and 8 had other refractory epilepsies. The average number of previous anti-seizure medications used was 8.5, and the average age of the patients was 9 years. Of these, 15 patients had intellectual disabilities. None achieved seizure freedom; 37.5% were responders with more than a 50% reduction in seizures, 43.7% were responders with less than a 50% reduction, and 18.7% showed no response. The average duration of CBD use was 14.6 months. Seventy-five percent reported cognitive and behavioral improvements. In the group with more than a 50% seizure reduction, 100% reported cognitive improvement while 83% noted enhancements in language, behavior, and physical condition. Fifty percent experienced improvements in sleep (with no correlation to reductions in nocturnal seizures), and 83% reported enhanced quality of life. In the group with less than 50% seizure reduction or no improvements, 85% noted cognitive improvements, 57% reported better interaction abilities, 71% stated behavioral improvements, and 42% experienced physical improvements. Sleep remained unchanged in all patients, and 57% reported improvements in their quality of life.

Conclusions It is essential to know, diagnose, and treat neurodevelopmental comorbidities in patients with refractory epilepsies through specific diagnostic tools and targeted treatments. New anti-seizure drugs like CBD might have beneficial effects on cognition and behavior. A holistic approach with effective treatments targeting not only seizures but also comorbidities is necessary to improve the quality of life of patients and their families.

ABSTRACTS

Topic: Infectious and Inflammatory Diseases/ Neuroimmunology

EPNS25_1005 - Unusual cerebral involvement in a patient with acute myeloid leukemia (AML): Immune reconstitution inflammatory syndrome (IRIS)

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Objectives

"Immune reconstitution inflammatory syndrome" (IRIS) refers to a group of inflammatory conditions characterized by the paradoxical exacerbation of an existing infection. It commonly occurs in human immunodeficiency virus (HIV) patients after initiating antiretroviral therapy (ART) but can also affect non-HIV immunocompromised patients when immunosuppression is reduced. Here, we aim to present the case of an eleven-year-old female patient diagnosed with IRIS during follow-up for acute myeloid leukemia (AML).

Methods

Clinical, laboratory and imaging characteristics of the case were obtained from the hospital database.

Results

An eleven-year-old girl with AML and neutropenia developed severe headache and left hemiparesis while being treated for a pulmonary fungal infection that developed during chemotherapy. Brain magnetic resonance imaging (MRI) showed a midline shift to the left and a FLAIR hyperintense edematous area adjacent to the right lateral ventricle. As signs of a raised intracranial pressure syndrome developed, extraventricular CSF drainage was performed in addition to anti-oedema treatment. Biochemical CSF parameters and cell count were within the normal limits. There was no growth in CSF culture. As the findings progressed, the neurosurgeon performed a decompressive craniectomy, a brain biopsy was performed, and a ventriculoperitoneal shunt was placed. The differential diagnosis included leukemic involvement, other brain malignancies and IRIS. Leukaemic involvement was excluded when CD34 and CD117 were negative in the CSF sample. In the pathological examination of the excisional biopsy specimen, non-specific findings such as reactive gliosis, increased capillary vessels, focal necrosis were observed. Also, Alcian blue/periodic acid-Schiff (AB-PAS) staining and Epstein-Barr encoding region (EBER) signal were negative. So central nervous system (CNS) tumours were excluded. Dexamethasone was started with a presumptive diagnosis of IRIS. Under steroid treatment, clinical and neuroimaging findings gradually improved. The case is still being followed without neurological sequelae.

Conclusions

Patients with an absolute neutrophil count (ANC) below 500 per microliter face increased risk of opportunistic fungal and viral infections (e.g., Aspergillus, cytomegalovirus). These infections may initially be latent or subacute but become clinically evident as IRIS once neutrophil counts improve. In the context of leukemia patients nearing the end of their neutropenic phase, it is crucial to include IRIS in the differential diagnosis when encountering unexplained cerebral manifestations. Expeditious exclusion of leukemic involvement and secondary malignancies is essential in leukemia patients to prevent delays in the administration of highly effective corticosteroid treatment for IRIS.

ABSTRACTS

Topic: Cerebrovascular Disorders

EPNS25_1006 - Neurological outcome prediction models after childhood ischaemic stroke

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Objectives

Arterial ischaemic stroke in children has an incidence of 1.6-2.4/100,000 children/year and is associated with significant morbidity. The modified Alberta Stroke Program Early Computed Tomography Score (modASPECTS) was developed to describe lesion size and location in a simple semi-quantitative scoring system. This score has been widely used as a predictor of neurological outcome in children with arterial ischaemic stroke.

This project asks whether, among 168 childhood arterial ischaemic strokes in our registry with good quality baseline charactaristics and neurological outcome data after 24 months, we can improve outcome prognosis by combining radiological and clinical data into a model compared to using the radiological score as a prognostic model alone.

Methods

To this end, we calculated the modASPECTS score on the first available diffusion-weighted imaging and its prognostic value. Further we collected baseline signs and symptoms, initial pedNIHSS score, and neurological outcome of these children at 24 months as measured by the Paediatric Score Outcome Measure (PSOM). We then constructed a logistic regression model to predict favourable or unfavourable outcome by PSOM. We used backward stepwise selection based on Bayesian Information Criterion (BIC) to identify significant predictors. We used multiple imputation with predictive mean matching for missing values.

Results

The logistic regression model using the modASPECTS score alone showed a significant association with unfavourable neurological outcome at 24 months (complete cases: OR = 1.36, $p < 0.001$; after multiple imputation: OR = 3.66, $p < 0.001$). However, its predictive power was moderate (AUC ≈ 0.76).

In full logistic regression including all available symptoms and signs, only pedNIHSS at presentation remained a significant predictor in addition to modASPECTS score ($p < 0.001$ for both variables) using backward stepwise selection. The final model had strong discriminatory power (AUC = 0.815 before imputation, 0.801 after imputation). DeLong's test showed no significant difference between the models with and without multiple imputation ($p = 0.77$), suggesting robustness.

Conclusions

In conclusion, paediatric NIHSS and supratentorial modASPECTS score reliably predict long-term neurological outcome and interestingly, clinical characteristics at presentation improve model performance independently of stroke lesion size and location as measured by modASPECTS score.

ABSTRACTS

Topic: Infectious and Inflammatory Diseases/ Neuroimmunology

EPNS25_1007 - Atypical Presentation of Guillain-Barré syndrome variant: Miller-Fisher Syndrome in Children Under Three Years of Age

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Objectives: Miller-Fisher syndrome (MFS) is characterized by a triad of symptoms: areflexia, ataxia, and ophthalmoplegia. This condition suggests a rare variant of Guillain-Barré syndrome (GBS), which is characterized as an acute immune-mediated nerve disorder. Recognition of atypical presentations of MFS is important for rapid diagnosis and treatment as the syndrome can be confused with other neurological disorders. Three cases featuring atypical clinical components and a rare presentation age of under three years are presented.

Methods: Case 1: A 2-year-old male and Cases 2 and 3: 3-year-old males arrived at the clinic with acute-onset ataxia. Neurological examinations conducted upon hospital admission revealed ataxia and ophthalmoplegia in Cases 1 and 2, while Case 3 exhibited isolated-ataxia. All cases experienced a viral illness one week prior and showed normal deep tendon responses (DTR). The diagnosis encompassed acute ataxia and/or incomplete Miller-Fisher syndrome (MFS), a variant of Guillain-Barré syndrome (GBS), attributed to an atypical clinical presentation and age-related factors.

Results: To rule out postinfectious cerebellitis or intracranial lesions as a result of acute ataxia and ophthalmoplegia, brain magnetic resonance imaging (MRI) was applied. The results were unremarkable. All patients areflexia on day two of hospitalization. Based on ataxia, ophthalmoplegia, and areflexia in Cases 1 and 2, and ataxia with areflexia in Case 3, atypical GBS/incomplete MFS presentations were considered, prompting serum, CSF, and spinal MRI evaluations. Case 3 had spinal MRI hyperintensity to the cauda equina, while the other two had normal results. In Cases 1 and 3, CSF analysis showed high albumin levels (89 mg/dL, 82 mg/dL; normal range: 10–30 mg/dL) and IgG indices. Case 2 had triad of MFS, although CSF IgG index and albumin were normal. The ganglioside antibody panel, including GQ1b, is limited and expensive in our nation, thus only Cases 1 and 2 were tested, producing negative results. Case 3 had EMG data consistent with widespread peripheral sensorimotor neuropathy, while the other two had normal results. After analysis, all patients received 400 mg/kg/day IVIG for five days. Clinical improvement was significant in all patients. At follow-up outpatient visits, areflexia and ophthalmoplegia resolved after one month.

Conclusions: Most patients with MFS achieve full recovery within several weeks to a few months. Prompt initiation of IVIG therapy is advisable for favorable prognostic outcomes. The significance of suspecting and identifying MFS, particularly in early-onset pediatric patients, and recognizing it as a differential diagnosis for ataxia and acute-onset ophthalmoplegia has been emphasized.

ABSTRACTS

Topic: Epilepsy: Diagnosis and Investigations

EPNS25_1008 - Enhancing Executive Function in Dravet Syndrome: The Impact of Fenfluramine on Seizures, Behavioral Performance and Quality of Life

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Objectives

Fenfluramine (FFA) has proven to be highly effective in controlling seizures in patients with Dravet syndrome (DS). This single-center longitudinal study aims to evaluate its impact on executive functions, attention, participation, and overall quality of life (QOL) in these patients.1,2,3

Methods We followed a cohort of 33 patients with DS treated with add-on FFA. The median duration of treatment was 44.5 months (range 2-82 months). We assessed both seizure-related and non-seizure-related QOL domains after initiating FFA treatment in 22 of the 33 patients (ages 4–30 years, M = 15.85, SD = 7.02). 23% of the participants underwent pre- and post-treatment cognitive assessments. Raw scores were standardized using normative data ($\mu = 100$; $\sigma = 15$) and analyzed qualitatively. Changes in standardized scores were examined in relation to treatment duration and patient age. Additionally, a semi-structured caregiver interview was conducted to collect insights into the patient's attention, social skills, and overall QOL.

Results

After FFA treatment, seventy-five percent of the patients had a significant reduction in seizure frequency. Of those who completed cognitive assessments, 60% showed significant improvements in standardized scores, while 40% with shorter treatment durations experienced mild declines. Caregiver interviews revealed statistically significant improvements in cognition, attention, speech, social skills, and both patient and caregiver QOL. Patients without side effects demonstrated greater behavioral improvements ($p = 0.019$) and better social communication ($p = 0.046$). Minor improvements were also observed in motor function.

Conclusions

The best outcome of this drug therapy was observed in seizure control. Fenfluramine treatment in DS patients is effective not only in managing seizures but also in improving overall quality of life. Long-term treatment showed more pronounced and statistically significant improvements across various domains. The excellent results in cognitive function are likely due to the reduced negative impact of seizures on this patient cohort.

ABSTRACTS

Topic: Cerebrovascular Disorders

EPNS25_1009 - Risk factors for recurrence in paedaitric arterial ischaemic stroke: a systematic review

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Objectives To conduct a systematic review to identify the incidence of recurrent paediatric arterial ischaemic stroke (PAIS) and which risk factors predict recurrence in children from 1 month to 18 years

Methods This review followed PRISMA guidelines. 6 electronic databases (CINAHL, EMBASE, MEDLINE, PsychINFO, Scopus and Web of Science) were searched for English-only articles published after the year 2000 with data on recurrent PAIS in children who had had at least one PAIS. Case reports, literature reviews, and expert opinions were excluded. Results were checked and compared to eligibility criteria. Data was collected for study characteristics and for recurrence in relation to vascular diagnosis. The included studies were assessed for their quality using the QUIPS tool.

Results Of the 7,627 studies, 11 were included. 6 were prospective, and 5 were retrospective. Two included only patients with only posterior PAIS while the remainder included anterior PAIS. 2,868 patients were included with median follow-up for 22 months, of whom 358 (15%; range 1-52%) had stroke recurrence, 182 (50.8%) with vasculopathy and 35 (9.8%) with cardiac disease. From 182 recurrent stroke patients with vasculopathy, vasculopathy type was not specified in the majority (n=150, 82.4%). Moyamoya disease was the most commonly reported vasculopathy type associated with recurrent PAIS (n=14, 7.7%), followed by vertebral dissection in posterior PAIS (n=6, 3.3%).

Conclusions Recurrence remains common after PAIS and the risk is of concern to families as well as physicians..Vasculopathy was the strongest associated risk factor for PAIS recurrence, requiring detailed diagnosis and early referral for optimum treatment. Vascular pathologies include dissection, often following trauma, focal cerebral arteriopathy following infection, and moyamoya, with a genetic basis but the type was not specified in the majority of studies. Recognising the role of vasculopathy and the associated causal factors may aid in prevention of developing PAIS recurrence.

ABSTRACTS

Topic: Epilepsy: Diagnosis and Investigations

EPNS25_1010 - Not all epileptic encephalopathy with stereotypic hand flapping are of Rett Syndrome:an infant with Heterozygous de novo pathogenic MEF2C mutation related dystonic epileptic encephalopathy diagnosed by R14 Rapid Genome Sequencing Pipeline

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Objectives

1. To raise awareness on Heterozygous de novo pathogenic MEF2C mutation associated with global developmental delay, motor coordination difficulties, seizures and intellectual disability. Only sixty individuals have been reported till 2018[1,2,3]
2. To share usefulness of Rapid Genome Sequencing R14 panel, the “Time Saver & Game Changer” in diagnosing rare monogenic condition specifically for immediate therapeutic implications in perinatal and early infanthood, epileptic encephalopathy, neuro-regression and future family planning.[5,6,7,8,9]

Methods

Case report after early input of multidisciplinary team approach on clinical management, genetic counseling, Early start of antiepileptic medications,

Results

A 6 -week- old with uneventful neonatal and antenatal background, presented with startle episodes, unusual asynchronous bilateral wandering & rolling eyes to different direction, poor eye contact, stiff truncal tone with normal peripheral tone & poor head control. Over the infant and toddler period, dystonia progresses with gradually evolving repetitive stereotypic flapping hand movement similar to Rett Syndrome, No other neurocutaneous features or microcephaly. Maternal Older brother with CHARGE syndrome, Dandy Walker Malformation passed away at Age 6. 1 older sister, Age 10 is now seizure free for 5 years. Due to video evidence, investigations for seizure panel & Tertiary Neurology team input was requested. Electroencephalogram (5 month) showed predominant left symmetrical focal burst 4-5Hz, 200 uV, superimposed upon moderate amount of 0.9-2Hz , 140 uV in posterior emphasis (Awake Phase).Vertex Sharp waves during light sleep: occasional sharp bursts of frequency 2-5Hz, 500uV, overall high amplitude over left parenchyma. Electrocardiogram normal and no cardiac issue. Non urgent MRI (Age 7 month) shows reduced corpus callosum but otherwise normal. USG abdomen (Age 12 month) after serial follow up confirmed bilateral undescended inguinal testes. Liver, Renal, Bone and Metabolic Panel including Ammonia, Biotinase are in normal range. Age 13 month, Rapid WGS, R14 panel as a special request , revealed this dystonic epileptic encephalopathy was most likely due to heterozygous de no vo pathogenic MEF2C variant while conservative WGS sent at 5 months was still pending. His left focal seizure is well controlled with Levetiracetam and Clobazam. Comprehensive and holistic care involving central and local neurology team, ophthalmology, occupational therapy, movement disorder team, neuro-disability team, and advanced care plan team input started as early as possible

Conclusions

Rapid Whole Genome Sequencing (R14 panel) is such a test to consider early for any neonatal, infantile epileptic encephalopathy. Not all the children with stereotypic hand flapping are autistic or of Rett Syndrome.

ABSTRACTS

Topic: Movement Disorders/ Cerebral Palsy

EPNS25_1011 - Molecular and Clinical Spectrum of the Epilepsy-Dyskinesia Syndromes – A Cross-Sectional Study of 563 Patients

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Objectives

Epilepsy-dyskinesia syndromes (EDS) are a heterogeneous group of neurological conditions characterized by co-occurrence of epilepsy and movement disorders. While over 100 genetic etiologies have been identified, the clinical spectrum, developmental and functional trajectories, and genotype-phenotype correlations remain poorly understood. This study aimed to systematically delineate the phenotypic and molecular spectrum of EDS in a large, international cohort, with a focus on movement disorder phenomenology, developmental and functional outcomes, and treatment responses.

Methods

A multicenter, cross-sectional study of 563 patients with genetically confirmed EDS was conducted across 30 centers in 22 countries (ClinicalTrials.gov ID NCT06585605). Cases were included based on pathogenic variants in 102 predefined genes associated with both epilepsy and movement disorders. Standardized clinical data were collected through a standardized survey completed by pediatric neurologists and movement disorder specialists, integrating retrospective medical record reviews and video-based assessments. Movement disorder phenomenologies were classified using expert consensus, and neurodevelopmental milestones, motor function, and treatment outcomes were systematically documented. Statistical analyses included pathway cluster and genotype-phenotype correlation analyses, and time-to-event modeling of developmental and functional outcomes. Treatment responses were evaluated through comparative analyses, identifying gene-specific therapeutic effects and adverse outcomes.

Results

Patients harbored pathogenic variants in 72 genes, with MECP2 (15.8%), ATP1A3 (7.3%), and PRRT2 (6.9%) as the most frequently affected. Epilepsy was present in 63.8% of cases, with 41.0% classified as developmental and epileptic encephalopathy. Movement disorders were highly diverse, with dystonia (33.8%), stereotypies (23.3%), and ataxia (15.8%) as the most common leading phenomenologies. Over 50.6% of patients had a mixed movement disorder. Significant gene-specific developmental and functional trajectories as well as phenotypic signatures and treatment responses were identified through unbiased comparative analyses.

Conclusions

This study represents the largest systematic, movement disorder-focused characterization of EDS to date, highlighting distinct phenotypic signatures, disease trajectories, and treatment responses. The findings underscore the need for expert movement disorder evaluation, as movement disorders contribute significantly to disease burden and treatment complexity. The study provides a framework for improved diagnosis, patient stratification, and targeted therapeutic approaches. Future longitudinal studies are needed to refine these insights and guide clinical trial readiness in this evolving field.

ABSTRACTS

Topic: Neurometabolic Disorders

EPNS25_1012 - Clinical and Neuropsychological Outcomes of Eladocagene Exuparvovec gene therapy in Paediatric Patients with Aromatic L-Amino Acid Decarboxylase Deficiency (AADCd): A Systematic Review

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Objectives
Aromatic L-amino acid decarboxylase deficiency (AADCd) is a rare severe neurometabolic disorder due to DDC gene mutations. The recently approved gene therapy with eladocagene exuparvovec increases AADC enzymatic activity, with good safety and tolerability profiles. This systematic review aims to explore the efficacy and clinical outcomes of gene therapy in pediatric AADCd patients.
Methods
Following the PRISMA protocol, a systematic search was conducted in PubMed, WOS, Cochrane, Scopus, EMBASE, ClinicalTrials.gov and EuClinicalTrials.eu. Original studies reporting clinical outcomes of gene therapy in AADCd patients aged 0-18 were included.
Results
Out of 483 records, 7 studies (2012–2022) met the inclusion criteria, involving 48 patients (54.2% M) with a mean age at therapy of 5.3 yrs. Most studies (85.7%) were single-arm with OCEBM-Level 3 evidence (100%). Eladocagene exuparvovec was delivered via one-time intracerebral infusion using an AAV2-hAADC vector. The putamen was the main infusion site (85.4%), with 14.6% receiving infusions in the substantia nigra (SN) and ventral tegmental area (VTA). Volumes ranged from 50 to 100 µL per hemisphere.
Motor function improved in all patients assessed by PDMS-2, dystonia resolved in 70% of cases, whereas oculogyric crises in all. Autonomic symptoms improved or resolved in 54.6%, sleep disturbances in 53.8%, gastrointestinal symptoms in 66.7%, and mood disturbances in 53%. Cognitive and language function (assessed in 18 patients) improved over time, with Bayley-III scores increasing at 1, 2 ($p<0.001$), and 5 years ($p=0.006$). FDOPA-PET revealed increased dopaminergic metabolism in 68.1% of cases. Biochemical analysis showed a significant rise in cerebrospinal fluid homovanillic acid (CSF-HVA) levels ($p<0.001$, $r=0.95$). Age at therapy negatively correlated with post-treatment HVA levels ($\rho=-0.439$, $p=0.028$), while vector volume positively correlated with HVA levels ($\rho=0.643$, $p<0.001$). CSF-HVA levels were higher in patients with SN+VTA than putaminal infusions ($p<0.001$); vector dose showed no significant difference ($p=0.760$). Finally, 64.6% of cases had transient postoperative dyskinesia.
Conclusions
Eladocagene exuparvovec proved effective in improving psychomotor function, autonomic stability and biomarkers, with no major safety concerns. Early intervention, dose, and infusion localization were key factors, though the low evidence quality highlights the need for further high-quality studies.

ABSTRACTS

Topic: Neuromuscular Disorders

EPNS25_1013 - Genetic Phenotype Relationship of Patients with Limb-Girdle Muscular Dystrophy

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Objectives Limb-girdle muscular dystrophy (LGMD) is an autosomal inherited neurogenetic disorder involving the proximal muscles of the hip and shoulder region with different subgroups. It is classified as autosomal dominant and autosomal recessive. Different symptoms and phenotypes can be observed in the same family members even with the same mutations. Although the disease is known to involve the prosimal hip and shoulder muscles, distal involvement is predominant in some types. It may present with different symptoms such as cardiac arrhythmias, cardiomyopathy, cardiac failure, respiratory failure, exercise intolerance, muscle cramps, contractures, facial and bulbar weakness, cataracts, cognitive retardation, ocular findings and epilepsy. LGMD progressively affects skeletal muscles in particular, often leading to muscle fiber loss with proximal muscle weakness. Creatine kinase (CK) is usually elevated, leading to histologically dystrophic changes in the muscles. Bipap device in patients with impaired respiratory function, beta-blockers can be applied to some patients with cardiac symptoms, nutrition should be adjusted according to the needs of the patient. Many potential treatments such as stem cell transplantation, exon skipping, gene therapies are being investigated. In this study, it was aimed to discuss the clinical findings, genetic analysis and disease course of patients diagnosed with LGMD in our clinic and the genetic phenotype relationship with the literature.

Methods The electronic files of patients with LGMD in the Pediatric Neurology Clinic of Bursa Uludag University were retrospectively analyzed. Demographic characteristics, symptoms and findings, CK levels, histopathologic results, echocardiography (ECHO) reports, rhythm holters, and genetic analysis were included as data.

Results Data of 11 patients with complete file information were evaluated. Male gender was found to be 64% (n:7) of the patients. The median age of the patients was 13 years (min:3 years max:20 years). The median follow-up period was 3 years (min:1 year max:10 years). Consanguinity was present in 77% (n:9) of the patients. The main presenting symptoms were frequent falls while walking, tiptoe walking, and difficulty in squatting and standing. All patients underwent genetic analysis and 81% (n:9) had an autosomal recessive (OR) genetic mutation. The median CK value at diagnosis was 1000 IU/L (min:60, max:7011).

Conclusions LGMD may occur with different mutations in different genes. In our series, we found a high rate of consanguinity and, accordingly, a higher proportion of LGMD patients with autosomal recessive inheritance. Calpain 3 gene mutation was the most common mutation.

ABSTRACTS

Topic: Cerebrovascular Disorders

EPNS25_1014 - Paediatric Cerebral Venous Thrombosis: Anticoagulation Timing, Imaging, and Outcomes

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Objectives
The study aimed to identify common presenting features and risk factors for CVST, evaluate the efficacy of treatments, especially direct oral anticoagulants (DOACs), and assess morbidity and mortality.

Methods
Patients under 18 with confirmed CVST were identified retrospectively from electronic records. Data included demographics, co-morbidities, presenting symptoms, diagnosis timing and method, and anticoagulants treatment (where applicable). Primary outcome was CVST-related mortality; secondary outcomes included neurological morbidity (neurodisability, epilepsy), raised intracranial pressure (ICP) identified through ophthalmological assessment, anticoagulation complications, recanalisation and residual thrombus on follow-up imaging.

Results
57 patients (mean age 7 years; 13 neonates; 24 females (42%), 33 males (58%)) were included. Primary symptoms: headache in 19 patients (33.3%), seizure in 9(15.8%), asymptomatic in 5(8.8%), fever in 5(8.77%). Diagnosed using CT venogram and MRI/V.
Risk factors: infections in 14(24.5%) including 8 (14%) with mastoiditis, malignancy in 11(19.3%), congenital heart disease in 6(10.5%), isolated CVST in 5(8.8%), thrombophilia in 3(5.25%). CVST was in a single location in 23(40%)of cases, most commonly the superior sagittal sinus. 14 had extracranial thrombi, 10(71%) in internal jugular veins.
Treatments: IV heparin in 17 patients(29.8%), subcutaneous low molecular weight heparin (LMWH) in 34(59.6%), no anticoagulation in 5(8.8%). Long-term: DOAC in 30 patients(52.6%), LMWH 26 (45.6%), warfarin in 1(1.8%). Median anticoagulation duration: 94 days.
There were 3 deaths (sepsis, malignancy, heart failure), none attributed to CVST or anticoagulation-related. Follow-up: 48 patients(84%) were followed up, 30 (75%) showed recanalisation, 22(55%) had residual thrombus. Raised ICP in 14(34%), 3(6%)needed ongoing management. 3(6%) had haemorrhagic venous infarcts, 4(8%) developed new epilepsy.

Conclusions
CVST can be safely treated with heparin and LMWH. DOACs are a safe and effective alternative, reducing the need for injections, bruising, and theraputic monitoring, with no bleeding risk in this cohort. No CVST-related mortality in our cohort. Follow-up imaging showed most patients achieved recanalisation. Routine follow-up MRI may not provide additional benefit clinically stable patients.

ABSTRACTS

Topic: Neuromuscular Disorders

EPNS25_1015 - Lack of efficacy of Disease-Modifying Treatments in SMA pediatric population reported at the French SMA Registry

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Objectives: Nusinersen (Ns, 2016) was the first disease-modifying treatment (DMT) approved for spinal muscular atrophy (SMA). Later, Onasemnogene abeparvovec gene therapy (GT, 2019) and Risdiplam (Rs, 2020) were also available. The aim of this study was to identify and describe the cohort of children who have shown a lack of efficacy (LoE) of DMT.

Methods: Patients included in the SMA-France Registry with age at treatment initiation < 18 years and with reported LoE of DMT were studied. Data analysed: DMT (in monotherapy (MT) or combined), SMA type, *SMN2* copy number, medical context at the age of arrest/change of DMT, reason, pre/post motor and respiratory function scales, need of respiratory/nutritional support, and presence of scoliosis or spinal surgery.

Results: As for 01/01/2025, 1052/1383(76%) patients included in the registry had received at least one DMT (603 pediatric). Out of 603 pediatric patients 406 received Ns, 239 Rs and 126 GT. DMT distribution in MT: 244 NsMT, 84 RsMT and 105 GTMT. The following combinations/changes were observed: 1)switch from Ns to Rs (139); 2) return to Ns after switching Ns to Rs (Ns-Rs-Ns) (8); 3)Ns 'bridge' before GT (13); 4)Rs add-on after GT (8); 5)Ns add-on after GT (2). LoE was reported in 8.7% patients. 3SMA1 (1.2%) with NsMT and 2SMA1 (1.9%) with GTMT experimented early LoE and died, without being able to exclude severe disease severity. 1SMA2 (1.2%) with RsMT discontinued two years after initiation. Within the 28% switches Ns-Rs, 5 were SMA1 who had an initial positive response in motor capacities with Ns but needed a gastrostomy at the end of the first year of life, experimenting bulbar improvement with Rs; the rest (10SMA1, 19SMA2, 5SMA3) switched after a mean of 3.3 years with Ns due to global LoE. Considering the 8 Ns-Rs-Ns, 7 switched due to technical difficulties, 1 of them due to LoE related with scoliosis aggravation. This patient and 5 more (2SMA1, 3SMA2, 1SMA3) returned to Ns due to LoE, mainly in motor upper-limbs capacity and 2 because of side effects. All the patients who received Rs or Ns add-on after GT were due to LoE (all SMA1), without significant improvement after the add-on.

Conclusions: LoE of the 3 DMT was unfrequently reported in this exhaustive national real-life registry. Preliminary results suggest that bulbar deterioration is a better and earlier marker of LoE in SMA1 infants while motor function is first affected in older and less severe phenotypes.

ABSTRACTS

Topic: Epilepsy: Diagnosis and Investigations

EPNS25_1016 - Phenotypic spectrum in individuals with chromosome15-long-arm-duplication-syndrome

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Objectives: We investigated the electroclinical phenotype of a novel cohort of patients with chromosome15-long-arm-duplication-syndrome (dup15q).

Methods: We collected previously unpublished patients with interstitial (intdup15) and isodicentric (idic15) duplication. Demographic, genetic and electro-clinical data were retrospectively reviewed, and long-term follow-up of comorbidities was evaluated.

Results: We identified 20 patients (9 males) with idic15 and 7 (3 males) with intdup15, with median age 11.5 years (range: 3-41 years) and 12 years (range: 4-32 years). For patients with idic15, epilepsy was diagnosed in 18/20 (90%) with a median onset of 7 years. Seizures at the onset were spasms in 8/18 (44%) of patients, generalized tonic-clonic in 5/18 (28%), focal seizures in 4/18 (22%). Syndromic classification was possible in 9/18 (50%): 4 West syndrome (WS), 5 Lennox-Gastaut syndromes (LGS), 1 evolving from WS. The remaining patients presented with a developmental and epileptic encephalopathy. Pharmaco-resistant epilepsy was present in 13/18 (72%). Beta-band rapid-rhythms (RR) was present in 18/20 (90%) patients, localization shifted from diffuse to anterior. Severe developmental delay/intellectual disability (DD/ID) was observed in 100%. Behavioral or psychiatric comorbidities were present in 18/20 (90%); autism spectrum disorder (ASD) or autistic features were the most prevalent (17/20; 85%). In contrast, 2/7 (29%) patients with intdup15 suffered from epilepsy with a onset of 10 and 15 years, respectively; a single patient developed LGS. A patient showed febrile seizures. DD/ID affected 100% of patients mostly affecting speech and cognition and to a lesser degree motor skills: mild in 2/7 (29%), moderate in other 29%, severe in 3/7 (42%). ASD or autistic features were diagnosed in all patients. EEGs were performed in all patients and RR was present in 5/7 (71%)

Conclusions: We outline the electroclinical features in both interstitial and isodicentric duplications of dup15q syndrome, a rare condition that can encompass drug-resistant epilepsy, ASD and DD/ID.

ABSTRACTS

Topic: Miscellaneous

EPNS25_1017 - Low vitamin D levels in children and adolescents with neurological manifestations

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Objectives

Vitamin D deficiency has been a global health problem for several years. The pleiotropic effect of this essential fat-soluble steroid nutrient was investigated in infectious, immunological, and chronic diseases, as well as metabolic conditions such as dyslipidemia and obesity. According to research, in children with migraine and pervasive developmental disorders, its beneficial neuroprotective influence is possible, while the data in children with epilepsy controversial. We aimed to investigate the association of potential warning neurological manifestations with lower vitamin D values in pediatric populations after early neurodevelopmental age.

Methods

A five-year (2019-2023) retrospective data survey was conducted in pediatric patients (1-18 years) with vitamin D values lower than recommended (below laboratory reference values). Patients were treated in our tertiary center due to neurological manifestations. Age, gender, calcium, phosphate, alkaline phosphatase values, and a lipid panel were evaluated. Descriptive statistics was used. The statistical difference was tested by Kruskal-Wallis test in SPSS Statistics 21.

Results

Among 2591 tested pediatric patients with lower vitamin D values, a total of 973 children, median age of 12.5 years (girls 58%), were treated in our center during the study period, mostly because of headache (44.5%), epilepsy (11.3%), syncope (7.4%), cerebral seizures (7.3%). Vitamin D values ranged from 12.7 to 70 nmol/L. Mild vitamin D deficiency (30-49 nmol/L) was detected in 46.5% of children, while 14.5% of our patients had severe vitamin D deficiency (<30 nmol/L). In 55% of children, lower values were observed in autumn and winter. A negative correlation of vitamin D values and triglycerides was found. Depending on the group of symptoms, lower values of vitamin D were determined in children with developmental disabilities. Lower vitamin D levels were found significantly in preschool children ($p = 0.002$) and puberty ($p = 0.028$).

Conclusions

Preliminary research data point to the importance of monitoring vitamin D levels in children with neurological manifestations after the first year of life, especially in puberty and those with neurocognitive deviations. A comprehensive assessment is essential during neurological and somatic developmental changes with rational approach in reaching health well-being, not laboratory values. The effect of vitamin D in children is reflected in the regulation of triglycerides.

ABSTRACTS

Topic: Epilepsy: Diagnosis and Investigations

EPNS25_1018 - Pediatric Epilepsy Surgery: Global Trends in Invasive Explorations

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Objectives

Invasive presurgical evaluation is essential in pediatric epilepsy surgery, guiding resections and disconnections and optimizing outcomes. This study provides an updated international overview of current practices in invasive explorations.

Methods

Group-level data were collected from representative centers worldwide on children and adolescents undergoing presurgical evaluation and epilepsy surgery in 2023.

Results

A total of 55 centers from 25 countries across 6 continents contributed data on 2,274 patients. Invasive explorations were performed in 21.5% of cases, with the highest rate in North America (32.6%). The primary indication was seizure onset localization (86.9%), followed by functional mapping of motor/sensory (17.4%) and language areas (15.0%). Among patients who underwent invasive explorations, 60.7% (highest in South America at 80.0%) had no detectable abnormalities on MRI. Stereoelectroencephalography (SEEG) was the predominant approach (20.1%, highest in North America at 29.0%), while subdural electrodes were rarely used (0.7%, highest in South America at 1.7%). A combination of depth and subdural electrodes was applied in 0.7% of cases, more frequently in North America (2.4%). SEEG-guided thermocoagulation was performed in 15.3% of cases,with the highest rate in Australia (25.0%). Following invasive explorations, 43.8% of patients did not proceed to resective or disconnective surgery, with the highest rate in Asia (65.4%). Complications related to electrode implantation occurred in 4.1% of cases.

Conclusions

This study provides a comprehensive overview of the global distribution of invasive presurgical explorations in pediatric epilepsy surgery. These findings highlight international trends, emerging advancements, and areas requiring further development.

ABSTRACTS

Topic: Movement Disorders/ Cerebral Palsy

EPNS25_1020 - FGF13: a new gene of paroxysmal dyskinesia with peculiar hypokinetic / hypotonic spells

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Paroxysmal dyskinesias (PxD) are a heterogeneous group of rare hyperkinetic movement disorders characterized by recurrent and sudden attacks of dystonic and/or choreic involuntary movements. The etiological diagnosis of PxD is established in around 50% of cases with currently known genes, so there are still causes to be identified.
Pathogenic variants of the *FGF13* gene are a rare cause of X-linked developmental encephalopathy and epilepsy (DEE90), reported in 9 patients. To date, they are not been implicated in PxD.

Objectives We report the first three patients presenting with PxD linked to missense variants in *FGF13* gene.

Methods The patients were collected through networking on rare diseases, including an ITHACA call for collaboration. *FGF13* variants were identified by genome or exome sequencing.

Results We propose a clinical and video presentation of three boys from three unrelated families harbouring missense variants in *FGF13* gene.
Kinesigenic and non kinesigenic PxD occurred in the first year of life (between 5 and 9 months) in children with normal development and neurological examination.
PxD have a peculiar clinical presentation: they start with a «classical» generalized hyperkinetic phase with choreo-dystonic movements lasting less than 1 minute. An hypokinetic phase lasting several minutes follows, associated with generalized hypotonia, clenched hands, aphasia and sometime with drooling. The children presented 2 to more than 60 episodes/day.
One of the children had nocturnal hyperkinetic spells, too.
MRI was normal and ictal EEG ruled out epileptic seizures in all patients.
Two patients shared the same p.(Ser8Leu) missense variant; interictal examination showed mild generalized dystonia and myoclonus, mild intellectual disability (ID) in one, no ID in the other.
One patient had a p.(Ala3Val) missense variant, he had a normal interictal examination and no ID. In this 3rd patient, the peculiar bi-phasic PxD episodes were observed in the 1st year of life; later on, PxD presented only with the hypokinetic/hypotonic phase.
Acetazolamide, carbamazepine, topiramate, levetiracetam, valproate, ketogenic diet were ineffective; partial improvement was observed with caffeine or methylphenidate treatment.

Conclusions We expanded the phenotype related to *FGF13* gene variants and we highlight a new gene presenting with PxD with peculiar hypokinetic/hypotonic spells.

ABSTRACTS

Topic: Neuromuscular Disorders

EPNS25_1021 - Prevalence and Clinical Characteristics of Paediatric-Onset Neuromuscular Disorders in Ireland

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Objectives

To date, there have been no Irish studies of the epidemiology of paediatric neuromuscular disorders and no Irish patient registries in paediatric onset neuromuscular disorders exist. This lack of data hampers our ability to plan health resources, plan for allocation of emerging therapeutics and clinical trial eligibility, and disease registry planning.

This study aims to describe the prevalence and clinical characteristics of paediatric onset neuromuscular disorders in the Irish population.

- Prevalence and distribution of paediatric neuromuscular disorders in the Irish population
- Neuromuscular diseases will be categorised into those of spinal cord, motor neuron, neuropathies, neuromuscular junction disorders and muscle disorders.
- Clinical characteristics will be compared to known international studies of disease characteristics and natural history studies.
- Proposals and recommendations about the planning of health resources, allocation of emerging therapeutics and clinical trial eligibility, and disease registries

Methods

There are three main clinics in Ireland for the diagnosis and management of paediatric neuromuscular disorders: the Central Remedial Clinic in Dublin, Children's Health Ireland (CHI) at Tallaght and Enable Ireland in Cork and the Neuromuscular Respiratory Clinic in CHI at Temple Street. Informed consent was completed for all participants, and participants' assent forms were completed. The patients' lists for the clinics were reviewed to confirm the diagnosis and collect relevant clinical and demographic data. Data collection was completed on the REDCap platform.

Results

In total, we had 477 patients on the lists, 83 in CHI at Tallaght, 92 in the respiratory clinic at CHI at Temple Street, and 302 in the Central Remedial Clinic. Not all these patients met our inclusion criteria, and some were duplicates. 51 patients in the CRC and 4 in Tallaght reached 18 years of age before they were approached by the research team for consenting to the study and were excluded.

The number of patients included in this analysis is 284. 183 patients from the CRC, 67 patients from CHI at Tallaght and 34 patients from CHI at Temple Street. This number will increase when the prevalence data on patients attending the neuromuscular clinic in Enable Ireland, Cork.

Conclusions

This is the first study on the prevalence and clinical characteristics of paediatric-onset neuromuscular disorders in Ireland. The prevalence data will be based on recent national census data.

ABSTRACTS

Topic: Neurogenetics

EPNS25_1026 - Functional Characterization of a Novel Familial DHDDS Variant with Incomplete Penetrance Associated with Drug-resistant Epilepsy

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Objectives

The dehydrodolichyl diphosphate synthase (DHDDS) gene encodes for the catalytic subunit of a key enzyme for the synthesis of dolichol and dolichol-dependent protein glycosylation. To date, 45 patients with 12 different DHDDS variants have been reported. We present the case of a patient and his family who are carriers of a DHDDS variant classified as of uncertain significance (VUS). Our main goal was to assess this variant's pathogenicity, and our secondary objective was to describe our patient's phenotype.

Methods

We retrospectively collected data from the family members and performed electron microscopic analysis of our patient's skin fibroblasts and a functional yeast-based complementation assay of the DHDDS variant.

Results

Our patient is a 7-year-old boy with an unremarkable perinatal history and later speech delay. At 4 years of age, he developed epilepsy with eyelid myoclonia, and tried several anti-seizure medications without clear benefit. Finally, acetazolamide was added to the ongoing therapy, with a modest clinical improvement and a significant electroencephalographic response. Brain magnetic resonance imaging and intellectual profile were normal. An epilepsy genetic panel revealed the frameshift DHDDS variant c.874del in heterozygosity, not previously reported and classified as a VUS with unclear effect on the gene transcript. Segregation analysis found the same variant in the mother and maternal grandmother, who are asymptomatic, and in the younger brother, who had psychomotor retardation, attention deficit, and autistic features. Ultrastructural analysis of fibroblasts showed only minor changes. The yeast-based complementation assay of the DHDDS variant demonstrated its role in inhibiting cell growth.

Conclusions

In this study, we describe a novel heterozygous DHDDS variant with incomplete penetrance and successfully demonstrate its pathogenicity through functional studies. Unlike most reported DHDDS cases, our proband and his brother exhibit a milder clinical phenotype, as suggested by ultrastructural analysis of fibroblasts. This may be due to the reduced pathogenicity of the specific gene variant. Finally, we are the first to describe the successful use of acetazolamide in the treatment of DHDDS-related drug-resistant epilepsy.

ABSTRACTS

Topic: Neurogenetics

EPNS25_1027 - The cognitive changes in children with microduplication of chromosome 16

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Objectives: Microduplication syndromes are a heterogeneous group of genetic etiology characterized by changes in the number of copies of a section of chromosomes. They are most often characterized by impaired cognitive functions, delayed speech development and stunted growth, various kinds of stigmas, dysmorphisms and malformations affecting a wide range of systems and organs.

The aim of the study was to determine the developmental features of children with the microduplications of 16 chromosomes. The study was conducted at the Central Children's Hospital in Crimea for 15 years.

Methods: The study included 100 patients aged 7 to 17 years with the microduplications of chromosome 16. The number of boys – 58 (51,7%) prevailed over the number of girls – 32 (48,3%). The children were examined by laboratory, instrumental and genetic methods. Various methods are used to determine microduplications of chromosome 16 by FISH (fluorescent in situ hybridization) and CHMA (chromosomal micromatrix analysis) on DNA microarrays. The following forms the microduplication of chromosome 16 were found in the study: 16p11.2 dup – 46 (46%), 16q22.1 dup – 34 (34%), 16q24.3 dup – 20 (20%).

Results: In our study, microduplication of 16p11.2 is associated with dysmorphic features autism (20%), ID (16%), CNS disorders (7%) and schizophrenia (3%). Background EEG of children with impaired receptive speech is characterized by a decrease in the amplitude of the alpha rhythm of the parietal and occipital leads. 16q22.1 duplication correlates with ID (13%), epilepsy (12%) and learning disabilities (4%), micrognathia (3%), microdentia (2%). The impaired receptive speech in children with 16q22.1 dup demonstrated on EEG the increased amplitude of the theta rhythm in the frontal and temporal zones. In the group of children with16q24.3 dup and sensory alexia, there is no resynchronization of alpha and beta activity in the sensorimotor zones, which is observed in typically developing children during the perception of words in correct sentences.

Conclusions: In conclusion, it is important to note that the microduplication syndromes that have been described and recognized in recent years with the aim of summarizing their main characteristics and chromosomal regions involved. Detected EEG features in children with microduplications and speech disorders are important for the differential diagnosis of diseases with cognitive dysfunction.

ABSTRACTS

Topic: Fetal and Neonatal Neurology

EPNS25_1030 - Long term neurological outcomes in survivors of foetomaternal haemorrhage: A systematic review

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Objectives Foetomaternal haemorrhage (FMH) is an obstetric emergency which, if acute and massive can lead to stillbirth or neurological sequelae in survivors, but data is scarce. A systematic review was undertaken to evaluate reported long-term neurological outcomes on neonates after foetomaternal haemorrhage and their predictors.

Methods Publications were identified via EMBASE, PsycINFO, PubMed, Web of Science, Scopus, OVID and the Cochrane library, using terms relating to foetomaternal haemorrhage and neurological outcomes. Papers were screened by 2 reviewers, initially by titles and abstract, then by full texts. Included studies focused only on survivors with a minimum of 12 months follow up. Data were extracted and a binary logistic regression was performed to compare clinical and laboratory variables in poor and good outcome patients. Studies were quality assessed via the CASP or Joanna Briggs criteria for case reports.

Results Seventeen studies were included, comprising 6 retrospective case series with outcomes: (4 only reporting FMH (n=31, 18, 11, 6), and 2 focusing on foetal (FMH in 1/127 cases eligible for in utero transfusion) or neonatal (FMH in 16/20 cases) anaemia. Five presented individual laboratory data, and were included in the individual data analysis, alongside 11 case reports. Of 63 cases with median long-term follow up of 24 (12-112) months, 41 (65%) demonstrated favourable outcome and 22 with poor outcome 35% (15 (24%) had cerebral palsy and 7 (11%) had other adverse cognitive-behavioural sequelae). Apgar score at 1 minute (OR=0.79; [95% CI 0.61-0.99]) and low neonatal haemoglobin (OR=0.97 [95% CI 0.93-1.0]) independently predicted poor outcome. Transfusion in the neonatal period was mentioned in 20 cases.

Conclusions This systematic review suggests that haemoglobin levels and Apgar 1 minute scores are associated with neurological outcome. However, the available data lacks clarity on the timing of neonatal haemoglobin measurements and transfusions. A recent matched case-control retrospective study by Pettway et al (PMID:39532114), published after this search, reviewed the developmental and cognitive outcomes of 260 neonates surviving FMH in comparison to those not exposed. Interestingly, of 137 with clinically significant FMH, 80 were intrauterine deaths while 57 were transfused as neonates; four died in the neonatal period but there was no observed difference in neurodevelopmental diagnoses in the 53 long term survivors in comparison to the matched unexposed infants. Longer follow up is needed for survivors of FMH. This review highlights the need for more focused, prospective studies so that appropriate guidelines to improve outcome can be developed.

ABSTRACTS

Topic: Infectious and Inflammatory Diseases/ Neuroimmunology

EPNS25_1031 - Immunomodulatory therapy in management of Paediatric autoimmune neuropsychiatric disorder associated with streptococcal infection (PANDAS)

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Objectives Paediatric acute onset neuropsychiatric disorder associated with streptococcal infection (PANDAS) is a controversial diagnosis and management of these patients is debated. The primary treatment is antibiotic therapy. It is not always sufficient, especially in patients with recurrent symptoms. We investigated the effect of the immunomodulatory therapy, i.e. non-steroidal anti-inflammatory drugs (NSAID) and oral corticosteroids.

Methods This is an observational study on paediatric patients evaluated at our clinic between 2023 and 2024. A cohort of 11 patients with persisting symptoms after antibiotics were treated with immunomodulatory therapy. Patients with mild symptoms were treated with ibuprofen (10mg/kg/dose 3 times a day, 7 days), patients with moderate symptoms were treated with oral Prednisone (1mg/kg for 5 days).

Results Patients were 4-13 years old. One patient was diagnosed with Sydenham chorea and rheumatic fever. 9 patients were treated with NSAID: in 2/11 patients the effect was abrupt within 1 week, in 2/9 children the symptoms resolved within 4 weeks, in 4/9 children NSAD therapy was followed by oral Prednison, however their disorder lasted several months. 1/9 patient did not show any improvement on NSAID and did not tolerate the Prednisone treatment. 1 patient (with a history of several preceding streptococcal infection and neuropsychiatric disorder lasting for several months) was treated by oral Prednisone from the start, with 80% improvement intensity and frequency of the within 1 week, but persistent mild symptoms, despite additional oral Prednisone pulse. The patient with Sydenham chorea was treated by concurrent NSAD and Prednisone, the symptoms decreased significantly in 2 weeks and resolved in 10 months. Complete resolution was observed in 8/11 children. 3/11 children reported previous episode of neuropsychiatric impairment associated with streptococcal infection. The symptom duration was significantly shorter when immunomodulatory treatment was added to antibiotic treatment.

Conclusions Our observations support the data revealing benefits of immunomodulatory therapy such as NSAID and oral corticosteroids in patient with PANDAS. Also, our results show that children with acute onset of complex neuropsychiatric disorder should be screened for a history or ongoing streptococcal infection and receive adequate therapy.

ABSTRACTS

Topic: Neuromuscular Disorders

EPNS25_1033 - Single Sural Nerve Response: A Reliable and Practical Method for Diagnosis of Diabetic Peripheral Neuropathy in Children with Type 1 Diabetes

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Objectives

Type 1 diabetes mellitus (T1DM) is a significant global health issue, particularly due to its association with microvascular complications such as diabetic peripheral neuropathy (DPN). Sensory nerves in the lower extremities are primarily affected by DPN, with the sural nerve being particularly impacted. The conventional method for diagnosing DPN involves evaluating four motor and four sensory nerves in the upper and lower extremities. Motor tests use dual-point high-intensity stimulation to elicit a compound muscle action potential, while sensory tests apply a single, lower-intensity stimulus to assess depolarized nerve fibers. The aim of this study was to define the efficacy of using a single sural nerve response for diagnosis of DPN in pediatric T1DM patients compared to conventional method.

Methods

This retrospective study analyzed data from 242 patients, including 204 with T1DM and 38 controls. For T1DM patients, we evaluated risk factors for DPN include age, gender, Hemoglobin A1c levels, lipid parameters, and body mass index. Nerve conduction studies were evaluated in both groups.

Results

The examination of a single sural nerve achieved a sensitivity of 83.3% and a specificity of 97.2% in diagnosing DPN. Multivariate logistic regression analysis identified HbA1c level as the only significant predictor of DPN. Comparison of sural nerve responses between non-neuropathic T1DM patients and the control group indicated pre-electrophysiological nerve abnormalities within the T1DM cohort.

Conclusions

Evaluation of a single sural nerve response in pediatric T1DM patients can replace conventional nerve studies. The study supports the use of point-of-care devices for DPN detection, potentially simplifying and enhancing clinical practices.

ABSTRACTS

Topic: Neurometabolic Disorders

EPNS25_1036 - A Case of Adrenoleukodystrophy in a 20-month old Filipino Male

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Objectives

This paper aims to investigate the clinical presentation and diagnostic process of adrenoleukodystrophy in a Filipino patient, exploring the challenges in identifying and diagnosing the disease in a resource-limited setting and to assess the availability and effectiveness of treatment options for adrenoleukodystrophy in the Philippines, including both medical and genetic counseling approaches, and the role of early diagnosis in improving patient outcomes.

Methods

In this case report, a comprehensive approach that included detailed patient history, clinical examinations, diagnostic imaging, laboratory tests, and genetic analysis was used to evaluate the presentation, diagnosis, and management of adrenoleukodystrophy in a Filipino patient.

Results

A 20 month old male was initially seen at the Outpatient Department due to stiffening of extremities and regression of milestones. Adrenoleukodystrophy was considered in the patient and referrals were made to Neurology and Genetics. However, the patient was again seen at the Emergency Room due to persistence of stiffening and increased irritability. A 2H VEEG was done showing intermittent focal slowing seen coming from both occipital regions. The patient was placed on seizure precaution and workup was done. Cortisol and ACTH levels were within normal. A very long chain fatty acid test was ordered to be done as an outpatient and was discharged. The patient was again seen at the outpatient department with noted elevated very long chain fatty acid tests. The patient was advised palliative care.

Conclusions

Adrenoleukodystrophy is a complex genetic disorder affecting the nervous system and adrenal function. While there still is no cure for the disease, stem cell transplantation and ongoing research offer hope for slowing or halting disease progression. In our case, the child had advanced disease, hence only symptomatic management and palliative care was possible. Since there is also a lack of laboratory facilities here, we could not run the very long chain fatty acid test sooner, causing delays in diagnosis. Since developmental regression is a hallmark of ALD, we suggest that pediatric patients with unexplained developmental delay should undergo neurological follow-up to explore possible ALD-related issues since early diagnosis and prompt intervention are crucial for achieving the best possible prognosis

ABSTRACTS

Topic: Neurorehabiltation

EPNS25_1040 - A Neuropediatric rehabilition clinic as non University training centre for rare and common neuropediatric acute and chronic diseases

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Objectives

The very few neuropediatric rehabilitation clinics in Germany offer multiple chances of training for pediatric residents and those in further neuropediatric training to come in close contact to the very rare and very common neurological diseases, that keep the SPZ and neuropediatric ambulance at University clinics and all the others very busy and in high demand. Main aspects of neuropediatric training happen there quasi on the go.

Methods

Analyzing the status quo from the given example in Brandenburg an der Havel in relation to experience in the other few places.

Results

By analyzing the daily tasks and the complexity of aspects of the main disease, in stadiums of ongoing diagnosis or treatment measures and procedures, of social interactions and the focus on the broadening of daily-life participation for children and young adults with more or less complex disabilities, a neuropediatric rehabilitation clinic grows into another kind of research lab, training center, post-acute hospital.

Conclusions

A network of acute clinics and post-acute clinics could provide a better outcome for the training and personal, individual development of coming to be neuropediatric physicians and medical professionals, including therapists. This network would benefit from a formal structural, financial and professional backup, like a structural program for (neuro) pediatric training between the different players like Universities, SPZ, other acute clinics and rehabilitation centers.

ABSTRACTS

Topic: Neurorehabiltation

EPNS25_1042 - Start of project FAST 103 in Uzbekistan

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Objectives : The FAST 103 project is an important part of ESO. For many years, young children have been taught how to recognize the first signs of stroke in adults.

Methods: For 5 weeks, children were taught in kindergartens in the city of Tashkent in Uzbekistan. Materials (books, booklets, posters with FAST superheroes) were used throughout the training. During the training, the children learned to recognize the first signs of a stroke (slanted face -F, arm stiffness - A, loss of speech - S, and that you need to act quickly -time- T)

Results : The training was conducted for children from 3 to 6 years old . More than 750 children have been trained. Among them, 60% were boys and 40% were girls who completed 5 weeks of training in a playful way with FAST superheroes. After the training, about 35% of the trained children were able to reach 103 and call an ambulance for their grandparents. In turn, the medical staff was able to provide the necessary assistance in a timely manner.

Conclusions: Based on the above research, it is worth noting that the FAST103 project has a significant role in preventing the prevention and timely assistance to the elderly with the help of children, and it also helps to train children to recognize the first signs of stroke, which can help increase productivity in the country.

ABSTRACTS

Topic: Neuromuscular Disorders

EPNS25_1046 - Neurodevelopmental and mental disorders in individuals with Duchenne muscular dystrophy: a cohort study

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Objectives: Over the last few years there has been increasing attention to the involvement of central nervous system in Duchenne muscular dystrophy. The aim of this study was to assess the spectrum of neurodevelopmental and mental disorders and possible required intervention in our cohort of 264 boys and adults with Duchenne muscular dystrophy

Methods: We retrospectively analyzed clinical notes and psychological assessments, including routinely performed cognitive tests and clinical observations. Intelligence quotients and site of mutations were also noted.

Results: 103/264 individuals (39%) had symptoms compatible with one of the following diagnosis: Attention deficit and Hyperactivity disorder (ADHD) (n=26), Autism spectrum disorder (ASD) (n=11), Depressive mood/Disruptive mood dysregulation disorder (n=27), Anxiety disorder (n=17), Obsessive-compulsive disorder (n=2), Psychosis Risk Syndrome (n=7), thirteen had a more complex phenotype. ADHD and ASD were more frequent in infancy, emotional dysregulation during early adolescence and psychosis and more severe phobias in older boys and adults. The risk of developing these disorders did not increase with the concomitant involvement of the dystrophin isoforms Dp140 and Dp71. Pharmacological treatment was suggested for 48 individuals but was started only in 24, as it was refused by the remaining 24 families

Conclusions: Our findings confirm that neurodevelopmental and mental disorders are common in Duchenne and are likely to have a multifactorial nature. These findings support the need for disease specific assessments, and the need to increase awareness of the possible behavioral and social difficulties among families and health care professionals

ABSTRACTS

Topic: Fetal and Neonatal Neurology

EPNS25_1048 - Postnatal outcome of fetuses with small head circumference: retrospective analysis of a single-center cohort

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Objectives

The antenatal discovery of a small head circumference (HC) is a major red flag that leads to multiple investigations (amniocentesis, fetal MRI) to detect microcephaly as early as possible. This single-center retrospective study conducted from 2015 to 2024 aims to i) determine the proportion of postnatal microcephalies, ii) explore the associated genetic profiles, and iii) identify predictive antenatal factors.

Methods

The cohort includes 45 pregnancies monitored for small head circumference, defined as a head circumference below the 3rd percentile (French College of Fetal Ultrasound) and below the 1st percentile (WHO and INTERGROWTH-21). The median follow-up duration was 3.5 years (range: 0.25 - 9 years).

Results

Among the 45 fetuses followed, 35 (70%) exhibited a small head circumference in the second trimester, and 15 (30%) in the third trimester. Furthermore, 40% of the fetuses had intrauterine growth restriction (IUGR), often associated with a small head circumference detected in the third trimester. Amniocentesis was performed in 64% of the pregnancies, revealing a 7% rate of genomic imbalance, while brain MRIs were conducted for 70% of the fetuses, with 30% showing abnormalities. Eight medical terminations of pregnancy were performed due to various genetic anomalies and syndromes, while two fetal deaths and three neonatal deaths were recorded.

Postnatally, 19 newborns (60%) had confirmed microcephaly, with 40% associated with IUGR. Among them, 40% had an identified cause, primarily genetic, including mutations in the FBX011, MCPH1, ZNF292, SMAD6, and IGFR1 genes, or a Feingold syndrome diagnosis. The only predictive factor for postnatal microcephaly in this cohort appears to be a decrease in head circumference during follow-up.

Conclusions

Antennatal small head circumference is an early indicator of microcephaly in over 60% of cases. However, a significant proportion of genetic causes remains unidentified by standard prenatal testing, underscoring the importance of exome sequencing in these situations.

ABSTRACTS

Topic: Epilepsy: Medical and Surgical treatment

EPNS25_1049 - Efficacy and Safety of the Ketogenic Diet in Young Infants of less than 3 Months of Age

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Objectives

The ketogenic diet (KD) was previously not recommended for children under 2 years due to concerns about developmental impact and potential nutritional deficiencies. However, recent evidence, particularly focusing on infants with West syndrome, demonstrates the effectiveness and safety of the KD. Nonetheless, there is limited information on younger infants, especially those less than 3 months old. Therefore, this study aimed to share the experience of using the KD in such patients.

Methods

A retrospective chart review was conducted, including patients who started the KD before the age of 3 months at Severance Children's Hospital between 2009 and 2020. Seizure control efficacy was assessed by collecting seizure frequency data from the previous month. Patients with a ≥ 50% reduction in seizures were considered responders, while non-responders included those who discontinued the KD due to poor compliance, adverse events, or the need for epilepsy surgery.

Results

Out of 26 patients who started the KD before 3 months of age, 22 patients were included in the efficacy assessment after 3 months, with a response rate of 72.7%. After 6 months, 18 patients were assessed, and the response rate was 72.2%. When comparing clinical characteristics, Ohtahara syndrome showed a significant difference in response to the KD ($p = 0.010$), although this difference was not statistically significant when controlled for etiology. Adverse events leading to KD discontinuation were observed in 3 patients (11.5%) within 6 months, including hypoglycemia, aspiration pneumonia, and significant weight loss due to recurrent diarrhea.

Conclusions

The ketogenic diet can be effectively and tolerably administered to young infants less than 3 months old.

ABSTRACTS

Topic: Basic Science

EPNS25_1054 - Visual Disturbances Following Mild Head Trauma in a Pediatric Patient - Atypical Presentation of Glutaric Acidemia Type I

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Objectives

Glutaric Acidemia Type I is a rare autosomal recessive metabolic disorder resulting from mutations in the GCDH gene, which encodes glutaryl-CoA dehydrogenase—an essential enzyme in the catabolism of lysine and tryptophan. Enzyme deficiency leads to the accumulation of neurotoxic metabolites, primarily glutaric acid and 3-hydroxyglutaric acid, which can cause significant neurological impairment. Although GA1 typically manifests in early childhood, late-onset cases have been documented beyond six years of age and even during adolescence, with some individuals remaining asymptomatic.

Methods

We report the case of a previously healthy 9-year-old girl who was diagnosed with Glutaric Acidemia Type I (GA1).

Results

Patient presented to the Emergency Department with a 10-day history of subjective visual disturbances in her right eye, occurring after a minor head trauma sustained during judo practice. Neurological and ophthalmological examinations revealed homonymous hemianopsia on the right side and macrocephaly (head circumference >99th percentile, +3.3 standard deviations). While suspected macrocephaly had been noted in infancy, no further investigations had been pursued at that time. By the following day of hospitalization, the visual disturbances spontaneously resolved, and the patient remained asymptomatic. Brain MRI with spectroscopy revealed extensive white matter demyelination in the periventricular and subcortical regions of the frontal, parietal, and occipital lobes. Additional findings included bilateral temporal lobe polymicrogyria and arachnoid cysts. Metabolic testing showed significantly elevated urinary levels of glutaric acid, 3-hydroxyglutaric acid, 2-hydroxyglutaric acid, and alpha-ketoglutaric acid. Genetic analysis confirmed two pathogenic variants in the GCDH gene, establishing the diagnosis of GA1. The patient was advised to follow a dietary restriction of lysine-containing foods.

Conclusions

This case presents an unusual manifestation of Glutaric Acidemia Type I (GA1) in a pediatric patient with transient visual disturbances following minor head trauma. It underscores the heterogeneity of clinical presentations in metabolic disorders and emphasizes the importance of timely diagnosis, which enables the implementation of targeted dietary interventions to potentially mitigate further neurological decline.

ABSTRACTS

Topic: Infectious and Inflammatory Diseases/ Neuroimmunology

EPNS25_1059 - Caspr2 Antibodies and Glomerulonephritis: Exploring a Potential Immunological Link in Morvan Syndrome

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Objectives

Morvan Syndrome is a rare autoimmune disorder affecting the peripheral, central, and autonomic nervous system, primarily associated with antibodies against Caspr2 and LGI1. While traditionally considered an adult disease, increasing evidence suggests that Morvan Syndrome also occurs in children, where it may be underdiagnosed due to its variable presentation. Recent reports indicate a possible link between Caspr2 antibodies and renal involvement, particularly glomerulonephritis. This study aims to investigate a potential causal relationship by analyzing Caspr2 expression in kidney tissue and assessing its role in disease pathophysiology.

Methods

We conducted immunohistochemical analyses of kidney biopsies from an index pediatric Morvan Syndrome patient with glomerulonephritis, alongside control samples (healthy individuals and patients with focal-segmental glomerulosclerosis, FSGS, or Wilms tumors). Immunofluorescence studies were performed using murine brain and kidney tissues incubated with patient-derived serum and Caspr2 antibodies. RNA sequencing was applied to evaluate Caspr2 expression in renal tissue. Additionally, a literature review and further patient recruitment were undertaken to systematically assess Caspr2-associated nephropathy.

Results

Preliminary findings suggest Caspr2 expression in renal tissue, supporting the hypothesis of an autoimmune response contributing to glomerular damage. The index patient presented with proteinuria, hypertension, and biopsy-confirmed FSGS, showing a marked response to immunotherapy (IVIG, Rituximab). A review of published cases identified four additional patients with Caspr2 antibodies and renal involvement, suggesting that this association may be more common than previously assumed.

Conclusions

Our study provides novel evidence for a potential immunopathogenic role of Caspr2 antibodies in glomerulonephritis, possibly through direct autoimmune mechanisms or secondary autonomic dysregulation. If confirmed, these findings could significantly impact the diagnosis of Morvan Syndrome by prompting early renal screening in affected patients. Additionally, recognizing renal involvement as part of the Morvan spectrum may influence treatment strategies, emphasizing the importance of early immunomodulatory therapy to prevent long-term organ damage. Further studies are needed to establish the exact pathomechanism and clinical implications of Caspr2-related nephropathy.

ABSTRACTS

Topic: Miscellaneous

EPNS25_1062 - Spinal Ultrasound as a Tool for Localizing Cauda Fibers in Older Children with Suspected Tight Filum

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Objectives

Our clinic specializes in dysraphic disorders and pediatric urology, with a particular focus on continence issues. The potential presence of occult spina bifida is often considered in these cases. MRI has diagnostic value, but a tight filum terminale may not always be definitively identified. The decision for surgical intervention is challenging and would benefit from additional diagnostic tools to improve the preoperative assessment of tethered cord syndrome.

Methods

Patients suspected of having tethered cord syndrome undergo interdisciplinary evaluation by a dysraphism board comprising neurosurgery, pediatric neurology, and pediatric urology experts. Electrophysiological testing, specifically evoked somatosensory potentials (SEPs), is routinely performed. Additionally, alternative imaging approaches have been explored, including prone MRI, which has been limited by motion artifacts. Based on clinical experience, we investigated the feasibility of using segmental ultrasound in a kyphotic posture ("playing cat" position) with a 10 MHz longitudinal transducer to assess the ventral shift of cauda fibers in prepubertal children.

Results

Our observations indicate that lumbar segmental ultrasound in the kyphotic position allows visualization of the cauda fibers in children aged 3 to 11 years in 30-80% of cases, depending on factors such as adherence, mobility, weight, and age. This technique provides a potentially reliable, non-invasive, and inexpensive bedside diagnostic tool for assessing tethered cord syndrome.

Conclusion

Segmental ultrasound of the lumbar spine in prepubertal patients represents a promising alternative for evaluating surgical indications in cases of severe constipation where tethered cord syndrome is suspected. A larger standardized study is planned to assess its utility in a broader cohort of unaffected children, aiming to establish its role in guiding the decision for invasive filum incision.

ABSTRACTS

Topic: Epilepsy: Diagnosis and Investigations

EPNS25_1064 - THE CLINICAL UTILITY OF HOME-VIDEO AMBULATORY EEG IN CHILDHOOD

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Objectives

To evaluate the clinical utility of home-video ambulatory electroencephalogram (HVAEEG) in children.

Methods

Retrospective data from 280 referrals for a paediatric HVAEEG were reviewed, since it's introduction in March 2019 to November 2024. Information was gathered on various aspects of the referral process, the characteristics of the children referred, as well as recording information for the test. Clinical utility was calculated as the percentage of cases in which the investigation provided useful information with respect to the question asked in the test. Deprivation stratification analysis was also performed using the Scottish Index of Multiple Deprivation (SIMD 2020).

Results

The HVAEEG was found to be useful in 73.93% of patients and there was a change of clinical management from the test in 52.86% of patients. A clinical question was asked in 98.21% of patients, and it was answered in 72% of those. There were 31 (11.07%) new diagnosis of epilepsy after the use of the test. Out of the 280 patients, 157 (56.07%) had at least another neuropsychiatric diagnosis, with learning disability/developmental delay being the most frequent (93 cases, 33.21%), followed by autism spectrum disorder (39 cases, 13.39%), attention deficit and hyperactivity disorder (18 cases, 6.43%) and anxiety (7 cases, 2.5%). The test was not useful in 26.07% of cases and the most common reason was failure to capture an event (45 cases, 16.07%), followed by technical issues (10 cases, 3.57%), recording of an atypical event only and not the event in question (9 cases, 3.21%) and the procedure was not tolerated in only 9 cases (3.21%).

Conclusions

The HVAEEG system was found to be useful in almost three fourths of cases. Failure to capture events appears to be the most significant limiting factor, so performing this test when the frequency of events is higher is an important consideration.

Given it is effective as well as convenient, accessible, and lower cost than inpatient EEG monitoring, we believe HVAEEG should be considered for paediatric patients.

ABSTRACTS

Topic: Neuromuscular Disorders

EPNS25_1065 - Mexiletine Paediatric Investigation Plan, PIP4 Study: Efficacy findings in children aged 0–<18 years with myotonia

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Objectives

The PIP explores mexiletine use in children with myotonic dystrophy (DM) or non-dystrophic myotonia (NDM). Here, efficacy findings in PIP4 are presented.

Methods

PIP4 (EudraCT2019-003757-28): 12-week, open-label, non-comparative study of mexiletine in sequential cohorts. Cohort 1: 12–<18y; Cohort 2: 6–<12y. Study design: 4 weeks' screening; 4 weeks' mexiletine 62, 83 or 167mg once-daily titrated to maximum 3-times-daily; 4 weeks' maintenance (best-tolerated dose). Efficacy endpoints (baseline to end of study): relaxation time measured by handgrip dynamometer; patient-reported visual–analogue scale [VAS]0–100 scores [stiffness, pain, weakness/fatigue]); Myotonia Behavioural Scale (MBS); Pediatric Quality of Life Inventory™(PedsQL); Clinical Global Impression (CGI).

Results

PIP4 Cohort 1 (N=7): 2 with DM1, 5 with NDM (mean age 13y; 4 female; max dose range 186–500mg). Cohort 2 N=5 with NDM (mean age 8y; 3 female; max dose range 186–249mg).

Mexiletine treatment improved relaxation time (all cohorts) PIP4 VAS scores (n=10): stiffness, 33.7–78.5% improvement; pain improvements, 85.4% (Cohort 1); 61.3% (combined cohort); weakness/fatigue, 43.2–60.2% improvements. MBS scores improved (n=8; 67%), were stable (n=3; 25%) or worsened (n=1; 8%). Overall, MBS scores decreased across cohorts. Improvements were observed for PedsQL, especially physical domain (most impacted at baseline) and among older children. PedsQL neuromuscular scores also improved, especially in Cohort 1. For CGI, mexiletine was rated very efficient (25%), good (58%), fair (17%) (all cohorts).

Conclusions

PIP4 confirms that mexiletine is efficacious treatment for myotonia in children aged 6-<18 years. PIP4 completers are being followed for ≥2 years in PIP7.

ABSTRACTS

Topic: Epilepsy: Medical and Surgical treatment

EPNS25_1067 - Long-term Experience of VNS Therapy in Children

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Objectives: Evaluate effectiveness of Vagus Nerve Stimulation Therapy (VNS) at 24 months in neuro implant naive (NIN) patients < 18 years of age enrolled in the prospective, multicenter, multinational observational study, CORE-VNS (NCT03529045).

Methods: Seizure frequency for all types of seizures and patient-reported outcome measures, (quality of life and quality of sleep) were collected at baseline and 3, 6, 12, 24, and 36 months. The 24-month outcomes are compared to the pre-implant baseline and presented here.

Results: 312 (54% male, 46% female) children were included. Of those who received a VNS Therapy device, 240 (77%) were considered NIN. 40.8% of all children underwent VNS Therapy in Europe, 27.5% in the Americas, and 25.8% in the Western Pacific. The median age for children receiving their first implant was 9.7 years (range 1 to 17.99) and the median duration between epilepsy diagnosis and informed consent was 5.5 years (range 0-16.5 years). The median number of prior failed anti-seizure medications (ASMs) for this group was 6 (range 2-17). 63.4% of these children had at least moderate cognitive impairment, 87.1% had no prior brain or epilepsy surgery, and 88.3% of NIN children received a responsive VNS Therapy device (i.e., SenTiva, AspireSR). With a median time to labeled target dose (combination of output current and pulse width) of 6 months, the NIN responder rate (≥50% reduction in seizure frequency) at 24 months was 53.9% (all seizures), 54.4% (generalized), and 58.7% (focal seizures). A ≥80% reduction in seizure frequency was also noted in 31.3%, 36.7%, and 39.9% for all seizures, generalized, and focal. The median seizure frequency reduction at 24 months for NIN was 55.3% across all seizures, 61.1% for focal, and 60% for generalized. Most reported either improved quality of life at 24 months (43%) or no change (44.3%). Overall sleep quality trended towards improvement as measured by CSHQ. VNS was well-tolerated, with 24.2% of NIN children reporting at least 1 treatment-emergent adverse event. 3.8% were reported as related to the investigation device or procedure. The most common (> 5% reported) included respiratory, thoracic, and mediastinal disorders, primarily dysphonia.

Conclusions: Adjunctive VNS Therapy reduced seizures, regardless of type, over the course of 24 months in NIN children with DRE. Most NIN children had a >50% reduction in seizures at 24 months. Quality of life was also improved in 43% of children and remained stable in the remaining.

ABSTRACTS

Topic: Basic Science

EPNS25_cr7 - STEROID RESPONSIVE ENCEPHALOPATHY ASSOCIATED WITH AUTOIMMUNE THYROIDITIS (SREAT) PRESENTING AS STATUS EPILEPTICUS IN AN ADOLESCENT BOY

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Case report

Background and aims:Steroid-responsive encephalopathy associated with autoimmune thyroiditis (SREAT), also termed Hashimoto's encephalopathy (HE), is a rare immune-mediated disorder characterized by altered mental status, seizures, and cognitive dysfunction.Therapeutic options include steroid treatment. We present a case of 11 year old adolescent boy who presented with a seizure and was successfully diagnosed as SREAT and managed with corticosteroid therapy.

Materials and methods: Case report

Results: 11 year old presented with generalised tonic-clonic seizure of bilateral upper limbs, with uprolling of eye balls.There was no history of trauma,fever,drug intake or any intoxication. On examination, patient was in comatose state with GCS score of 4.Bilateral pupils were equal in size and reacting to light, tone was hypotonic, plantars upgoing. Child was immediately intubated and put on ventilatory support and administered phenytoin,acyclovir and Ceftriaxone.In lab investigations haemogram, blood sugar levels and electrolytes were normal. Cerebrospinal fluid analysis done, showed a normal cell count with mildly raised proteins approx 81.4 mg/dl.MRI brain was normal. EEG showed mild diffuse encephalopathy. Post-extubation child displayed an unstable gait, ataxia and visual hallucination. Thinking phenytoin toxicity as cause for unsteady gait, blood phenytoin levels were done and came out to be normal. Review of history revealed that patient was diagnosed with hypothyroidism one year back and was on thyroxine.Anti thyroid peroxidise antibody (anti TPO) levels were measured and turned out to be elevated 600 IU/ml (normal: < 20 IU/ml). At this point of time, possibility of Hashimoto's encephalopathy was considered and patient initiated on intravenous pulse methylpredinisolone for 3 days. Child showed a remarkable improvement and his gait started to stabilise. Child was discharged on oral prednisolone.

Conclusion: All patients with unexplained acute or subacute encephalopathy, or atypical psychiatric manifestations, especially patients who have autoimmune thyroid disease, Steroid-responsive encephalopathy associated with autoimmune thyroiditis must be included in the differential diagnosis.

ABSTRACTS

Topic: Basic Science

EPNS25_cr8 - A Case Report of Spinal Epidural Lipomatosis Presenting with Gait Disturbance

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Case report

Objective: Gait abnormalities are a prevalent reason for presentation to pediatric neurology outpatient clinics. Although idiopathic or benign aetiologies are most common, the presence of spinal diseases should be examined. Spinal epidural lipomatosis is an uncommon condition marked by excessive accumulation of fat in the extradural region causing compression of neural systems.

Method: In this case report, a patient who presented with gait disturbance and was diagnosed with spinal epidural lipomatosis is presented.

Results: A 2-year-old male child was admitted to our outpatient clinic with irregular gait disruption since he started walking. The patient's gait abnormality developed after a particular period of time (average 15-30 minutes) after activity. The neurological examination showed no aberrant results, save for a scissoring gait pattern, particularly in the right leg. Deep tendon reflexes were normoactive. The prenatal, natal, and postnatal history was uneventful. His neurodevelopmental milestones were compatible with his peers. Neuroimaging was performed on the patient. The lumbar MRI indicated grade 2 spinal epidural lipomatosis. The patient was consulted to the neurosurgery department. The decision was made to proceed with surgery for the patient. The patient underwent evaluation one month post-operation. The gait abnormality has nearly fully resolved. The patient continues to receive follow-up care.

Conclusion: The aetiology of spinal epidural lipomatosis may involve obesity in adults, endogenous corticosteroid elevation, or exogenous steroid use in children; however, it may also be idiopathic. Spinal diseases may exhibit numerous manifestations. Neuroimaging, particularly spinal imaging, is indicated for patients exhibiting gait disturbances.

ABSTRACTS

Topic: Basic Science

EPNS25_cr11 - A novel PTEN frameshift mutation in a family with Cowden syndrome and autism

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Case report

Objectives:

Germline mutations of the PTEN gene are responsible for several PTEN hamartoma tumor syndromes. They are also implicated as a cause of macrocephaly, mild to severe developmental delay and autsim, regardless of the presence or absence of hamartomas in childhood.

Methods:

We conducted whole-exome sequencing on the proband, the child's parents.

Results:

A 4-month-old boy presented macrocephaly. From birth, the height, head circumference, and weight were all in the 99th percentile. There were no facial dysmorphisms, and the physical examination was normal. During outpatient follow-up, the head circumference remained in the 99th percentile, and although there was mild motor developmental delay, the child eventually caught up. There was a language delay, and features of autism were observed later. The brain was normal at 40 months. Whole-exome sequencing identified a heterozygous novel frameshift mutation, c.408del (p.Cys136TrpfsTer11) in PTEN. After confirming the genetic mutation in the patient, testing was performed on the parents. At that time, the patient's mother was 32 years old and was undergoing chemotherapy after being diagnosed with breast cancer. The patient's mother also showed macrocephaly, and thyroid nodules were observed on ultrasound. While the BRCA1 and BRCA2 genes were negative, the same PTEN mutation as the patient was identified. The boy also exhibits autistic behavior and mental retardation, while his mother has a normal intelligence and social interaction pattern. No PTEN frameshift mutation was observed in the patient's father. In the family history, the patient's maternal grandmother passed away while being treated for breast cancer. She also had thyroid nodules and skin lesions that appeared to be trichilemmomas.

Conclusion:

We report on a mother with Cowden syndrome and a son with autism who have a novel PTEN frameshift mutation. We review the scanty literature data on the association of Cowden syndrome and autism and emphasize that the association of macrocephaly and autism spectrum disorder seems to be an indication for screening for PTEN mutations.

ABSTRACTS

Topic: Headache / Migraine

EPNS25_cr15 - When Vitamin supplementation is a troubling headache -A case of intracranial hypertension due to Vitamin A supplementation

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Case report

Objective: Idiopathic intracranial hypertension is commonly overlooked as a cause of headaches in the pediatric population given its low incidence**.** The exact pathogenesis of intracranial hypertension and its other causative factors also remain in discussion. Research has postulated potential links to use of certain medications or supplements. Use of retinol or Vitamin A has been implicated in many cases of intracranial hypertension.

Result: We report a case of a pre-pubertal child with intracranial hypertension secondary to chronic low-dose vitamin A supplementation.

Conclusion: This case report highlights the importance of considering infrequent etiologies of headaches in children. Idiopathic intracranial hypertension is hard to diagnose unless an invasive lumbar puncture is done and thus can be easily overlooked as an etiology of headaches in the pediatric population. Idiopathic intracranial hypertension can be associated with a range of medication or supplementation usage and a thorough drug history is vital during history-taking. Prolonged usage of Vitamin A derivatives are strongly associated with increased risk of intracranial hypertension.

ABSTRACTS

Topic: Traumatic Brain Injury

EPNS25_cr17 - Traumatic brain injury mimicking Canavans disease

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Case report

Objectives

Canavan disease is a genetic leukodystrophy that presents in infancy with neuroregression. It is characterized by persistently high N-Acetylaspartate (NAA) in both body fluids and brain MRS due to a deficiency of aspartoacelase breaking down NAA. This finding is so characteristic that it is frequently felt to be diagnostic. Here we present a differential diagnosis that can present with the same MRS and organic acid profile.

Method

Here we present a case of a developmentally normal 5month old boy who presented with sudden encephalopathy associated with seizures. As part of his investigations into his epileptic encephalopathy, he had MRI, MRS, MRA of his brain.

He was found to have widespread cortical low signal on his ADC map and NAA peak on his MRS. His MRA, MRV was normal. Metabolic screening found extremely high urine NAA (10x control) initially at day 1, reduced to 4xcontrol day 3 and normalise 2 months later.

His seizures was difficult to control initially but later stablised. He was subsequently discharged home on nasal gastric feed and was followed up with the rehabilitation team.

He did not have any fractures on skeletal survey but had bilateral retinal haemorrhages on opthalmology exam. Parents declined genetic testing. His mother had 3 other children from a different relationship who are all normal.

Conclusion

It was later discovered that this child had suffered a non-accidental injury resulting in his presentation. This case illustrates that acute brain injury can result in temporary increase in urinary NAA that may mimic Canavans disease in investigation and presentation

ABSTRACTS

Topic: Neuromuscular Disorders

EPNS25_cr18 - Becker Muscular Dystrophy Presenting with Rhabdomyolysis: An Atypical Initial Manifestation

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Case report

Objective
To describe a rare presentation of Becker Muscular Dystrophy (BMD) with rhabdomyolysis as the initial symptom, emphasizing the importance of recognizing atypical features, performing early diagnostic testing, and initiating appropriate monitoring to prevent disease progression.
Method
This is a case report of a pediatric patient with atypical manifestations of Becker Muscular Dystrophy.
Result
We describe a 12-year-old boy who presented with recurrent episodes of leg muscle cramps since the age of 5 years, often triggered by exertion and alleviated by rest. Over time, symptoms worsened at age 12, the patient experienced a severe episode of rhabdomyolysis following strenuous uphill walking. The episode was characterized by severe leg muscle pain and dark-colored urine, with serum creatine kinase (CK) levels markedly elevated at 201,018 U/L. On clinical examination, the patient retained normal motor function and muscle strength graded as 5/5 in all extremities. Deep tendon reflexes were normal at 2+, and no Gower's sign.
Further investigations revealed persistently elevated serum creatine kinase levels ranging from 3,872 U/L to 201,018 U/L during follow up. Whole-body muscle MRI showed no demonstrable muscle abnormality, indicating preserved muscle structure despite biochemical abnormalities. A muscle biopsy revealed findings consistent with muscle dystrophy. Genome sequencing identified a hemizygous deletion of *DMD* exons 45-48 which is predicted to be inframe causing Becker Muscular Dystrophy phenotype. Cardiac echocardiography demonstrated normal systolic function with no evidence of cardiomyopathy at this stage.
Conclusion
This case demonstrates that rhabdomyolysis, persistent hyperCKemia, and exercise-induced muscle cramps can precede significant muscle weakness in Becker Muscular Dystrophy, with normal muscle MRI findings. Early recognition through clinical symptoms, CK screening, and genetic testing is critical for timely diagnosis, cardiac surveillance, and implementation of preventative measures to improve long-term outcomes.

ABSTRACTS

Topic: Infectious and Inflammatory Diseases/ Neuroimmunology

EPNS25_cr19 - Cryptic but Overt: A Case report of Cryptococcal Meningoencephalitis in an Immunocompetent Child

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Introduction: Cryptococcus is an infection that can affect the central nervous system and commonly occur in immunocompromised individuals. Symptoms of cryptococcal meningoencephalitis include fever, vomiting, and headache, progressing to altered mental status or seizures in later stages.

Objective: This study reports a case of cryptococcal meningoencephalitis in a child with malnutrition.

Method: Clinical evaluations, laboratory tests, imaging studies, and lumbar puncture procedures were performed.

Results: A 10-year-old boy presented with acute alteration of mental status, with a previous history of generalized seizure accompanied by loss of consciousness, fever, headache, vomiting, and drowsiness which progressively worsened. His anthropometric status indicated malnutrition, with a weight-for-height measurement of 73% according to CDC standards. Physical examination showed the patient was somnolent with GCS 10/15, positive signs of nuchal rigidity, reactive bilateral pupils, isochoric pupils 3 mm / 3 mm and hyperreflexia. Fundoscopic examination showed papilledema. Laboratory tests showed elevated white blood cell count (13,200/mm^3), hyponatremia (117 mEq/L), hyperglycemia (203 mg/dl), and positive C-Reactive Protein (32.6 mg/L). HIV test was negative. Abdominal ultrasound showed mild ascites, chest X-ray was normal, electroencephalography showed generalized low voltage, and MRI of the brain revealed cerebral atrophy. Lumbar puncture was performed with the result of CSF India ink preparation showing Cryptococcus spp. GeneXpert for CSF was negative. Mantoux tuberculin skin test, HSV CSF, and anti-NMDAR CSF tests were negative. The patient was admitted to the Pediatric Intensive Care Unit and diagnosed with cryptococcal meningoencephalitis. Intravenous amphotericin B was administered for 14 days, however there was no clinical improvement observed.

Conclusion: Cryptococcal meningoencephalitis can occur in immunocompetent children, including those with malnutrition. Early recognition is crucial to prevent further progression. Antifungal therapy is the treatment of choice for this case.

ABSTRACTS

Topic: Cerebrovascular Disorders

EPNS25_cr20 - The Collagen Type IV Alpha 1 Chain (COL4A1) Mutation as a Rare Cause of Cerebral Small Vessels Disease in Adolescent: A Case Report

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Case report

Introduction: Cerebral small Vessel Disease (CSVD) is defined as an abnormality of small blood vessels in the brain, including arterioles, venules, or capillaries in the brain. It rarely occurs in children.CSVD can result from several factors such as genetics and environment. Several single-gene disorders have been linked to CSVD, one of which is caused by COL4A1 gene mutation, located on chromosome 13q34.

Objective : This study reports a case of a 17-year-old girl diagnosed with CSVD caused by a COL4A1 mutation.

Method : The patient underwent several examinations, including clinical, laboratory, imaging, and genetic testing.

Results: Patient's symptoms observed in this case included worsening slurred speech with difficulty chewing, recalling information, and tingling in both lower extremities. There is a family history of stroke in the patient's family. Physical examination showed paresis of the XII cranial nerve. Laboratory tests resulted in normal hemostasis profile with low platelet aggregation. Brain MRI showed hyperintense lesions on T2-weighted (T2W) and FLAIR sequences, hypointense lesions on T1-weighted (T1W) sequences, and multiple microhemorrhages in the frontotemporal lobes and bilateral cerebellar peduncles. Other imaging test, including thoracovertebral MRI, MRA, carotid Doppler ultrasound, and echocardiography, showed normal results. Genetic testing in patient identified a heterozygous *c.2417_24344del*(p.Ala806_Gly811del) variant in the *COL4A1* gene, classified as pathogenic, which was also detected in the patient's mother. Patient was treated with piracetam and a low-dose anticoagulant for a short duration. After one year of follow-up, patient had no more XII cranial nerve paresis, although patient still continued to experience intermittent tingling and had difficulty in concentrating.

Conclusion : Mutation in the *COL4A1* gene is associated with abnormalities in the vascular basement membrane, which can lead to CSVD. This mutation can be inherited in familial patterns. Genetic testing of the patient's family members is necessary to prevent its risk. Early diagnosis and treatment of the disease in the patient can significantly improve their prognosis.

ABSTRACTS

Topic: Infectious and Inflammatory Diseases/ Neuroimmunology

EPNS25_cr23 - First pediatric case of AQP4-antibody positive neuromyelitis optica spectrum disorder presenting with area postrema syndrome in South Korea

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Case report

Introduction: Neuromyelitis Optica Spectrum Disorder (NMOSD) is severe autoimmune inflammatory diseases of the central nervous system characterized by episodes of optic neuritis (ON), transverse myelitis (TM) and area postrema (AP) syndrome, such as hiccup, nausea, or intractable vomiting. AP syndrome is one of the core clinical characteristics in the diagnostic criteria of NMOSD. In children, it is rare for NMOSD to be diagnosed based on AP symptoms, without ON or TM. Here we report the first pediatric patient diagnosed with antibodies against aquaporin-4 (AQP4-Ab) NMOSD based on area postrema syndrome in South Korea.

Case: A 10-year-old female patient with unexplained prolonged vomiting was transferred to our hospital. After hospitalization, sudden right-eye esotropia occurred. Brain imaging revealed encephalitic lesions in the right posterior pons and both thalamus regions. Additionally, the serum AQP4-Ab test was positive. Orbit and spinal imaging results were normal. AP syndrome was suspected based on clinical findings. The patient was finally diagnosed with AQP4-Ab positive NMOSD even though there was no evidence of ON or TM. After treatment with intravenous methylprednisolone and immunoglobulin, patient showed significant improvement in symptoms.

Conclusion: AQP4-Ab is considered important factor of pathogenesis of NMOSD. According to the revised 2015 NMOSD criteria, only one core clinical characteristics is required in AQP4-Ab positive patients. The relapsing and aggressive nature of AQP4-Ab positive NMOSD in pediatric patients often results in a poor prognosis. Therefore, we recommend performing an AQP4-Ab test, if NMOSD is suspected based on area postrema syndrome, for accurate diagnosis and prognosis prediction.

ABSTRACTS

Topic: Epilepsy: Diagnosis and Investigations

EPNS25_cr24 - A rare cause of treatable epilepsy: Cerebral folate deficiency syndrome

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Case report

Objectives: Cerebral folate deficiency (CFD) is a rare neurometabolic condition characterized by decreased levels of 5-methyltetrahydrofolate (5-MTHF) in cerebrospinal fluid (CSF). CFD is responsible for folinic acid treatment.

Case: A 19-month-old girl with parental consanguinity was admitted to the child neurology outpatient clinic with seizures. Her neurodevelopmental milestones were almost normal until she had seizures. The seizures were repeated head drops and myoclonic-atonic character. Levetiracetam and clobazam were started. After these seizures, her cognition, speech, and walking abilities were deteriorating. She had an unsteady gait and an appearance of autistic behavior. She was born at 39 weeks of gestational age from uneventful pregnancy and delivery. Birth weight was 3500 gr (50–75th percentile), length was 49 cm (25th percentile), and head circumference was 33 cm (3rd percentile). On laboratory examination, there were no abnormalities on hemogram, biochemical parameters (AST, ALT, urea, creatinine, glucose, uric acid, calcium, magnesium, creatine kinase, B12, folate, TSH, f-T4), acylcarnitine profile, urine organic acid analysis, biotinidase activity, homocysteine, very-long-chain fatty acids (VLCF), serum amino acid analysis. There were calcifications on the brain tomography. The brain magnetic resonance imaging (MRI) showed mild cerebellar atrophy and delayed myelination. Electromyography (EMG), electrocardiography (ECO), and eye examination were normal. The electroencephalography (EEG) determined generalized epileptiform activity with voltage suppression. In her genetic test result, FOLR1 (NM_016724) c.505T>C (p.C169R) homozygote gene mutation was detected, which confirms the diagnosis of cerebral folate deficiency. Folinic acid was started, then gradually increased to the present dose of 1 mg/kg/day orally. At this dose of folinic acid, seizures became better controlled (less frequent and less duration). Besides, the symptoms, including unsteady gait and cognitive level, were improved.

Conclusion: CFD should be kept in mind for patients who have typical brain MRIs and tomography findings, such as cerebellar atrophy and calcification, which can cause treatable epilepsy.

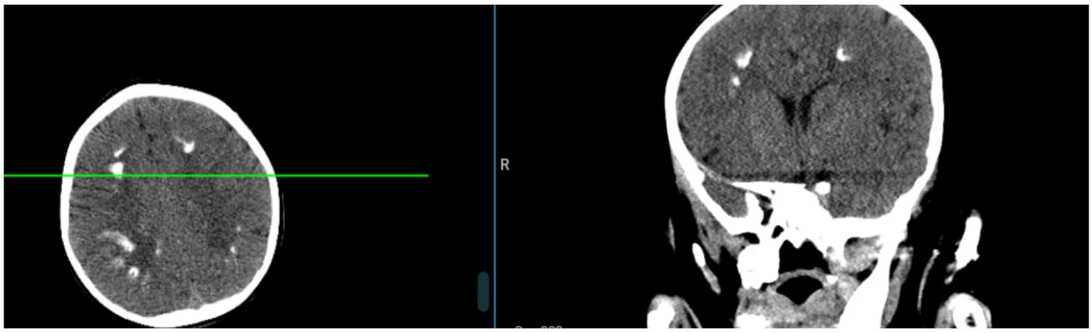

Figure 1: Brain tomography with common calcifications

ABSTRACTS

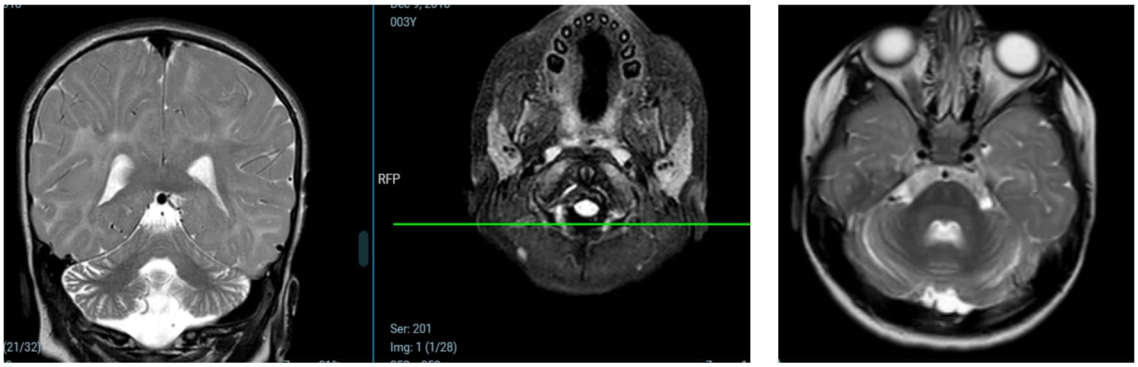

Figure 2: Brain MRI shows mild cerebellar atrophy and delayed myelinations

ABSTRACTS

Topic: Neurometabolic Disorders

EPNS25_cr26 - A rare case of GLUT-1 deficiency with only language delay

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Case report

Objections: GLUT1 deficiency syndrome-1 (GLUT1DS1) is a neurological disorder showing wide phenotypic variability. The most severe 'classic' phenotype comprises infantile-onset epileptic encephalopathy associated with delayed development, acquired microcephaly, motor incoordination, and spasticity. The onset of seizures, usually characterized by apneic episodes, staring spells, and episodic eye movements, occurs within the first four months of life. Other paroxysmal findings include intermittent ataxia, confusion, lethargy, sleep disturbances, and headaches.

Case: Twin brothers who were born at 38 gestational weeks, had no problems in the prenatal, natal, and postnatal period, and had first-degree consanguinity between mother and father were presented. They applied for speech and neurocognitive deficiency, according to their peers, and they suffered from dizziness, especially in the morning when they were hungry. On their physical examination, there was tiptoeing and unsteady gait, mental and speech delay, and autistic appearance. On laboratory examination, there were no abnormalities on hemogram, biochemical parameters (AST, ALT, urea, creatinine, glucose, uric acid, calcium, magnesium, creatine kinase, B12, folate, TSH, f-T4), acylcarnitine profile, urine organic acid analysis, biotinidase activity, homocysteine, very-long-chain fatty acids (VLCF), serum amino acid analysis. The brain magnetic resonance imaging (MRI) and spectroscopy were normal. In the electroencephalography (EEG), both patients have generalized epileptiform activity with epileptic encephalopathy. Levetiracetam was started for both. In their genetic test result, SLC2A1 NM_006514.4 c.1199G>A (p.R400H) (p.Arg400His) autosomal dominant mutation was detected of both.

Conclusion: We kept in mind GLUT1 deficiency in every patient who has generalized epileptic discharges and displays ataxic symptoms, especially when they are hungry.

ABSTRACTS

Topic: Infectious and Inflammatory Diseases/ Neuroimmunology

EPNS25_cr27 - Immune-mediated ataxia in a preschool girl - pitfalls and caveats

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Case report

Acute ataxia in a previously healthy child is a rare presenting complaint in the emergency department. Although the differential diagnosis is expanded, post-infectious etiologies are the most common, with acute cerebellar ataxia accounting for the vast majority of cases. Here, we present the challenging case of a 2.5year-old girl with acute ataxia, as well as the extensive diagnostic workup leading to a diagnosis of seronegative autoimmune cerebellar ataxia (CA).

We performed a detailed review of the patient's clinical history, imaging, and laboratory findings

Our patient was a 2.5-year-old girl who presented with severe, acute-onset ataxia. The patient had upper respiratory symptoms, and she was non-ambulatory at presentation. Her brain CT scan was normal and cerebrospinal fluid (CSF) analysis revealed elevated white blood cells and positive oligoclonal bands. She was treated with intravenous methylprednisolone for five days, with only minimal improvement. Repeating brain magnetic reasonance imaging (MRI), multiple extensive autoantibody panels in serum and CSF, as well as whole genome sequencing (WGS) were unremarkable. Due to residual deficits, the patient received six monthly courses of γ-globulin (IVIG) infusions, resulting in only moderate and infusion-related improvement. Indirect CSF immunohistochemistry (TIIF/IHC) was requested and revealed positive intracellular signal of Purkinje cells of the cerebellum, confirming the diagnosis of seronegative autoimmune CA. An extensive workup towards occult malignancies come back negative. Sustained remission was achieved with prolonged oral corticosteroid therapy.

In conclusion, seronegative autoimmune CA with normal brain MRI, although rare and challenging to diagnose, should be incorporated in the differential diagnosis of children with acute and subacute ataxia. We highly recommend that TIIF/IHC should be included in all pediatric autoimmune workups, as it validates the diagnosis in antibody-negative cases and guides personalized immunomodulatory treatment.

ABSTRACTS

Topic: Neuromuscular Disorders

EPNS25_cr28 - Severe neonatal hypotonia – x lynked myotubular myopathy

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Case report

We present a case of a 12 months old boy, the first child of a healthy parents, abnormal pregnancy (reduced fetal movements, polyhydramnios), but birth at therm, without perinatal asphyxia (weight 3630 g, Apgar score 8/9, head circumference 35 cm). Signs of the disease appears in the first hours of life with marked weakness and hypotonia, weak cry and external ophthalmoplegia without respiratory failure in the neonatal period.At the age of 6 weeks old the boy is with motor regression with musculotendinous retractions, proximal muscular deficit and severe hypotonia. The MLPA test for spinal muscular atophy (SMA) was negative and the cerebral MRI showed pontocerebellar hypoplasia, sow first our diagnostic was SMAnon5Q, but the whole exome sequencing showed hemizygous mutation in gene MTM1 c.535C>T, p.(Pro179Ser), which is likely pathogenic. The patient had respiratory support, bilevel positive airway pressure (BIPAP) type of ventilation and was tested every 3 months with the scale Children’s Hospital Of Philadelphia Infant Test Of Neuromuscular Disorders. Disease caused by MTM1 variants is inherited in an X-linked recessive manner; males hemizygous for a disease-causing MTM1 variant are affected, whereas heterozygous females are typically unaffected or mildly affected.We recommend carrier testing of the patient’s mother and the results showed that the mother is a carrier, heterozygous for MTM1 c.535C>T, p.(Pro179Ser).We have reported a case with severe congenital muscle disease caused by mutation in the MTM1 gene. No approved treatment exists for this congenital myopathy, but doctors need to deliver better standards of care for this patients.

ABSTRACTS

Topic: Neurogenetics

EPNS25_cr29 - X-linked adrenoleukodystrophy with fabry disease : a case report

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Case report

X-linked adrenoleukodystrophy (X-ALD) is a neurodegenerative disorder caused by accumulation of very long-chain fatty acids (VLCFA) in the brain and the adrenal cortex. It typically occurs in boys and it initially presents with cognitive disabilities, learning and behavioral problems and then in the later stages, with severe neurologic manifestations.

This is a case of a 7 year old male, born full-term to a 33 year old primigravid with an uncomplicated pregnancy. His expanded newborn screening (ENBS) test was normal and developmental milestones were at par with age. He was apparently well until about 6 years of age when he presented with gradual blurring of vision followed months later by difficulty in writing and ambulation.

He was seen by a neurologist when there was already progressive deterioration in his motor, receptive and expressive language skills. Supportive management was initiated however, this did not prevent or delay his neurologic deterioration. Currently, the patient is blind, bed-ridden with muscular atrophy and decrease in overall tone and is fed through a percutaneous endoscopic gastrostomy (PEG) tube. He also requires full time care from his relatives.

Data from studies show that X-ALD can be reliably identified through newborn screening; however in our country, X-ALD is not included in the ENBS test.

As part of the work-up, genetic testing was also done and the patient was positive for Fabry disease (FD). FD is a progressive inborn error of metabolism but in contrast to other lysosomal storage diseases, patients remain clinically asymptomatic during their early years. With age, progressive damage to vital organ systems including the brain, heart and kidneys develops. Enzyme replacement therapy (ERT) is the cornerstone for treatment however because of the advanced state of our patient's neurologic status, he is no longer a candidate for such.

X-ALD and FD are both rare genetic disorders that affect the body's ability to process fatty acids but as of this writing, a combination of both in one patient has not yet been reported in literature. This case report aims for the following: 1) inform the community that X-ALD and FD can be present in one patient 2) shed light on the rapid disease progression and poor prognosis of individuals with X-ALD who were diagnosed at a later stage 3) recommend that X-ALD be incorporated in diseases detected in the ENBS test offered in our country.

ABSTRACTS

Topic: Neurometabolic Disorders

EPNS25_cr30 - Expanding the phenotypic spectrum of Zellweger Spectrum Disorders: A Case Report of PEX13-Related Disease

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Case report

OBJECTIVES: The Zellweger spectrum disorders (ZSDs) are a heterogeneous group of autosomal recessive disorders characterized by a defect in peroxisome metabolism and are caused by pathogenic variants in one of 13 *PEX* genes. From a clinical point of view, ZSDs are a continuum ranging from severe to mild phenotypes with multiorgan involvement including the nervous system. Common neurological findings are hypotonia, seizures, developmental delay and leukodystrophy MRI pattern. Given its variable phenotype and rarity, differential diagnosis with other genetic leukodystrophies is challenging and usually relies on biochemical findings and confirmatory genetic testing.

This report describes a child with compound heterozygous *PEX13* pathogenic variants, presenting with a novel phenotype and specific neurophysiological and radiological pattern.

METHODS: we describe clinical and instrumental findings in a patient with molecularly confirmed ZSD diagnosis due to pathogenic variants in the *PEX13* gene, identified through whole-exome sequencing (WES).

RESULTS: the patient was first evaluated to our department at 4 years of age because of sensorineural hearing loss and mild cognitive delay. No focal neurological signs were observed. MRI disclosed cerebellar white matter (WM) involvement, and a demyelinating sensorimotor neuropathy was detected. Over the following year, the patient developed cerebellar signs (ataxia and dysmetria), along with pyramidal signs (Babinski sign and increased deep tendon reflexes). Instrumental follow up showed worsening of peripheral neuropathy and progression of cerebellar lesions. Serum analysis revealed normal levels of very long-chain fatty acids (VLCFA), phytanic acid, and pristanic acid. WES detected two compound heterozygous pathogenetic variants in the *PEX13* gene, c.472T>A (p.Phe158Ile) and c.676C>T (p.Arg226Ter), which segregated in trans in the proband's parents.

CONCLUSION: We present the first case of ZSD due to *PEX13* variants with exclusive subtentorial WM involvement and associated with demyelinating peripheral neuropathy. Our report expands the spectrum of the *PEX13* gene related disorders. This has significant implications in diagnostic work up of infantile leukodystrophy and ZSDs: *PEX13* pathogenic variants should be suspected in children with a neuroradiological pattern of leukodystrophy and no supratentorial WM involvement, even in the absence of biochemical findings suggestive of ZSDs.

ABSTRACTS

Topic: Epilepsy: Diagnosis and Investigations

EPNS25_cr32 - Electroclinical pattern of pcdh19 related epilepsy: a case report of a rare refractory epilepsy

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Case report

We present a case of an 8 years old female child, hospitalized at the age of 11 months due to her first febrile epileptic seizure. Due to epileptiform discharges in EEG, and repetitive seizures, treatment with antiepileptic drug was started. Neuroimaging of the brain showed normal findings. Genetic testing (WES), revealed pathogenic variant c.462C>G, p. (Tyr154*) in exome 1 of PCDH19 gene, present in mosaic form, de-novo mutation. These changes indicated association with developmental and epileptic encephalopathy 9, inherited X-linked. Electroencephalographic (EEG) characteristics were analyzed both at the beginning and during follow-up assessments.

The aim is to evaluate the electroencephalographic (EEG) and clinical features of PCDH19-related epilepsy in pediatric patient by examining its early signs and evaluating treatment effectiveness.

The first two EEGs showed multifocal bihemispheric discharges of high voltage spike and wave complexes when treatment with Levetiracetam was started. In the following EEGs generalized discharges were present, when Valproate was added. Afterwards, followed couple of years of electroclinical stabilization. At 6- and 8-years old destabilization followed with recurrent febrile tonic-clonic generalized seizures. Most of the seizures occurred with febrile state due to respiratory infection. Respectively, the EEGs showed multifocal bihemispheric discharges of spike and wave complexes. Nowadays, she is stable and receiving Levetiracetam and Valproate.

This case emphasizes the essential role of genetic testing in diagnosing de-novo PCDH19 epilepsy, recognizing EEG patterns and seizure types, and customizing treatment plans. Prompt diagnosis and individualized care can greatly enhance the prognosis and quality of life for patients. PCDH19-related epilepsy, also known as Girls Clustering Epilepsy (GCE), is a rare genetic disorder mainly affecting females, caused by mutations in the PCDH19 gene, inherited in an X-linked dominant pattern. It leads to clustered seizures often triggered by fever, starting in infancy. The condition also involves developmental delays, intellectual disability, and autism spectrum disorders, which in our patient are not noted.

ABSTRACTS

Topic: Neurogenetics

EPNS25_cr34 - A Rare Case KCTD7-Associated Progressive Myoclonic Epilepsy

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Case report

A previously healthy 19-month-old female patient presented with eyelid tremors, imbalance, and falling while walking. It was stated that her symptoms started 1 month ago. The eyelid tremors last about 10-15 seconds and occur many times during the day. She was born to consanguineous parents (first cousins) at 37 weeks gestation with a 3750 gram birth weight. Pre and post-natal history was unremarkable. Neuromotor development stages were normal. His mother's cousin had epilepsy. We determined that the patient, who previously walked normally and had speech skills appropriate for her age, had lost these abilities for 2 months.

Her general condition was good, she was oriented and cooperative. She was hypotonic and she has microcephaly (41 cm <-2SD). Cranial nerve examination was normal and she has increased deep tendon reflexes. Her gait was in an ataxic pattern. No pathology was detected in metabolic tests. There were no findings such as retinal deposits or optic atrophy in the eye examination. Global developmental delay was detected in the Denver developmental test. Brain magnetic resonance imaging (MRI) showed bilateral mild dilatation of the ventricles and prominence of the cerebellar foils. Electroencephalogram (EEG) of the patient taken at different times showed generalized spike-slow wave discharges and multifocal spike-slow wave discharges. Karyotype analysis revealed 46,XX. There was no pathology in microarray analysis. Whole exome sequencing (WES) showed homozygous pathogenic variant in the *KCTD7* gene. (c.280C>T) This gene has been associated with progressive myoclonic epilepsy (PME) type-3 and NCL type-14 in the literature. In cases without ocular involvement, PME is primarily considered. This variant was identified as pathological in gene databases. We found that the mother and father were heterozygous for the same pathological variant in their genetic results. The family was referred for genetic counseling, they has a healthy child now.

Levetiracetam was chosen as the initial drug in the patient's treatment. Sodium valproate was added to the treatment after metabolic diseases were excluded because of the persistent persistence of seizures. Despite this, the patient's seizures continued and clobazam and topiramate were added to the treatment because of their anti-myoclonic activity. The patient was included in the physical therapy program from the moment of admission. After the age of five, the seizure frequency decreased and she entered a stable phase. The patient continues to be followed up with the diagnosis of *KCTD7*-related progressive myoclonic epilepsy.

ABSTRACTS

Topic: Palliativ Care

EPNS25_cr36 - Central respiratory dysregulation as a life-limiting condition in Krabbe disease

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Case report

Objective: Krabbe disease (Globoid Cell Leukodystrophy) is a neurodegenerative disorder characterized by demyelination of the peripheral and central nervous system. Little knowledge exists about which symptoms finally lead to death. Here, we describe the occurrence of central apneas in Krabbe disease as a potentially life-limiting symptom in a palliative care context.

Methods: Case report of three patients diagnosed with early onset Krabbe disease confirmed by MRI and genetics who developed central apneas in the course of the disease.

Results: Case 1: Male, disease onset 4 months. At the age of 17 months, he developed central apneas without any signs of dyspnea, and died at 18 months of age.

Case 2: Male, disease onset 8 months. Supported by the specialized home pediatric palliative care (SHPPC) team, he experienced almost three years of low symptom load. At the age of 47 months, he developed apneas and died a few days later, presumably from central respiratory failure.

Case 3: Female, disease onset 6 months. At the age of 15 months, she developed symptoms of central respiratory dysregulation, showing no dyspnea. The family was supported by SHPPC, focusing on the treatment of stressful symptoms and avoiding hospital admissions. She is still alive at 10 months of age. A shared decision was taken not to monitor vital parameters and to withhold mechanical ventilation in the case of respiratory deterioration.

Compatible with clinical findings, the MRI showed demyelination extending into the medulla oblongata and cervical spinal cord in all three patients.

Conclusion: Central respiratory dysregulation appears to be a relevant symptom and possible cause of death in Krabbe disease, not necessitating symptomatic opioid therapy due to the absence of dyspnea. Parents were grateful for the information that that death due to central apneas can come without pain or suffering.

ABSTRACTS

Topic: Epilepsy: Medical and Surgical treatment

EPNS25_cr38 - Successfull treatment of child with scn2a-related developmental and epileptic encephalopathy with apparent gain-of-function effects

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Introduction: SCN2A has emerged in recent years as a key causative gene for pediatric epilepsy. Loss-of-function (LoF) variants are typically associated with later-onset seizures, and gain-of-function (GoF) variants are more closely associated with early-onset epilepsy in the neonatal or infantile period. SCN2A GoF potentiates NaV1.2 activity and is most closely associated with early infantile epileptic encephalopathy (EIEE) and self-limited familial and nonfamilial infantile epilepsy (formerly benign familial infantile seizures).

Objective: We report an infant who presented with migrating focal seizures in the neonatal period. She was found to have a mosaic c.4534C>Gp.Pro1512Ala variant in SCN2A. Functional studies on this variant revealed a mixture of gain- and loss-of-function effects.

Clinical Description. A 6-week-old girl was hospitalized in our department due to experiencing daily seizures in multiple areas, which started on the 5th day after birth. She had no notable personal history. Prior to her admission to our clinic, she had been given Levetiracetam and Phenobarbital within the recommended therapeutic levels but it did not effectively control her seizures. Upon undergoing electroencephalography, bilateral and multifocal epileptiform discharges were observed. Prompt seizure management was achieved using Phenytoin, in accordance with recent literature suggesting the use of sodium channel blockers for SCN2A-related epileptic encephalopathies. The child remained free from seizures but experienced delayed development in motor and cognitive skills. Genetic investigations identified a de novo SCN2A missense pathogenic variant with predicted GoF effect.

Conclusion: This case illustrates the dramatic response to sodium channel blockers suggested an underlying channelopathy.

ABSTRACTS

Topic: Cerebrovascular Disorders

EPNS25_cr39 - Recurrent Ischemic Stroke in a 3-Year-Old Boy with ACTA2-related Smooth Muscle Dysfunction Syndrome: Clinical Manifestations and Diagnostic Challenges

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Case report

Objectives: This case report aims to present the clinical manifestations of a 3-year-old boy diagnosed with an *ACTA2*-related multisystemic smooth muscle dysfunction syndrome, focusing on the challenges encountered in diagnosing this rare genetic condition in pediatric patients.

Methods: We reviewed the clinical course, diagnostic evaluations, and management of a 3-year-old male patient. The child presented with recurrent ischemic strokes and had a significant medical history, including patent ductus arteriosus (PDA), bronchomalacia, intestinal malrotation, and developmental delays. Trio-genome sequencing (GRCh38) identified a *de novo* heterozygous pathogenic variant c.536G>A (p.Arg179His) in *ACTA2* (NM_001613.4).

Results: The patient experienced recurrent episodes of focal motor weakness. Neuroimaging revealed progressive cerebrovascular anomalies consistent with moyamoya-like arteriopathy, including severe narrowing of the supraclinoid internal carotid arteries and diffuse involvement of the small vessels in the middle and anterior cerebral arteries. Systemic features included history of patent ductus arteriosus, pulmonary arterial hypertension, and intestinal malrotation. Despite an extensive initial workup, the diagnosis of Multisystemic Smooth Muscle Dysfunction Syndrome (MSMDS) was established only after genetic analysis. The patient underwent right superficial temporal artery (STA)-middle cerebral artery (MCA) bypass surgery with EDAMS (encephaloduroarteriosynangiosis) and continued antiplatelet therapy, resulting in the resolution of ischemic episodes and stabilization of neurological symptoms.

Conclusions: This case highlights the diagnostic complexity associated with *ACTA2* mutations in pediatric populations. Early genetic evaluation and comprehensive imaging protocols are essential for timely diagnosis and management. This report emphasizes the need for heightened clinical awareness of *ACTA2*-related disease to improve outcomes in affected children.

ABSTRACTS

Topic: Cerebrovascular Disorders

EPNS25_cr40 - A Rare Case of Achalasia with Moyamoya Syndrome 6: Clinical, Radiological, and Genetic Insights

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Case report

Objectives:
To present a comprehensive clinical case of Achalasia with Moyamoya Syndrome 6 (OR, OMIM #615750), emphasizing the diagnostic complexities and importance of genetic testing in identifying rare syndromes associated with recurrent strokes, achalasia, and refractory hypertension.

Methods:
All patient information was obtained from the hospital data system.

Results:

The patient was born full-term with an unremarkable prenatal history, experienced transient vision loss at 13 months following minor head trauma, resolving within two hours without intervention. At 15 months, after a febrile diarrheal episode, the patient presented with somnolence and right-sided hemiparesis. Cranial MRI revealed restricted diffusion and T2 hyperintensities in the right temporal, left frontoparietal, and left occipital regions. EEG showed delta-theta waves in the posterior hemispheric regions, which is consistent with encephalopathy. Despite treatment with ceftriaxone and acyclovir for suspected encephalitis, cerebrospinal fluid analyses were inconclusive for infectious agents.

Between 15 months and 7 years of age, the patient had three episodes of acute weakness and speech difficulties due to ischemic stroke, with cranial imaging indicating Moyamoya disease. Persistent emesis and constipation led to an endoscopic diagnosis of achalasia, which was treated with balloon dilatation on three occasions, and improved symptoms. By the age of 7 years, the patient had developed refractory hypertension with normal renal Doppler findings.

Given the patient's recurrent stroke, mitochondrial disease, especially MELAS, was initially considered; however, the mitochondrial disease panel yielded normal results. Subsequent whole-exome sequencing (WES) revealed a homozygous pathogenic frameshift variant, c.1649_1653del p.Ala550AspfsTer10, in GUCY1A1. Consequently, the patient was diagnosed with Akalasia with Moyamoya Syndrome 6 (OR, OMIM #615750).

Further medical history revealed additional clinical findings, including severe cyanosis of the lips in cold environments and Raynaud phenomenon. The current therapeutic management includes aspirin, arginine, propranolol, enalapril, and amlodipine.

Conclusions:
This case highlights the effectiveness of whole-exome sequencing for diagnosing rare syndromes with overlapping systemic and neurological symptoms. Achalasia with Moyamoya Syndrome 6 should be considered in patients with recurrent stroke, achalasia, and resistant hypertension. We think that this gene defect should be considered in the differential diagnosis of MELAS-like conditions.

ABSTRACTS

Topic: Infectious and Inflammatory Diseases/ Neuroimmunology

EPNS25_cr42 - Paediatric miller fisher syndrome presenting with bulbar palsy: a case report

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Case report

Miller Fisher syndrome (MFS), a clinical variant of Guillain Barre syndrome (GBS) is an acute, autoimmune, self-limiting disorder characterized by a clinical triad of ophthalmoplegia, ataxia and areflexia. MFS, Bickerstaff's encephalitis and GBS are closely related and overlap syndromes occur. A subset of patients have bulbar palsy (BP), which often develops within a week of symptom onset. We report a case of MFS with unique presentation of BP as presenting symptom.

This was a retrospective study of patient with MFS in Children's Clinical University Hospital in 2022 using institutional information data system.

A previously healthy 14 year-old boy presented to the Emergency Department (ED) with 1 day complaint of being able to speak only with his nose pinched. At home, nasal regurgitation of water had occurred. He was afebrile with no other symptoms. A week prior, he had loose stools without fever or vomiting. He was neurologically intact and was discharged after neurologist, otorhinolaryngologic and psychiatric evaluations. He presented to ED 3 days later with new-onset diplopia. He was consulted by an ophthalmologist, who described lateral gaze ophthalmoplegia, ptosis OD and decreased OU pupillary light reflex. Neurologically, he also had decreased palatal elevation, dysarthria and stocking-glove hypoesthesia. MRI of the brain was unremarkable. Cerebrospinal fluid showed albuminocytologic dissociation. Next day, patient had areflexia in legs. Nerve conduction studies were normal. A differential diagnosis of botulism was considered and antitoxin serum was acquired. Risk factors for botulism were not identified in history. Patient then developed ataxia in legs, making diagnosis of MFS more likely. Intravenous immunoglobulin (IVIG) 2 g/kg was administered over 5 days. Anti-GQ1b and anti-GT1a were positive in serum. After first IVIG dose, patient developed facial nerve palsy *dextra* and dyspnoea. However, the patient's condition gradually improved and he was discharged 8 days after admission. A week after discharge, he had no neurological sequelae.

We report a boy with MFS and an unusual BP presentation making eventual diagnosis of MFS challenging. The differential diagnosis of MFS should include botulism, especially in atypical MFS variants. MFS is described as a self-limiting disease, however, initiation of immunotherapy should be considered in patients with BP due to potential risk of complications.

ABSTRACTS

Topic: Epilepsy: Medical and Surgical treatment

EPNS25_cr44 - With Rituximab Treatment

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A previously healthy 18 month old female patient presented with a focal tonic seizure. She was born to consanguineous parents (first cousins) at 37 weeks gestation. Pre and post natal history was unremarkable. Several members of the family had epilepsy. Neurodevelopmental stages were normal. Brain magnetic resonance imaging (MRI) revealed was normal. An electroencephalogram (EEG) showed focal epileptic discharges. Valproic acid was given as treatment. During the patient's follow-up period, we saw that she continued to have resistant seizures. Carbamazepine, lamotigine, levetirecetam and topiramate were add to the treatment due to refractory seizures. Then, when she was 14 years old, she was admitted to the pediatric emergency department due to seizures. Her seizure was myoclonic with focal clonic in the mouth. During the follow-up it occured to status epilepticus. We initiated antiseizure drug treatments for this. After the she was admitted to the intensive care unit, drug loadings and infusions were given accorfing to the status epilepticus protocol. The current anti-seizure drugs she was using were; carbamazepine, topiramate and levetirecetam. Brain MRI performed during this period, showed suspicious cortical dysplasia in the right temporal area, edematous apperance oft he right hemisphere compared to the left, effacement of the sulci and signs of inflammation. In this period of EEG, epileptiform potentials originating from the frontocentrotemporal regions of the right hemisphere were seen. These potentials occasionally spread to the frontoparietooccipital regions of the same hemisphere. Hemispheric asymmetry was detected in this EEG and MRI.

On the fifth day of follow-up, was given intravenous immune globulin (IVIg) treatment with a preliminary diagnosis of autoimmune encephalitis. The patient responded to this treatment, the number of seizures decreased by more than 50 percent. A few days later since the seizures continued pulse metilprednisolon (PMP) was given 1000 mg/day for seven days. All autoimmune encephalitis antibodies except the GAD65 were negative. The patient benefited greatly from this treatment and Rasmussen Encephalitis was considered. Due to prolonged intubation the patient underwent a tracheostomy and was swithced to home type mechanical ventilation. We administered Rituximab 375 mg/m^2 weekly for 4 weeks. After this treatment the patient started talking and we saw %90 reduction in seizures. Whole exome sequencing (WES) was planned for the etiology.

We are currently preparing the patient for epilepsy surgery. We presented this case because it was an anti-GAD65 positive Rasmussen Encephalitis case that benefited significantly from Rituximab.

ABSTRACTS

Topic: Palliativ Care

EPNS25_cr46 - The effect of dynamic neuromuscular stabilization on the symmetry of muscle activity in children requiring palliative care

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Case report

Background. Little is known about the effect of dynamic neuromuscular stabilization (DNS) on the functions and muscle activity of children requiring palliative care.
Objectives: To assess the effect of the dynamic stabilization method on the symmetry of muscle activity in children requiring palliative care.

Methods: The research was carried out between Oktober and December 2024 at the Budget institution Klaipėda Children's Home for Children with Impaired Development. A retrospective review and analysis of the clinical records of five patients (1-6 years old girls, mean age 4,2 years) with cerebral palsy (GMFCS IV-V) who underwent DNS was conducted and reported. Patients outcomes were evaluated and compared to pretest and post-test measurements based on clinical examination of electromyography, passive mechanical properties (MyotonPro), as well as gross motor function and classification system. Muscle activity (upper and lower trapezius, biceps and triceps, erector spinae) was recorded while lying on the stomach on the forearms; rectus abdominis and erector spinae - sitting; rectus abdominis - lying on the back; gluteus medius, rectus femoris, biceps femoris, gastrocnemius and tibialis anterior - while standing. All subjects were placed in the Deadbag position, lying on their stomach with the child resting on their forearms. Sitting position with or without assistance. The positions were applied for six weeks 5 t/week. The mean and standard deviation of the data are represented. The difference between pre- and post-test and left/rigth sides were analysed with Student criteria ($p<.05$).

Results: Gross motor function did not change during the study. Six weeks is not enough to improve the gross motor function and level of children requiring palliative care. Six weeks was not enough to reduce the asymmetry of the passive mechanical properties and electrical activity of the trunk and leg muscles, except for the upper and lower trapezius, biceps brachii muscles. A small difference in the asymmetry of the electrical activity and passive mechanical properties of the trapezius, biceps brachii muscles on both sides of the upper and lower parts of the body after six weeks of DNS revealed that the chosen intervention is effective in reducing the asymmetry of the shoulder girdle muscles in children with cerebral palsy.

Conclusions: Although gross motor function did not change during the study, the results of muscle electrical activity and passive mechanical properties revealed the importance of consistency in the application of DNS therapy positions in the rehabilitation process.

ABSTRACTS

Topic: Neurogenetics

EPNS25_cr47 - When genetic testing is negative... think about somatic mosaicism!

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Case report

We present the case of a 10 y.o. male patient, born at 36 weeks of gestational age via emergency cesarean section due to abnormalities in the cardiotocographic trace. At one month of age he was hospitalized for episodes of hypotonia and focal epileptic seizures with gaze deviation. Brain MRI revealed bilateral perisylvian and perirolandic polymicrogyria associated with ectopia of the neurohypophysis. A replacement therapy for panhypopituitarism was started.

At the age of 7 years the physical examination revealed spastic-dystonic hypopostural tetraparesis, delayed language development, neuromotor developmental delay, and dysmorphic features such as left-sided hemihypertrophy of the face, sparse eyebrows, double-row eyelashes, hypertelorism, posteriorly rotated ears, broad nasal bridge and wide forehead, malar hypoplasia, small spaced teeth, hand asymmetry with the left hand being larger, and scoliosis.

He had episodes of head and trunk collapse in the three months prior, consistent with clusters of epileptic spasms confirmed by video-EEG. Brain MRI confirmed the known findings. Array-CGH analysis yielded normal results, and next-generation sequencing (NGS) for cortical malformations performed on a blood sample was also negative.

The patient was started on valproate, vigabatrin, and nitrazepam, resulting in an improvement in spasms. At the age of 10 years, due to the observation of asymmetry in the face and limbs, a karyotype analysis was performed on a skin biopsy. This revealed chromosomal mosaicism with a cell line showing a tetraploid configuration (96,XXYY) in approximately 5% of the analyzed cells, the only world-known case to date according to our knowledge.

Somatic genetic anomalies may occur in any cell of the body, excluding the germline. They arise in the post-zygotic phase and can be associated with both mutations in single genes or chromosomal abnormalities. While germline alterations can be identified by analyzing any tissue, somatic alterations are more challenging to detect. They may not be evident in blood samples and often require cytogenetic or molecular analyses of other tissues.

This result highlights the importance of considering not only germline genetic mutations but also chromosomal and somatic alterations in the diagnostic process when clinical suspect is relevant. In our case, the clinical presentation characterized by asymmetry not only in the face but also observed in MRI imaging suggested the possibility of chromosomal mosaicism.

and now? The child developed a form of LGS on structural/malformative basis with persistence of negative myoclonus and tonic spasms, decreased head control, atypical absences and reflex seizures triggered by noises.

ABSTRACTS

Topic: Neurodevelopmental Disorders / Developmental Neuroscience

EPNS25_cr49 - Unraveling the Uncommon: A Rare Case of Renpenning Syndrome in a Young Boy

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Case report:

Objective:
This case report aims to describe the clinical presentation, diagnostic process, and genetic findings of a child diagnosed with Renpenning syndrome, emphasizing the role of WES in confirming this rare diagnosis, with estimated incidence less than 1 in 1,000,000 live births.

Methods:
We report on a 7-year-old child presenting with multiple congenital haemangiomas on the right lower limb and furthermore asymmetric right lower limb overgrowth, which required further diagnostics with angiography and Doppler ultrasound. Due to showing moderate intellectual disability and display behavioral discrepancies as repetitive- stereotypical movements and speech delay, also neurological evaluation, EEG and MRim was performed. Whole-exome sequencing was indicated to confirm the suspect of the diagnosis.

Results: Lower limb ultrasound Doppler imaging confirmed the presence of venous malformations and angiography further characterized the vascular abnormalities. MRI of the brain was conducted to rule out associated central nervous system involvement, which revealed ventricular dilation. Electroencephalography was also performed due to observed stereotypical movements, but no significant pathologic graphoelements were detected. Whole-exome sequencing was performed and identified a pathogenic variant in the ***PQBP1*** *gene c.459_462del, p.(Arg153Serfs*41*) inherited from his mother, confirming the diagnosis of Renpenning syndrome.

Conclusion:
This rare X-linked genetic disorder caused by mutations in the ***PQBP1*** *gene*, typically presenting with intellectual disability, developmental delays, speech impairments, and stereotypical movements. Due to its rarity and the variability of its clinical manifestations, early diagnosis can be challenging, often requiring advanced genetic testing such as whole-exome sequencing (WES). Although the prevalence is low, identifying the genetic mutation provides crucial insights into the etiology of the disorder, allowing for better-informed management strategies and genetic counseling. Multidisciplinary care is essential to address the developmental and behavioral needs of affected individuals, ultimately enhancing their quality of life and providing support for affected families.

ABSTRACTS

Topic: Cerebrovascular Disorders

EPNS25_cr53 - Mineralizing Angiopathy: A Rare Stroke Etiology Triggered by Minor Head Trauma

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Case report

Pediatric arterial ischemic stroke (AIS) is an uncommon neurological disease with diverse etiologies, the most frequent of which includes infections, vasculopathies, congenital heart diseases, and coagulopathies. Mineralizing angiopathy, an exceptionally rare cause of AIS in children, has gained increasing attention in the recent years. This condition has been predominantly documented in otherwise healthy children who present with acute basal ganglia infarction after a minor head trauma. The underlying pathophysiology is thought to involve the occlusion of calcified lenticulostriate arteries, which demonstrate a heightened vulnerability to mechanical injuries. The characteristic clinical presentation involves acute-onset monoparesis/hemiparesis following minor head trauma in children under two years of age. Loss of consciousness or language disturbance occurred at a lower frequency. Diagnosis is established through the demonstration of basal ganglia calcification on computed tomography(CT). The prognosis is very good, particularly in younger patients. The proposed protective factors include aspirin therapy and the treatment of iron deficiency.

We present the case of a 20-month-old developmentally normal boy diagnosed with mineralizing angiopathy following a second ischemic stroke in the territories of the lenticulostriate arteries. At 10 months of age, he presented to the pediatric neurology clinic with decreased mobility of the left arm. This symptom appeared acutely after a fall from a couch one month earlier and improved gradually. MRI showed chronic ischemic infarction in the inferior right putamen, and extensive etiological investigations were normal. At 16 months of age, he presented with acute decreased mobility in the right upper and lower extremities following a fall from a sofa, along with agitation and excessive crying. Diffusion-weighted MRI revealed acute ischemic infarction in the left putamen, whereas conventional MRI demonstrated no findings indicative of calcification. Cranial CT revealed calcifications in the bilateral basal ganglia, leading to a diagnosis of mineralized angiopathy. Aspirin prophylaxis and physical therapy were initiated and the final clinical examination results were normal.

Mineralizing angiopathy should be considered in the differential diagnosis of infants presenting with acute focal neurological deficits and basal ganglia infarction, particularly after a minor head trauma. In suspected cases, targeted neuroimaging such as cranial CT is recommended along with prophylactic therapy despite the lack of established efficacy in this context.

ABSTRACTS

Topic: Neurodevelopmental Disorders / Developmental Neuroscience

EPNS25_cr54 - Cowden Syndrome, case report

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Case report

Cowden Syndrome (CS) is a rare inherited disorder marked by the presence of hamartomas and an increased risk of cancer. The inheritance is autosomal dominant and 25% of the cases are caused by germline mutations in PTEN.

Disease manifestations occur between the second and third decades of life but can appear at any age. The symptoms are diverse, in children the most common is macrocephaly, Global Developmental Delay (GDD) as well as benign tumors.

A quantitative scoring system for adults and a separate pediatric criteria system have been created for an early detection. However, diagnosis remains a challenge, especially in childhood when hamartomas or other tumors have not yet appeared.

The purpose of this case report is to be aware of the existence of this syndrome during childhood and the importance of its early detection.

The first case is a 2 years old North African boy, referred due to a gait disorder. On examination he presented macrocephaly (+5 SD) and GDD with features of Autism Spectrum Disorder (ASD), as well as inguinal hernia. Brain MRI was requested, which was reported as normal. Initially, it was requested a microarray in which no alteration was detected, and subsequently a Clinical Exome Sequencing (CES), revealing a Pathogenic Variant (PV) in the PTEN gene. The child was followed up by oncologists due to risk of tumor appearance and during surveillance a thyroid nodule was detected at 4 years of age, revealing the biopsy a follicular adenoma. A segregation study was carried out in the parents who did not initially reveal any health problems, and the same PV in PTEN was detected in the father who was diagnosed with intestinal polyposis.

The second case is a 2 years old North African girl, referred for GDD and macrocephaly. During the examination, she presented macrocephaly (+6 SD), supraumbilical hernia and ASD features. In this case, brain MRI revealed the presence of a pinealoma. A genetic panel was requested for Sotos and Becwith-Wiedemann Syndrome, and no alteration was found. Subsequently, in the CES, a PV in the PTEN gene was found.

These two cases are presented to improve the detection of CS in childhood. The main symptoms are macrocephaly, GDD and a type of hernia (last sign not included in the literature).

In conclusion, CS is an underdiagnosed disorder and the early diagnoses is important for a correct management as well as to give genetic counseling.

ABSTRACTS

Topic: Neurogenetics

EPNS25_cr55 - RCC1: An Ultra-Rare Genetic Mimic of Guillain-Barré Syndrome

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Case report

Objectives: Pathogenic variants in the regulator of chromosome condensation 1 (RCC1) gene predispose to abnormal nucleocytoplasmic trafficking during otherwise mild intercurrent infections leading to rapid neurological deterioration characterised by flaccid weakness and areflexia. We present two siblings with rapid and profound flaccid paralysis following a febrile illness, mimicking Guillain-Barre syndrome (GBS).

Methods: Retrospective analyses of case notes and literature review.

Results: Sibling 1 (female) presented at age 18 months following an uneventful birth and developmental progress. After a trivial respiratory illness, she developed rapid paralysis and areflexia requiring ventilation. Her CSF protein was elevated and she was treated as GBS with IVIG and plasma exchange. No clinical improvement was seen and she developed encephalopathy. Brain/spinal imaging, neurometabolic work-up and muscle biopsy studies were unremarkable. Neurophysiology studies were atypical for GBS or infantile neuroaxonal dystrophy. A homozygous variant of RCC1 (Gly43Ser) was identified on genome sequencing. She remains severely hypotonic on assisted ventilation at home.

Sibling 2 (male) presented at the age of 8 months following an otherwise mild upper respiratory tract infection with progressive flaccid weakness, areflexia, and poor feeding developing over the course of two weeks, but did not require ventilation. Brain/spinal imaging, septic screen, and CSF studies were unremarkable. As his older sibling's variant has now been described as pathogenic, due to extensive cellular studies and the description of multiple affected individuals with biallelic variants in RCC1, he underwent targeted genetic testing and was found to have the same variant. At 2-month follow-up, although no longer requiring nasogastric feeding, he remains profoundly hypotonic.

In individuals with biallelic RCC1 variants, a raised CSF protein may be seen and although initial brain MR imaging is usually normal, progressive cerebral atrophy may occur. Nerve conduction studies usually reveal sensorimotor neuropathy. It is not unusual for a diagnosis of GBS to be considered first. Encephalopathy is more common, which may help distinguish from GBS. Limited improvement is seen in some, but recurrent episodes may occur with subsequent infections. There are no proven treatments.

Conclusions : Our cases reflect typical presentations of RCC1-related axonal neuropathy, where rapid and progressive flaccid weakness follows a non-specific infection. Unlike GBS, little to no improvement is seen and there are no proven treatments. RCC1 analysis should be part of the genomic work-up of children presenting with acute neuropathy with or without encephalopathy after an infection, especially where there is limited improvement or recurrent presentations.

ABSTRACTS

Topic: Infectious and Inflammatory Diseases/ Neuroimmunology

EPNS25_cr56 - A Rare Cause of Recurrent Meningoencephalitis: Sjögren Syndrome

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Case report

Sjögren Syndrome(SS) is an autoimmune chronic inflammatory disease that can affect the exocrine glands. Although neurological system involvement is rare, it can be an initial finding. We aimed to present a 16-year-old girl with recurrent meningoencephalitis attacks.

A 16-year-old girl patient presented with vomiting, confusion, and generalized tonic-clonic seizure. In blood tests, leukocyte 15400/mm, hemoglobin 10.3g/dl, hematocrit 33, MCV 86.2, CRP were negative, and serum electrolytes were normal. Cerebrospinal fluid (CSF) protein 68.3 mg/dl, leukocyte count 81, remaining CSF parameters were normal. Cranial MRI showed hyperintensity and edema in bilateral frontal medial sections and extending towards caudate nucleus. Viral markers sent from the respiratory tract and CSF were found to be negative. MOG and NMO antibodies sent for demyelinating involvement were negative. The patient was started on levetiracetam at 30 mg/kg/day and was given intravenous immunoglobulin (IVIG) at 2 g/kg with a preliminary diagnosis of autoimmune encephalitis. After IVIG treatment, clinical findings completely improved and cranial MRI taken 2 weeks later showed complete recovery. The patient presented with a second meningoencephalitis attack 7 months later, which started with headache and fever. In the following 5 months, she presented with 5 more meningoencephalitis attacks. Different findings such as ataxia, nystagmus, double vision, blurred vision, fever, seizure, and confusion accompanied the attacks. In each attack of the patient, cranial MRI showed involvement in different regions (frontal region, temporal region, basal ganglia, cerebellum, brainstem, leptomeningeal). Electroneuromyelography was found to be compatible with bilateral axonal neuropathy in the lower extremities. Hemogram results during each attack were consistent with chronic disease anemia. Blood tests showed Ro52, Ama-M2 and Dfs 70 were positive. Schirmer test was negative but salivary gland biopsy resulted in Chisholm score 4.The patient was diagnosed with Neuro-Sjögren's disease with recurrent meningoencephalitis attacks. IVIG treatment was given at each attack. Complete clinical and radiological recovery was observed in all attacks until the last attack. After the diagnosis of Sjögren's, cyclophosphamide and steroid treatment was added to the patient's treatment. In the last attack, rapid worsening of respiratory symptoms was observed and the patient was intubated and taken to intensive care. This attack didn‘t respond to IVIG treatment and the patient was treated with plasmapheresis.

The most common neurological manifestation of SS is peripheral neuropathy, but it can rarely cause central nervous system involvement. As a rare cause of recurrent meningoencephalitis in the pediatric age group, SS should be kept in mind.

ABSTRACTS

Topic: Miscellaneous

EPNS25_cr57 - Contaminated drugs beyond the tennis world: effects of unintentional use and withdrawal of tiapride-contaminated vigabatrin in children with epilepsy related to TSC.

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Case report

Objectives: In September 2023 the Polish Ministry of Health warned that two lots of Sabril (vigabatrin) powder for oral solution and tablets, released in 2021, contained trace amounts of tiapride. Tiapride is considered a safe treatment for psychiatric and neurological indications, such as agitation or movement disorders. However, it is not recommended in pediatric patients due to its antagonistic effect on prolactin release and therefore – possible inhibition of the process of puberty. Here we report the symptoms related to intake and sudden withdrawal of tiapride-containing-vigabatrin in pediatric patients with tuberous sclerosis complex.

Methods: We identified three children with TSC who had been treated with contaminated vigabatrin lots between December 2021 and July 2023. The effects of the exposure to contaminated medication and the rapid withdrawal of tiapride were assessed. The patients received respectively 900 tablets (equal to 450 000 mg of vigabatrin), 550 sachets (equivalent to 275 000 mg of vigabatrin), and 150 sachets (equivalent to 75 000 mg of vigabatrin) of tiapride-contaminated Sabril.

Results: The caregivers of the patients treated with contaminated vigabatrin did not report any adverse events during the exposure to the drug. However, when the contaminated lots were withdrawn from the market, all patients experienced symptoms possibly related to sudden tiapride withdrawal. The reported symptoms included increased frequency and severity of seizures, significant behavioral problems, insomnia, weight loss, and secondary amenorrhoea. One patient required admission to the intensive care unit due to drug-resistant status epilepticus.

Conclusions: Sudden and unexpected deterioration of seizure control and behavioral problems in patients treated with antiseizure drugs might be related to the adverse events of unintentional contamination of medications. Our observations suggest that rapid withdrawal of tiapride, even administered in low doses, may result in significant and life-threatening deterioration in patients with epilepsy.

ABSTRACTS

Topic: Epilepsy: Medical and Surgical treatment

EPNS25_cr60 - Tocilizumab in acute phase febrile infection-related epilepsy syndrome: a case report

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Case report

Febrile infection-related epilepsy syndrome (FIRES) is a subcategory of new-onset refractory status epilepticus (SE) characterized by super-refractory SE in previously healthy children without an identifiable cause. The pathogenesis is unknown, but a central role of innate immune system dysregulation has been proposed with elevated cytokines. Tocilizumab (TCZ), an interleukin-6 receptor antagonist, has been previously reported as effective in acute and chronic phase of FIRES. We report a case of FIRES with improvement after TCZ infusion.

A previously healthy 17-year-old girl presented with repeated generalised tonic-clonic (GTC) seizures following 6 days of upper respiratory infection with brief febrility. First and second line antiseizure medications (ASMs) were ineffective, therefore patient was admitted to the Intensive care unit (ICU) and intubated. Initial EEG showed electrographic SE. MRI of the brain was normal. Infectious work-up was negative. Cerebrospinal fluid was unremarkable. Oncological screening was done: gynaecological USG showed possible teratoma in right ovary, which was laparoscopically removed and histologically benign. PET-CT showed no abnormalities. Autoimmune and paraneoplastic antibodies were negative. Workup for metabolic diseases and whole-exome sequencing was undiagnostic. Immunotherapy was started with intravenous (IV) methylprednisolone, followed by plasma exchange, IV immunoglobulin, anakinra and rituximab due to suspicions of FIRES, but without improvement. Despite receiving extensive ASMs, the patient had multifocal electrographic and clinical seizures from both hemispheres. After 63 days in ICU, the patient received IV TCZ 8mg/kg. A week later, the patient started reacting to pain stimuli, executing voluntary movements. EEG showed decrease in epileptiform activity, improvement in background activity. Neurological status gradually improved and she was discharged with Glasgow Coma Scale 15. However, significant cognitive impairment remained (IQ 50). She received topiramate, phenobarbital and lacosamide for seizure control. 3 months later, she had repeated GTC seizures and received another dose of TCZ.

Our case highlights the potential efficacy of tocilizumab in acute phase FIRES. Immunotherapy should be promptly initiated in FIRES patients because ASMs alone are not sufficient for seizure control. Generally, the outcome of FIRES is poor with majority of survivors having acquired cognitive disability and refractory epilepsy.

ABSTRACTS

Topic: Infectious and Inflammatory Diseases/ Neuroimmunology

EPNS25_cr62 - Epstein–Barr virus meningoencephalitis in a pediatric patient: A Case Report

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Case report

Epstein-Barr virus (EBV), a widely distributed herpesvirus, is transmitted through intimate contact among susceptible individuals and asymptomatic carriers. It is the principal cause of infectious mononucleosis and can persist asymptomatically for life in nearly all adults. Primary infection with EBV may lead to a variety of clinical manifestations, complications, and several malignancies. Additionally, EBV has been recognized for its potential to cause neurological damage, with infections linked to various neurological manifestations that can range in severity, including encephalitis, meningitis, myelitis, and polyradiculitis.

A clinical case is presented involving a 7-year-old boy who exhibited symptoms such as dizziness, diplopia, fever (≥38°C), headache, sore throat, and dry cough. An initial evaluation revealed horizontal binocular nystagmus when looking left, right-sided anisocoria, and instability during the Romberg test. A head CT scan was unremarkable, leading to hospitalization with a diagnosis of left-sided vestibular neuritis.

On the second day of hospitalization, a brain MRI returned normal results, and treatment with prednisolone (1 mg/kg once daily) commenced. However, by day four, the patient developed febrile spikes (up to 40°C) and vomiting, although dizziness and double vision had improved. Meningeal signs were absent, and a lumbar puncture demonstrated cytosis (151 cells) with a predominance of lymphocytes.

By day seven, the boy's condition worsened, displaying increased lethargy and developing ataxia, prompting the initiation of intravenous immunoglobulins (0.4 g/kg/day), suspecting autoimmune encephalitis. On day eight, persistent fever and new pink skin spots emerged, with subsequent tests including repeat head MRI, chest CT, and bone marrow biopsy yielding normal results. A repeat lumbar puncture indicated undetectable EBV viral load in the cerebrospinal fluid (CSF) and a decrease in cytosis to 26 cells, with the autoimmune encephalitis panel returning negative.

On day fifteen, the child exhibited euphoric behavior and experienced a brief episode of muscle twitching in the right upper arm. An EEG indicated encephalopathy, leading to the administration of methylprednisolone (30 mg/kg/day) due to concerns of encephalitis. Imaging results revealed focal thalamic and temporal lesions consistent with encephalitis. PCR analysis of lumbar puncture findings validated the diagnosis of EBV meningoencephalitis.

The boy's condition improved, and he reported no further complaints or mood elevation; the muscle twitching did not recur. This clinical case highlights the challenges associated with diagnosing EBV encephalitis, a rare yet significant consideration, emphasizing the necessity to account for the impact of such infections in pediatric populations.

ABSTRACTS

Topic: Epilepsy: Medical and Surgical treatment

EPNS25_cr64 - Cerebral Folate Transport Deficiency and Epilepsy in Pediatric Patients

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Case report

Introduction: FOLR1 related cerebral folate transport deficiency (FOLR 1 CFTD), resulting from loss of function of the folate receptor alpha (FOLR1) protein, causes cerebral folate deficiency in the absence of systemic folate deficiency. Cerebral folate transport deficiency is rare, treatable neurodegenerative disorder which causes intractable seizures Treatment with 5 formyltetrahydrofolate 5 formylTHF also known as folinic acid or leucovorin can result in substantial improvement in neurologic findings when started at a young age. Only few case reports are available and there is a paucity of literature regarding this disorder in Turkish children.

Objective: Hence, we present to report five cases of genetically confirmed Turkish children with FOLR 1 CFTD. In this study, we aimed to share the treatment of patients with epilepsy and the effectiveness of vagal nerve stimulation (treatment, which will be included in the literature for the first time in FOLR 1 CFTD.

Case Report: Five pediatric patients who admitted to the our pediatric neurology and pediatric metabolism outpatient clinics and whose genetic diagnosis of FOLR 1 CFTD was confirmed were included in the study. All patients had drug refractory seizures There were generalized abnormalities in the EEG of all patients. 2 Upon diagnosis, all patients were started on oral folinic acid In two of the patients, there was no significant regression in seizures despite 6 months of treatment Vagal nerve stimulation (VNS) was applied to these patients Seizures significant decreased in these two patients after the VNS procedure.

Conclusion: FOLR1 CFTD is an important, rare and treatable clinical condition It should be taken into consideration in cases with refractory seizures, ataxia, neuromotor developmental delay, and hypomyelination detected on MRI. In this study, we aimed to contribute to this important treatable clinical condition by presenting Turkish patients. In addition, our study is the first article in which VNS was applied in the treatment of CFTD with current literature knowledge.

ABSTRACTS

Topic: Neurogenetics

EPNS25_cr65 - Expanding the Clinical Spectrum of TUBGCP6-Related Disorders

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Case report

Objectives: *TUBGCP6* gene (22q13.33) encodes tubulin gamma complex-associated protein 6. TUBGCP6 is a phosphorylation target of Pole-Like Kinase 4 (PLK4), a critical regulator of centriole biogenesis. Mutations in *TUBGCP6* are associated with Microcephaly and Chorioretinopathy, Autosomal Recessive 1 (MCCRP1), a rare disorder characterized by microcephaly, ophthalmological anomalies, dysmorphisms, developmental delay, and neuroimaging abnormalities. To date, only 18 cases of *TUBGCP6* mutations have been described in the literature. Here, we report a novel homozygous *TUBGCP6* variant, c.3914C>A (p.Ala1305Glu), and clinical phenotype.

Methods: Whole exome sequencing was performed on DNA extracted from the blood of the trios (parents and proband). Clinical, neuroimaging, and neurometabolic data were analyzed and compared to a literature review on *TUBGCP6*-related disease.

Results: The patient is a 5-year-old boy born at term to consanguineous parents from Bangladesh, following an uncomplicated pregnancy. From early infancy, he presented global developmental delay, and neurosensorial hearing loss. At 8 months, he developed infantile spasms, effectively managed with vigabatrin and topiramate. Additional clinical features included irritability, sleep disturbances, feeding difficulties, and motor stereotypies. Physical examination revealed intermittent esotropia, 4 *café au lait* spots, and dysmorphic traits such as thick eyebrows, dorsal hypertrichosis, and camptodactyly. Video-EEG revealed an abnormal background activity with interictal epileptiform discharges, while nerve conduction study showed mild demyelinating sensory neuropathy. Brain MRI detected hypoplasia of the corpus callosum and brainstem, and fundoscopy revealed optic disc pallor. Trio Whole-Exome Sequencing (WES) identified a novel *TUBGCP6* variant, c.3914C>A (p.Ala1305Glu), classified as a highly suspicious Variant of Uncertain Significance (VUS).

Conclusions: This case provides new insights into *TUBGCP6*-related disorder by reporting a novel TUBGCP6 variant and not previously reported features. These include the atypical brain MRI finding of brainstem hypoplasia, sensorineural hearing loss, infantile spasms, and sensory demyelinating neuropathy. These findings expand the clinical understanding of the disorder, emphasizing the variability in its expression.

ABSTRACTS

Topic: Neurogenetics

EPNS25_cr66 - Early Infantile Drug Resistant Epilepsy in Two Infants Caused by Pathogenic Mutation in the ASNS Gene

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Case report

Introduction: Asparagine synthetase deficiency (ASNSD) is a rare neurometabolic disorder caused by variants in the ASNS gene. It is characterized by microcephaly, severe developmental delay, and spastic quadriplegia. Seventy-one percent of ASNSD patients die in early infancy.

Objective: In this study, we aimed to raise awareness about this extremely rare condition in two Turkish patients with drug-resistant epilepsy, investigate the underlying mechanisms of the disease, and explore the mutations associated with it.

Case Presentation:

Twenty five-day-old male patient presenting with microcephaly, hyperexplexia, severe psychomotor retardation, hypotonia, spastic tetraplegia, and polydactyly. The patient was born at 38 weeks of gestation to healthy parents who were first-degree cousins. Due to dysmorphic features and respiratory distress required 20 days of NICU care. Seizures began three months after birth. Initially, seizure semiology included bilateral tonic-clonic and myoclonic seizures, which later evolved into epileptic spasms. The patient was drug resistant epilepsy and showed no significant response to a ketogenic diet. Whole-exome sequencing identified a homozygous autosomal recessive pathogenic variant in the ASNS gene: c.1193A>G (p.Tyr398Cys) (rs1166271142).

Our second patient involved a patient presenting at 15 days of age with hyperexplexia, microcephaly, severe psychomotor retardation, hypotonia, and spastic tetraplegia. This patient had drug-resistant epilepsy despite receiving appropriate doses of multiple conventional antiseizure medications. Brain MRI showed diffuse cerebral and cerebellar atrophy with a markedly hypoplastic and thinned corpus callosum. Routine laboratory tests were normal. Whole-exome sequencing revealed a "double trouble" scenario, with a homozygous autosomal recessive pathogenic variant in the ASNS gene: c.1193A>G (p.Tyr398Cys), and an autosomal dominant heterozygous pathogenic variant in the STXBP1 gene: c.324C>T (p.Asp108=). The patient, who did not respond to treatments including ketogenic diet, died at 48 months.

Conclusion:

In this study, we emphasize that Asparagine Synthetase Deficiency should always be considered in infants presenting with progressive psychomotor retardation, microcephaly, hyperexplexia, drug-resistant epilepsy, and dysmorphic features. Additionally, we have, for the first time in the literature, identified the coexistence of mutations in two different genes, ASNS and STXBP1, both contributing to seizures and psychomotor retardation in the second patient.

ABSTRACTS

Topic: Cerebrovascular Disorders

EPNS25_cr67 - Mechanical thrombectomy (MT) in a 10-year-old with acute ischemic stroke (AIS) and background of Langerhans Cell Histiocytosis (LCH)

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Case report

Background: Paediatric acute ischemic stroke (AIS) causes significant disability and mortality. In the acute setting the underlying cause of AIS is often unclear. The challenge lies in rapid management decision, including mechanical thrombectomy (MT) and medical management options.

Objective: We present a complex scenario of AIS who underwent MT under 6 hours of presentation with favourable outcome and emphasise the time critical MDT approach.

Case Presentation: A 10-year-old girl with a history of LCH in remission presented with the history of mild abdominal trauma followed by 3 days of nausea and headaches and sudden onset right-sided hemiparesis, aphasia, and GCS 8/15, NIHSS score 26. CT head showed early left middle cerebral artery (MCA) territory ischaemia. CT angiogram showed tapering of the left internal carotid artery (ICA) suggestive of likely dissection or delayed in-flow. Echocardiography was normal. CT chest demonstrated aspiration pneumonia. Infectious parameters were mildly elevated. Following Multidisciplinary team discussion huddle, she underwent successful MT at 5 hours post- presentation. There was carotid-T occlusion beyond the ophthalmic artery and partially collapsed ICA lumen proximally, with signs of vasospasm and no evidence of dissection. She was commenced on Aspirin 5mg/kg, Ceftriaxone for infection and observed on PICU overnight. GCS improved to 13/15 as well as speech and power 4/5 MRC, NIHSS score 4. MR angiography post MT showed Left ICA and MCA recanalization with no focal arterial abnormality and MCA territory acute ischemia. At this stage aetiology of AIS was presumed unlikely to be related to LCH and a definite cause for her stroke could not be identified. Thrombophilia came back unremarkable. She was transferred to her local hospital for further neurorehabilitation.

Conclusion: This case demonstrates the potential benefit of MT for AIS caused by large vessel occlusion in paediatric stroke early within the treatment window. There is an opportunity to collect evidence for observational study to record the number of paediatric strokes presenting within time window and reperfusion therapies (lysis +/- MT) should be considered where appropriate in paediatric neuroscience centres with A&E and adult stroke infrastructure.

ABSTRACTS

Topic: Epilepsy: Diagnosis and Investigations

EPNS25_cr68 - Tuberous sclerosis (TS) with autosomal dominant nocturnal frontal lobe epilepsy (ADNFLE) in a child

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Case report

Objectives: Tuberous sclerosis complex (TSC) is an autosomal dominant multisystem disorder caused by mutations in the *TSC1* or *TSC2* genes. The *KCNT1* gene is associated with autosomal dominant nocturnal frontal lobe epilepsy (ADNFLE). While seizures are common in TSC, ADNFLE is rare. We report a case of TSC with ADNFLE caused by *TSC1* heterozygous and *KCNT1* heterozygous mutations.

Methods: A 5-year-old boy with recurrent nocturnal seizures was evaluated. Clinical history, neurological examination, electroencephalography (EEG), genetic testing, and imaging studies were performed.

Results: The patient presented with recurrent seizures that are without loss of consciousness and dazed for about 30 seconds, only eyelid blinking at waking, or clonic movements of 15~20 seconds with loss of consciousness during sleep. Inter-ictal EEG showed 9-10Hz spike discharges from left and right central area for 3 seconds, followed by generalization of 7-8 spike discharges for 13 seconds. Continuous EEG showed frequent spike, spike and wave discharges from left or right frontal area and background attenuated followed by fast frequency activities from right central area spreading to both temporal areas for 90 seconds during sleep. We initially started levetiracetam but it was ineffective. So we discontinued levetiracetam and added oxcarbazepine, topiramate and valproic acid. Despite this, seizures persisted until doses were escalated (topiramate 75mg bid, oxcarbazepine 360mg bid, valproic acid 400mg bid), achieving seizure control for approximately one year. The physical examination revealed depigmented nevus on the trunk. The Next-Generation Sequencing panel identified *TSC1* heterozygous mutation (c.733C>T, p.Arg245Ter) and *KCNT1* heterozygous mutation (c.976C>G, p.Pro326Ala). Familial mutation analysis revealed that the *KCNT1* mutation was inherited from the mother, while the father had no mutations. Brain magnetic resonance imaging showed focal T2/FLAIR hyperintense lesion involving cortex, and subcortical white matter of both fronto-parietal lobes and left precentral gyrus.

Conclusions: This case demonstrates a rare combination of TSC with ADNFLE caused by both *TSC1* and *KCNT1* mutations.

ABSTRACTS

Topic: Neurometabolic Disorders

EPNS25_cr69 - Expanding the Spectrum of Leber's Hereditary Optic Neuropathy: A Pediatric Case with Cervical Spinal Cord Lesion

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Case report

Objectives:
We report a pediatric case of Leber's hereditary optic neuropathy (LHON) with spinal cord involvement, which is atypical for classic LHON and expands the clinical spectrum of LHON Plus Syndrome.

Methods:
All patient information was obtained from the hospital's data system.

Results:
This report describes the case of a 6-year-old male with subacute vision loss in the right eye and blurred vision in the left eye accompanied by spinal cord involvement at the C3-C6 levels on magnetic resonance imaging (MRI), which is atypical for classic LHON. Spinal and cranial MRI was taken to differentiate demyelinating optic neuropathies (MOGAD, NMO, MS) in the differential diagnosis of optic neuropathy. The patient's management included high-dose intravenous corticosteroids and plasma-exchange therapy, which failed to yield clinical improvement. Given the family history of a distant maternal relative previously diagnosed with LHON, genetic testing was conducted to confirm the diagnosis. Genetic analysis revealed a homoplasmic mt.11778G>A mutation in ND4 that is strongly associated with LHON. The presence of spinal cord involvement in this patient, in conjunction with optic neuropathy, led to the diagnosis of LHON Plus Syndrome. The diagnosis of LHON was genetically confirmed, and spinal involvement was also considered as LHON plus. Idebenone treatment was initiated at 900 mg/day and the patient was monitored closely. Genetic analysis of the patient's mother revealed a similar homoplasmic variant. The mother, who was asymptomatic, was closely monitored as a presymptomatic carrier.

Conclusions:
This case report of a 6-year-old male with LHON Plus Syndrome, characterized by severe visual impairment and atypical spinal cord involvement, shows the expanding clinical spectrum of LHON. Although LHON is conventionally characterized by isolated optic neuropathy, the presence of spinal cord involvement highlights the critical need for a thorough systemic assessment, encompassing neuroimaging and specific tests for alternative etiologies, to rule out conditions, such as NMO spectrum disorder or MOGAD. Pediatricians, pediatric neurologists, and ophthalmologists hould include LHON in their differential diagnoses when evaluating patients with unexplained optic neuropathy even when additional neurological symptoms or imaging findings are present.

ABSTRACTS

Topic: Neurorehabiltation

EPNS25_cr70 - The use of Hammersmith Scale in a Case of Non-Neurological Floppy Infant Syndrome in Kyrgyzstan

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Case report

Objective: This case study aims to demonstrate additional uses of the Hammersmith Scale in the assessment of floppy infant syndrome (FIS) and to emphasize the importance of evidence-based medicine (EBM), particularly in avoiding unnecessary medication prescriptions.

Methods: The patient is a 1-year-and-1-month-old girl presenting with complaints from her mother of a large head, delayed motor development (unable to stand or sit without support, not crawling), muscle weakness in both upper and lower extremities, a skin rash, and poor appetite, as reported by her mother. The child had been diagnosed with "Encephalopathy of combined genesis" at age 6 months and had been monitored by a regional neurologist. Concerned about her large head circumference, she underwent neurosonography (moderate enlargement of lateral ventricles) and MRI (normal findings). Based on neurosonography results, she was prescribed acetazolamide (2 mg/day) for six months. Additionally, the child was exclusively breastfed and had not been consuming solid foods due to refusal to eat. Upon assessment, the child scored 46 points on the Hammersmith Scale, showing no signs of neurological pathology. Head circumference was measured at 48 cm, which is +2 standard deviations according to the WHO growth chart. The head circumference at 1 month was recorded as 38.5 cm (+2 CO). The parents also reported that the child's head appeared unusually large. Further evaluations included a pediatric examination, which revealed iron deficiency anemia and hypocalcemia. Peripheral nervous system disorders were excluded. Following these findings, acetazolamide was discontinued, and the child was prescribed motor therapy using the Feldenkrais Method. Nutritional counseling was provided, and iron supplementation was prescribed by the pediatrician.

Results: One month after discontinuing acetazolamide, the child received treatment for anemia, improved nutrition, and rehabilitation. The child's Hammersmith Scale score increased to 69, indicating significant improvement in motor development. Her head circumference remained at 48 cm during the follow-up examination. According to the mother, the child became more active, and her appetite improved.

Conclusion: This case highlights the importance of evidence-based medicine in avoiding unnecessary drug prescriptions. The Hammersmith Scale proved useful in monitoring a child without neurological pathology, offering the mother a clear measure of progress. The case also underscores the value of a multidisciplinary approach, incorporating nutritional support and rehabilitative therapy, in achieving positive developmental outcomes, even in the absence of a definitive neurological diagnosis.

ABSTRACTS

Topic: Neurogenetics

EPNS25_cr71 - Biallelic Variants in the COLGALT1 Gene Cause Multiple Episodes of Bilateral Basal Ganglia Hemorrhage with White Matter Lesions Triggered by Dengue Infection: A Case Report

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Case report

Objective To describe the clinical presentation of a patient with brain small vessel disease 3 (BSVD3, OMIM# 618360) caused by biallelic variants in the *COLGALT1* gene, characterized by bilateral basal ganglia hemorrhages and white matter lesions. This report highlights evidence suggesting that dengue infection triggered this phenomenon.

Method This is a case report describing the phenotypic feature of a patient with brain small vessel disease 3, supported by an analysis of trio exome sequencing (Trio-ES).

Results We describe the clinical course of a 15-year-old girl with multiple episodes of bilateral basal ganglia hemorrhage and associated white matter lesions. The first episode occurred at 9 years of age, presenting with a severe headache without focal neurological deficits. During this episode, the patient was diagnosed dengue fever but platelet count was normal. A brain MRI revealed a deep bilateral basal ganglia hemorrhage with bilateral diffuse leukodystrophy. Over time, the patient experienced poor school performance and episodic headaches alleviated by oral acetaminophen.

At age 15, the patient presented with worsening headaches. The patient retained normal motor function. Cranial nerves and cerebellar function were intact. The WISC-IV test revealed a full-scale IQ of 73 (borderline). A brain MRI illustrated multiple petechial hemorrhages in the white matter and basal ganglia, acute to subacute left caudate hemorrhage with rupture into the left lateral ventricle, and a large confluent hyperintense T2/FLAIR signal involving bilateral cerebral white matter and bilateral basal ganglia. Trio-ES revealed compound heterozygous variants [c.261-1G>A];[c.1295T>C p.(Leu432Pro)] in the *COLGALT1* gene, consistent with a diagnosis of brain small vessel disease 3 (BSVD3).

Conclusion This report demonstrates the critical role of genetic testing in children presenting with recurrent basal ganglia hemorrhages accompanied by white matter lesions, where dengue infection triggered vascular damage. Recognizing the phenotype of *COLGALT1* variants enables early diagnosis and stroke prevention in the patient's future life.

ABSTRACTS

Topic: Infectious and Inflammatory Diseases/ Neuroimmunology

EPNS25_cr72 - Double Seropositivity in Autoimmune Neuropathy: Diagnostic Challenges and Treatment Response

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Case report

A previously healthy 14-years-old boy presented with progressive ascending limb weakness together with complaints of abnormal sensations and pain, and continence issues starting one week following a flu-like infection. Clinical examination revealed muscle weakness, areflexia and an ataxic gait. Cerebrospinal fluid analysis showed albuminocytological dissociation and electromyography revealed an acute inflammatory demyelinating polyneuropathy leading to the diagnosis of Guillain-Barré syndrome (GBS), later confirmed by positive antiganglioside antibodies. Despite initial treatment with intravenous immunoglobulins (IVIg) the patient's condition deteriorated, rendering him wheelchair bound. Therapy was escalated with nine sessions of plasma exchange, followed by a second IVIg course and a multidisciplinary rehabilitation program. Over several months, the patient showed gradual improvement including regained continence, pain relief, and mild recovery of muscle strength. However, he remained predominantly wheelchair bound. Follow-up spinal MRI revealed persistent pathological enhancement of the cauda equina nerve roots and conus medullaris, consistent with GBS, along with increased leptomeningeal enhancement throughout the spinal cord, indicating ongoing inflammation. Extended inflammatory screening identified contactin-1 autoantibodies, prompting a revised diagnosis of autoimmune nodopathy (AN). Treatment with steroids followed by rituximab led to significant recovery. Within one month, the patient resumed walking and, achieved unaided ambulation within six months. Subsequent MRI confirmed recovery, showing a marked reduction in contrast enhancement.

Conclusions

Autoantibody-associated disorders targeting paranodal proteins, such as contactin-1, are classified under autoimmune nodopathies (AN). Clinically, AN overlaps with chronic inflammatory demyelinating polyradiculopathy, although GBS-like presentation, particularly with contactin-1 autoantibodies, is reported. To our knowledge, double seropositivity for both paranodal and ganglioside autoantibodies has not previously been described and complicated the initial diagnosis in the presented case. AN is associated with aggressive onset, severe neurological deficits, and poor IVIg response. However, with intensive treatment at onset, preferable with rituximab, long-term prognosis is good, underscoring the importance of prompt and accurate diagnosis.

ABSTRACTS

Topic: Neurogenetics

EPNS25_cr75 - A Case Report on Late Infantile-Onset Metachromatic Leukodystrophy with a Novel ARSA Gene Mutation

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Case report

Objectives: This study presents a rare case of Late Infantile-Onset Metachromatic Leukodystrophy (MLD) in a pediatric patient, highlighting the significance of early diagnosis and genetic confirmation in managing neurodegenerative conditions.

Methods: A retrospective case study was conducted involving a child with a 2-month history of progressive loss of motor skills, speech regression, nystagmus, spasticity, hyperreflexia, and a positive Babinski sign. Neuroimaging and genetic testing were performed to confirm the diagnosis. The patient received symptomatic treatment with baclofen for spasticity and valproic acid for seizures. Follow-up assessments monitored disease progression and treatment adjustments.

Results: Neuroimaging revealed symmetric white matter abnormalities consistent with leukodystrophy. Genetic testing identified two pathogenic variants in the ARSA gene, confirming Late Infantile-Onset MLD. Five months post-diagnosis, the patient exhibited severe spastic diplegia, daily myoclonic seizures, and intermittent opisthotonic posturing. The family was educated about disease progression, and options for improving the patient's quality of life were discussed.

Conclusions: This case underscores the need for a high index of suspicion for neurodegenerative disorders in children with progressive neurological decline. The confirmation of MLD through genetic testing emphasizes the importance of precision molecular diagnostics in managing rare diseases. Currently, there is no curative treatment for MLD; however, early intervention with hematopoietic stem cell transplantation may slow disease progression. Regular follow-up and supportive care are essential for optimizing the patient's quality of life. This report contributes to the understanding of MLD and highlights the role of genetic testing in diagnosing and managing this condition effectively.

ABSTRACTS

Topic: Neurogenetics

EPNS25_cr77 - A family with a novel CACNA2D2 mutation presenting with different clinical findings within the same family

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Case report

Calcium Voltage-Gated Channel Auxiliary Subunit Alpha2delta 2 (CACNA2D2) gene encodes the alpha-2/delta subunit of the voltage-dependent calcium channel complex which tightly regulate the (Ca2+) entry into excitable cells. Biallelic mutation of CACNA2D2 gene is associated with cerebellar atrophy with seizures and variable developmental delay and early infantile epileptic encephalopathy. In recent years, it has been reported that synaptopathies are also effective in the pathogenesis of diseases associated with CACNA2D2 mutation. To date, five cases of infantile-onset epilepsy and cerebellar atrophy linked to bi-allelic mutations in CACNA2D2 have been reported in unrelated families.
We present clinical, genetic and radiological findings of two affected siblings with a novel homozygous CACNA2D2 mutation

The currently 19-year-old female patient first presented with fever-triggered epileptic seizures when she was 4 months old. Her family history was remarkable with a cousin marriage between her parents. She is currently wheelchair dependent and being followed up with refractory epilepsy and ataxia. All metabolic tests, karyotype, microarray and WES analysis performed until 2023 were normal. Brain MRI is characterized by marked atrophy of the cerebellar hemispheres and vermis. Her sister, who is 11 years younger, presented with a complaint of seizures triggered by fever when she was 2 months old. She is currently 8 years old, seizure-free with levetiracetam and able to walk with mild cerebellar ataxia. When WES was reanalyzed for ataxia and epilepsy in 2023, the novel homozygous variant NM_006030.4 c.632C>T (p.Pro211Leu) was detected in the CACNA2D2 gene in both siblings and parents were carriers.

Conclusion

CACNA2D2 should be considered as a differential diagnosis in individuals with cerebellar dysfunction and seizure that begin in the first year of life in those with a history of consanguineous marriage. However, Valence et al reported a patient with normal cognitive development and only 1 febrile seizure suggesting significant clinical variability of this disorder. CACNA2D2 c.632C>T (p.Pro211Leu) pathogenic mutation was reported for the first time in the literature. While the older sibling is characterized by refractory epilepsy and severe ataxia, the younger sibling is seizure-free only one antiepileptic drug and has mild ataxia. In other words, CACNA2D2 c.632C>T (p.Pro211Leu) mutation can present with different clinical presentations even within the same family.

ABSTRACTS

Topic: Neurodevelopmental Disorders / Developmental Neuroscience

EPNS25_cr78 - Do not Forget to Measure the Head: Hydrocephalus Can Phenotypically Mimic Developmental Coordination Disorder

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Case report

Objectives: Developmental Coordination Disorder (DCD) is a neurodevelopmental condition characterized by delayed motor development, poor motor skill acquisition, and impaired coordination from an early age. The diagnosis of DCD requires the exclusion of neurological conditions, including structural brain abnormalities, which could explain the observed phenotype. However, these neurological conditions may present with symptoms that closely resemble DCD, complicating the differential diagnosis. The aim of this paper is to highlight the possibility of hydrocephalus to phenotypically resemble DCD, and the importance of thorough diagnostic evaluation, including (longitudinal) head circumference (HC) measurements, in identifying treatable neurological conditions that mimic DCD.

Methods: In this retrospective case study, we describe a child in whom an initial diagnosis of DCD was withdrawn following the identification of acquired hydrocephalus.

Results: A seven-year-old girl, initially diagnosed with DCD, was referred to the Pediatric Neurology Clinic after experiencing status epilepticus. Despite normal motor milestones in infancy, her gait was stiff, with frequent falls. Cognitive and language development were normal. HC measured +0.00 SD at the age of 15 months. Due to gross motor impairments and the absence of objective neurological abnormalities, she was diagnosed with DCD at the age of six years. At that time, her HC was not measured. After the status epilepticus, brain imaging revealed hydrocephalus caused by an arachnoid cyst in the interpeduncular cistern, compressing adjacent structures. Neurological examination showed frontal bossing, a stiff gait, mild hypertonia, brisk reflexes, and esotropia. HC had increased to +2.25 SD. The diagnosis of DCD was withdrawn, and an endoscopic fenestration of the cyst was performed in consultation with the family.

Conclusions: In this patient, secondary macrocephaly was the clinical cue distinguishing acquired hydrocephalus from DCD. This study is the first to report hydrocephalus in a patient previously diagnosed with DCD, emphasizing the importance of considering underlying neurological diagnoses in children with phenotypes resembling DCD. Although children with DCD can present with minor neurological signs, the presence of macrocephaly and/or pronounced neurological impairments is generally indicative of an alternative neurological diagnosis. As such, in children with phenotypes resembling DCD, longitudinal HC measurements, along with neuroimaging when necessary, can aid the identification of treatable underlying neurological conditions like hydrocephalus, ensuring accurate diagnosis and timely intervention.

ABSTRACTS

Topic: Neurodevelopmental Disorders / Developmental Neuroscience

EPNS25_cr79 - Hemiplegic migraine induced by SON mutations in ZTTK syndrome: An evidence-based case report

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Case report

Objectives

To report recurrent hemiplegic migraine episodes in a patient with SON-related Zhu-Tokita-Takenouchi-Kim (ZTTK) syndrome and explore potential mechanistic links through literature review.

Methods

An evidence-based case report via an unsystematic literature review was conducted to explore the association between ZTTK syndrome and recurrent hemiplegic migraine.

Results

A 16-year-old girl with ZTTK syndrome presented with 4 episodes of left-sided weakness, facial droop, and recurrent headaches over 3 years, consistent with hemiplegic migraine. These episodes resolved spontaneously without permanent deficits. The patient exhibited global developmental delays and had heterozygous mutations in the SON and CHD7 genes. Neurological imaging, including CT, MRI, and CT angiography, revealed no structural abnormalities, suggesting a functional aetiology. Treatment with propranolol reduced episode frequency and severity.

ZTTK syndrome, first described in 2016, arises from heterozygous loss-of-function variants in the SON gene, which encodes an RNA-splicing regulator critical for development. SON mutations disrupt RNA splicing, voltage-gated ion channels, neurotransmitter release, and synaptic plasticity, contributing to neural hyperexcitability and predisposing to hemiplegic migraine. CHD7 mutations may amplify these effects. SON mutations also downregulate PRRT2, a known contributor to hemiplegic migraine.

Therapeutic options include beta-blockers, such as propranolol, that may stabilise neural excitability; calcium channel blockers; antiepileptics; and lifestyle modifications. Early intervention targeting hyperexcitability may mitigate recurrent episodes. Multidisciplinary care, involving neurology, developmental paediatrics, and physiotherapy is crucial for managing long-term neurodevelopmental outcomes. Regular follow-ups and early cognitive assessments can guide individualised educational plans.

Future research into gene-targeted therapies and neuromodulation may expand treatment options. Longitudinal studies are needed to establish the pathophysiology and evaluate current interventions.

Conclusions

This case highlights a link between ZTTK syndrome and hemiplegic migraine. Early diagnosis and propranolol treatment may reduce neurological symptoms and improve quality of life. Further research is necessary to elucidate ZTTK mechanisms and enhance therapeutic strategies.

ABSTRACTS

Topic: Neuromuscular Disorders

EPNS25_cr82 - CHAT Gene Mutation Leading to Recurrent Apnoeic Episodes in an Infant: A Case of Congenital Myasthenic Syndrome

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Case report

Objective:
Congenital myasthenic syndromes (CMS) are a group of rare, inherited neuromuscular disorders caused by genetic mutations that disrupt neuromuscular transmission. These conditions often present early in life with muscle weakness, respiratory difficulties, and apnoeic episodes, posing significant diagnostic challenges. Here, we present a case of CMS type 6 due to a choline acetyltransferase (CHAT) gene mutation in an infant, emphasizing the diagnostic complexities, the multidisciplinary approach, and the efficacy of targeted therapies.

Case:
A term infant, born via Caesarean section, remained well until 2 months of age when she experienced a life-threatening event characterized by sudden pallor, limpness, and respiratory arrest, requiring PICU admission. On admission, metabolic acidosis and atypical movements were noted, initially attributed to epileptic activity. She was empirically treated for sepsis and started on Levetiracetam. Extensive investigations, including a CT brain scan, EEG, CSF analysis, and MRI brain, showed no abnormalities. Cardiac assessments (ECG, Holter monitoring, echocardiography) and ENT and respiratory reviews, including sleep studies and microlaryngobronchoscopy, were unremarkable.

Despite normal development and the absence of myasthenic features, the patient continued to experience recurrent apnoeic episodes requiring intubation. Whole-genome sequencing ultimately confirmed a CHAT gene mutation, establishing the diagnosis of CMS type 6.

The patient was treated with pyridostigmine (6 mg/kg/day) and 3,4-diaminopyridine (3,4-DAP; 0.5 mg/kg/day). Multidisciplinary discussions avoided the need for tracheostomy by initiating nocturnal non-invasive ventilation (NIV). Following this targeted treatment, the patient has remained symptom-free for over five months, demonstrating significant clinical stability.

Conclusion:
This case highlights the importance of considering CMS in infants presenting with unexplained recurrent apnoeic episodes. CHAT mutations, although rare, account for 5–7% of CMS cases and can present with life-threatening events early in life. Early genetic testing, particularly whole-genome sequencing, plays a critical role in ensuring timely diagnosis and targeted therapy. This case emphasizes the role of pyridostigmine, 3,4-DAP, and multidisciplinary care in achieving stabilization and avoiding invasive interventions. However, ongoing monitoring remains essential to mitigate the risk of respiratory crises and ensure optimal long-term outcomes.

ABSTRACTS

Topic: Neurometabolic Disorders

EPNS25_cr83 - The complex landscape of aromatic L-Amino acid decarboxylase deficiency: A case series

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Case report

Objectives: Aromatic L-amino acid decarboxylase deficiency (AADC-D) is an ultra-rare disorder caused by *DDC* gene variants that typically presents in infants with hypotonia, oculogyric crises, global developmental delay, mood and sleep disturbances and autonomic dysfunction. Due to diverse symptoms, a considerable delay is reported between symptom onset and mean age at diagnosis (3.5 years; median, 13 months; range 2 months-23 years). We aimed to retrospectively review the diagnostic journey of our AADC-D patients.

Methods: We included three unpublished patients diagnosed between January 2023-January 2025 at our Division of Pediatric Neurology and Pediatric Metabolism. Age at symptom onset and diagnosis, work-up and course were documented.

Results: Patients 1 (P1) and 2 (P2), both female, presented with hypotonia and intermittent limb stiffness at age 4 months, while Patient 3 (P3), male, had upward gaze episodes at age 2 months. Patients showed seizures, increased secretions, frequent infections, temperature instability, or nasal congestion. Presentation ages were 19, 15, and 12 months, respectively. Findings included microcephaly (P1, P2), global developmental delay and axial hypotonia in all. P1 had spasms and involuntary movements; P2 and P3 had peripheral hypertonicity and cortical fisting. Routine laboratory tests and metabolic work-up were normal. MRI showed thin corpus callosum (P1) and dentate nuclei hyperintensity (P2) at 19 and 9 months of age, respectively. EEG showed epileptic activity in P3. A metabolic platform and CSF analysis were not accessible. Whole-exome sequencing identified compound heterozygous *DDC* variants (c.1040G>A;c.301A>T) in P1, and homozygous variants c.1040G>A and c.208C>T in P2 and P3. Diagnosis occurred 21, 8, and 10 months after symptoms began. P1 (3 years) did not respond to bromocriptine, pyridoxine, or pramipexole. P2 (2 years 2 months) was unresponsive to levodopa but partially responded to pramipexole. P3 was lost to follow-up. P1 and P2 can sit with support but remain nonverbal. Gene therapy is not currently accessible in Turkey.

Conclusions: Accurate diagnosis and early initiation of proper treatment require early recognition of symptoms and understanding the relation between *DDC* variants, their molecular impacts, and AADC-D phenotypes. The c.1040G>A and c.208C>T variants have previously been linked to severe course. Exome sequencing accelerates diagnosis in settings where biochemical and CSF diagnostic work-up for neurotransmitter defects are not accessible.

Key-words: AADC deficiency, *DDC* variants, diagnostic pathway

ABSTRACTS

Topic: Neuromuscular Disorders

EPNS25_cr84 - Polyneuritis Cranialis: A Rare Guillain-Barré Syndrome Variant in a 10-Year-Old Girl

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Case report

Introduction:

Polyneuritis cranialis, an uncommon variant of Guillain-Barré Syndrome (GBS), is characterized by cranial nerve involvement without limb symptoms. It is typically associated with antecedent infections and presents unique diagnostic and therapeutic challenges. We present a case of a 10-year-old girl with polyneuritis cranialis.

Material and Methods: A previously healthy 10-year-old girl experienced diplopia and a nasal voice two weeks after a self-limited diarrheal episode

Discussion

Clinical examination revealed bilateral abduction limitation, facial paralysis, and dysarthria, progressing to respiratory failure and requiring Pediatric Intensive Care Unit admission. Initial evaluations, including cranial CT and MRI, were unremarkable. Suspecting Miller-Fisher Syndrome (MFS), a Guillain-Barré Syndrome (GBS) variant, or botulism (due to homemade honey consumption), extensive investigations were performed. Treatment with botulinum antitoxin was administered, along with cycles of immunoglobulins (2g per kg for 5 days) and plasmapheresis. The neurophysiological studies suggest motor cranial nerve involvement, evidenced by low-amplitude responses in the blink reflex, and normal conduction studies and PAMC amplitudes in the extremities. Cerebrospinal fluid analysis showed no albumin-cytological dissociation. Stool cultures were positive for Campylobacter jejuni, and serum antiganglioside antibodies (Anti-GM1) were detected. Following initial improvement, the patient was transferred to Pediatric Neurology, where a second immunoglobulin cycle was administered, leading to further recovery. At two months post-onset, she exhibited only mild facial paresis and diplopia.

Conclusions:

This case emphasizes the importance of recognizing polyneuritis cranialis as a distinct GBS variant. Prompt clinical and neurophysiological evaluations, combined with timely immunotherapy, are crucial for achieving favorable outcomes in atypical GBS presentations.

ABSTRACTS

Topic: Movement Disorders/ Cerebral Palsy

EPNS25_cr86 - Bi-allelic variants in CCDC82 gene are associated to spastic paraparesis with intellectual disability and facial dysmorphism

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Case report

Objective: To report three new cases of an early-onset spastic paraparesis associated to a likely pathogenic variant in CCDC82 gene. Bi-allelic variants in this gene have been reported since 2017 related to intellectual disability (ID), microcephaly and spasticity, but disease is still not registered in OMIM, and little is known about the gene function.

Methods: Clinical and genetic description of three patients with progressive spastic paraparesis and literature review**.**

Results: Case 1. 17 years old girl. First consultation for motor delay at 7 months. No relevant perinatal history. Third child of second degree-related parents of gypsy-Portuguese ascendance. Coarse facies, macrotia and microcephaly were noted. At 1 year, spasticity of lower limbs, exaggerated reflexes and bilateral Babinski's sign were ascertained. She acquired stable seating at 19 months and assisted walking from 3 years. During school age, she presented language delay and moderate ID. She presented 2 febrile seizures at 4 and 7 years. Progression of lower limb spasticity from 9 years lead to a crouching gait, without improvement after surgery. She also developed moderate dysarthria with few word and short sentences from 12 years. Case 2. 3-yo girl followed since 14-mo for motor delay and axial hypotonia. Consanguineous parents of gypsy-Portuguese ascendance with no relevant perinatal history, unrelated to those from case 1. She presented coarse facies, macrotia and microcephaly. At 24-mo lower limbs spasticity and hyperreflexia were noted, with aided spastic gait from 26-mo. Expressive language delay and mild cognitive impairment were present at 3-yo. Case 3. 5-yo girl. First degree cousin of case 2. Apparently, non-consanguineous parents. She presented a motor delay with lower limbs hypertonia from 11-mo. Again, coarse facies with ear macrotia and microcephaly were noted. Surgery at 3-yo improved assisted crouching gait. In all 3 cases, exhaustive investigations were normal, including metabolic screening, microarrays and brain MRI. A trio-WES study revealed the same variant c.67C>T (p. Arg23*) in homozygosity in the CCDC82 gene in the 3 cases, which segregated in their parents. Healthy siblings were also studied, and none was homozygous for the variant.

Conclusions: The novel variant CCDC82 c.67C>T in homozygosity is related to an autosomal recessive progressive spastic paraparesis. Previous cases with ID with or without spasticity have been reported caused by frameshift and nonsense variants in CCDC82. Functional studies are needed to clarify the pathophysiological mechanisms underlying this disease.

ABSTRACTS

Topic: Neurometabolic Disorders

EPNS25_cr88 - Sanfilippo syndrome – a case report

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Case report

Mucopolysaccharidosis (MPS) type III, also known as Sanfilippo syndrome, is a rare autosomal recessive degenerative disease where fragments of partially degraded glycosaminoglycans (GAG) accumulate in the lysosomes, resulting in cellular dysfunction and clinical abnormalities.

There are limited data regarding cases of MPS III in Filipino children. Furthermore, this is the first diagnosed and managed case in our institution.

This is the case of an 11-year-old Filipino male child who presented with neurodevelopmental regression and seizures. Early signs and symptoms of hyperactivity, speech delay, and delayed gross motor skills were observed. Coarse facial dysmorphism, joint contractures, and neuroimaging findings of cerebral atrophy and hydrocephalus were present. A diagnosis of Mucopolysaccharidosis type IIIA was confirmed by molecular genetic testing and multidisciplinary management wasstarted.

This case report aims to present the patient's clinical history, physical examination findings, and diagnosis. A review of updated literature on MPS III treatment will also be discussed.

ABSTRACTS

Topic: Infectious and Inflammatory Diseases/ Neuroimmunology

EPNS25_cr90 - Anti MOG Associated Acute Disseminated Encephalomyelitis Mimicking Encephalitis

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Case report

Introduction: Antibodies (abs) against myelin oligodendrocyte glycoprotein (MOG) have been described in acquired demyelinating syndromes (ADSs). Myelin oligodendrocyte glycoprotein antibodies (MOG-Abs) were shown in over 50% of children with ADSs. MOG spectrum diseases manifest primarily in children with isolated or recurrent optic neuritis, isolated or combined with myelitis, or acute disseminated encephalomyelitis.
Case: A previously healthy five-year-old girl was admitted with two days of fever, fatigue, and increasing lethargy. She was diagnosed with hand-foot-mouth disease in another hospital a week ago because of "upper respiratory tract infection" which not improved with treatment. Her physical examination showed decreased alertness and lethargy. Cranial Magnetic Resonance (MRI) T2/FLAIR Images revealed increased signal without diffusion restriction and without contrast enhancement in the bilateral thalamus, sublentiform and both cerebral peduncles, and deep white matter in the right occipital region. MOG-Abs was found to be positive. Our patient with MOG-Abs and a clinical picture resembled encephalitis.
Discussion: We describe clinical, biochemical, and MRI findings in a girl presenting with encephalopathy due to the multiple white matter and deep white matter changes. Encephalitis mimicking presentations in MOG-Abs positive patients are recognized but rare, and few pediatric cases have been described.

Conclusions: Early detection of MOG-Abs in patients with a similar presentation and imaging features would enable rapid initiation of appropriate treatment and potentially reduce the need for comprehensive diagnostic procedures.

ABSTRACTS

Topic: Neuromuscular Disorders

EPNS25_cr91 - The Late Onset Form of Pompe Disease: Two Sibling Cases

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Case report

Introduction: Pompe disease (type II glycogenosis) is an autosomal recessive disorder caused by mutations in the *GAA* gene that lead to a deficiency in the acid alpha-glucosidase enzyme. Two clinical presentations are usually considered, named infantile-onset Pompe disease and late-onset Pompe disease (LOPD), which differ in age of onset, organ involvement, and severity of disease.
Case 1: Three years old boy was referred for elevated serum Creatinine Kinase (CK), alanine aminotransferase (ALT), aspartate aminotransferase (AST). His motor development was consistent with his peers, but his language development was delayed. The boy was delivered at term after an uneventful pregnancy. The family history was unremarkable. His parents were healthy, and there was no one with similar diseases in his relatives. His body weight was 18,6 kg (90.P), height was 102 cm (75.P), and head circumference was 50 cm (50.P). Neurological examination was normal. Laboratory evaluation was significant for abnormal liver function tests: AST 87,5U/L (0-40), ALT 67,2U/L (0-41), and CK 530 U/L (39-308). Electromyogram (EMG) showed mild myogenic involvement. The blood GAA activity was only 0.2 nmol/mL/h (normal reference range 1-7). Compound heterozygous pathogenic variants [c.-32-13T>G (IVS1-13T>G)/ c.1694_1697del (p.Leu565ProfsTer12)] in the GAA gene were detected. His parents were carriers for these variants.

Case 2: One-year-three-months-old boy who was admitted because of incidentally noticed elevated CK levels. His developmental milestones were normal. His body weight was 11 kg (50.P), height was 84 cm (90-97.P), head circumference was 50,5 cm (90-97.P). Neurological examination was normal, like his brother's. Laboratory evaluation was significant for abnormal liver function tests: AST 178U/L (0-40), ALT 121U/L (0-41) and, CK 1425 U/L (39-308). Echocardiography, electroencephalography, and magnetic resonance imaging were normal. EMG showed mild myogenic involvement. GAA activity was only 0.12 nmol/mL/h (normal reference range 1-7). The same compound heterozygous pathogenic variants [c.-32-13T>G (IVS1-13T>G), c.1694_1697del (p.L565Pfs*12)] in the GAA gene confirmed.

Discussion: Patients with late-onset may present at any age. The differential diagnosis is usually based on the age of onset of symptoms. The screening for late-onset Pompe's disease for asymptomatic CK elevation, allows the identification of affected patients in the preclinical stage.
Conclusions: Although there is an increased awareness about Pompe disease, its diagnosis is still challenging. LOPD may be asymptomatic in early childhood and diagnosis is often delayed and in patients with asymptomatic CK elevation. GGA enzyme activity, an easy and useful diagnostic test, should be considered.

ABSTRACTS

Topic: Infectious and Inflammatory Diseases/ Neuroimmunology

EPNS25_cr92 - "Exceptional cases of anti-lgi1 positive autoimmune encephalitis in two pediatric patients with atypical clinical progressions"

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Case report

Abstract
Background: Anti-LGI1 encephalitis is a rare but increasingly recognized autoimmune condition affecting the central nervous system, primarily in adults. Pediatric cases are exceptionally rare, with unique clinical characteristics and challenges in diagnosis and management.

Methods: We conducted a retrospective analysis of two pediatric patients diagnosed with Anti-LGI1 encephalitis at a tertiary care center.Clinical presentations, diagnostic findings, therapeutic approaches, and outcomes were reviewed and compared with existing literature. Diagnosis was confirmed via serum and cerebrospinal fluid (CSF) antibody testing using cell-based assays.

Results: These cases were noteworthy for their strikingly different clinical presentations, reflecting the heterogeneity of the disease. **Case 1** involved a 17-year-old female presenting with isolated eye movement abnormalities and atypical MRI findings. Diagnosis was confirmed with positive serum Anti-LGI1 antibodies, and treatment with steroids and intravenous immunoglobulin (IVIG) led to partial improvement.**With early immunotherapy, significant improvement in symptoms was observed, and the progression to typical Anti-LGI1 findings was effectively prevented. Case 2** involved a 13-year-old female with classic features of Anti-LGI1 encephalitis, including facio-brachial dystonic seizures (FBDS), memory loss, and hyponatremia. Initial immunotherapy with steroids and IVIG was supplemented with rituximab due to persistent symptoms, resulting in clinical improvement.

Discussion: Anti-LGI1 encephalitis in pediatric patients poses diagnostic challenges due to atypical presentations and its rarity. Case 1 highlights a unique presentation with minimal classic symptoms, while Case 2 illustrates the progression of classic features and the need for second-line immunotherapy. Early recognition and tailored treatment are critical for favorable outcomes.

Conclusion: This study underscores the clinical heterogeneity of pediatric Anti-LGI1 encephalitis and emphasizes the importance of prompt diagnosis and individualized management.

ABSTRACTS

Topic: Neuromuscular Disorders

EPNS25_cr94 - The Silent Signals: Diagnosing Guillain-Barré Syndrome When Electrophysiology Falls Short

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Case report:

Guillain-Barré Syndrome (GBS) is a rare immune-mediated neuropathy in children, often presenting as acute flaccid paralysis. Diagnosing GBS can be particularly challenging when nerve conduction velocity (NCV) and electromyography (EMG) studies yield normal results, necessitating a reliance on clinical, serological, and imaging findings. We report two pediatric cases highlighting these diagnostic challenges and the variability in disease progression and recovery.

The first case involved a child with progressive ascending weakness and bilateral ptosis following a respiratory tract infection. Despite normal NCV and EMG findings on days 2 and 23 of admission, elevated cerebrospinal fluid (CSF) protein of 0.77 g/L, spine MRI images showing anterior root enhancement, and positive anti-GM1 antibodies confirmed the diagnosis. Management with one course of 2 g/Kg intravenous immunoglobulin (IVIG) and neurorehabilitation resulted in significant recovery, with the child regaining near-normal gait and returning to full-time schooling.

The second case presented with progressive lower limb flaccid paralysis and gait instability over several weeks. NCV and EMG studies were normal throughout, but MRI revealed cauda equina nerve root enhancement, elevated CSF protein of 0.84 g/L, and positive anti-GQ1B antibodies confirmed the diagnosis. Due to poor outcome, the child required two courses of 2 g/kg of IVIG and intensive neurorehabilitation, achieving gradual improvement, with partial mobility restored using support.

These cases underscore the limitations of NCV and EMG in paediatric GBS, emphasising the need for a multidisciplinary diagnostic approach incorporating clinical assessment, serology, and imaging to avoid delays in treatment. They also highlight the variability in disease progression and recovery, with one case achieving near-complete recovery and the other demonstrating slower improvement requiring prolonged support. Timely initiation of multidisciplinary care, including physiotherapy and neurorehabilitation, was pivotal in optimising outcomes for both patients.

These reports underline the importance of awareness of atypical presentations, such as normal electrophysiological findings, in ensuring prompt and accurate diagnosis and treatment. Furthermore, they illustrate the critical role of individualised care plans tailored to the patient's clinical trajectory. While pediatric GBS remains a diagnostic and therapeutic challenge, these cases emphasise the potential for meaningful recovery with early, targeted interventions, even in the context of severe clinical deficits and diagnostic uncertainty.

ABSTRACTS

Topic: Infectious and Inflammatory Diseases/ Neuroimmunology

EPNS25_cr95 - The Immunology Future of GAD-associated Temporal Lobe Epilepsy

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Case report

Objectives: Glutamic acid decarboxylase (GAD) 65 plays a key role in gamma-amino-butyric acid (GABA) synthesis within the central nervous system and is highly expressed in GABAergic neurons in the spinal grey matter, brainstem, cerebellum, basal ganglia, and hippocampus. It is also present in pancreatic cells. Antibodies against GAD65 are frequently observed in patients with type 1 diabetes (T1D) and can also be detected in individuals with various neurological phenotypes. However, the pathogenicity of GAD antibodies remains debated, with cytotoxic CD8+ T cell-mediated neuronal damage proposed as a potential mechanism. The response to immunotherapy is often limited. Temporal lobe epilepsy (TLE) and limbic encephalitis (LE) are GAD- associated phenotypes observed in younger patients. However, in T1D, establishing a link between GAD antibodies and epilepsy is challenging, complicating the decision to initiate immunotherapy.

Methods: We present a case of a female with GAD-positive T1D since she was six, who later developed drug-resistant epilepsy with cognitive decline and was referred to our epilepsy center at age 14.

Results: Video-EEG revealed extensive epileptiform activity fronto-temporal left, and brain MRI 3T and FDG-PET showed mild structural changes in the left temporal and frontal lobes. While basic cerebrospinal fluid parameters were normal, flow cytometry showed an abnormal presence of B lymphocytes. A combination of various laboratory techniques, including cell-based assay, enzyme-linked immunoassay, and tissue sections methods, revealed abnormal intrathecal synthesis of GAD antibodies. The patient was treated with intravenous immunoglobulins and cyclophosphamide, resulting in a significant improvement in seizure frequency.

Conclusions: The case highlights the complexity of GAD antibodies in clinical practice and emphasizes the importance of early recognition of GAD-related neurological conditions, especially in pediatric T1D patients. Early immunotherapy during the active phase is crucial for the prognosis.

ABSTRACTS

Topic: Infectious and Inflammatory Diseases/ Neuroimmunology

EPNS25_cr98 - Juvenile myasthenia associated with antibodies against low-density lipoprotein receptor-related protein 4 (LRP4): two cases with ocular and generalised forms

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Case report

Juvenile myasthenia associated with antibodies against low-density lipoprotein receptor-related protein 4 (LRP4): two cases with ocular and generalised forms

Myasthenia gravis is the most prevalent disorder of the neuromuscular. The majority of juvenile patients have pathogenic antibodies against acetylcholine receptors (AChR), muscle-specific kinase (muSK) and as more recently described, against low-density lipoprotein receptor-related protein 4 (LRP4). We present two pediatric patients with ocular and generalised myasthenia whose serum was negative for acetylcholine receptor and muscle-specific kinase antibodies but positive for LRP4 antibodies.

Patient 1*

We reported a case with ocular myasthenia and LRP4 antibodies (1). Briefly, this was an 11 year old girl presenting with restriction of extraocular movements and ptosis which improved with the ice pack test and pysidostigmine administration. Serum was positive for anti-LRP4 IgG index (3,5, neg : <2,1) but negative for AChR, MuSK, thyroglobulin, and thyroperoxidase antibodies. Clinical remission was achieved with oral pysidostigmine and steroid treatments.

We present another case with generalised myasthenia.

Patient 2.

A 10-year-old girl presented with a one-year history of fatigue increasing in the evening and difficulty in climbing stairs. She had been evaluated by the general pediatrics, rheumatology, haematology and oncology departments. Neurological examination revealed mild weakness in the proximal upper and lower extremities. Other physical and neurological findings were normal. The patient is the first child of healthy, non-consanguineous parents. Her past medical and developmental history and school performance were satisfactory and a 11-year-old sister is healthy. Serum antibodies against AChR, MuSK, thyroglobulin, and thyroperoxidase tested negative, but the anti-LRP4 IgG index was positive at 4.42 (negative: <2.1) by enzyme-linked immunosorbent assay (ELISA), Electromyography (EMG) with repetitive stimulation of limb muscles yielded normal results. The chest computed tomography (CT) scan revealed thymic hyperplasia (Figure 1). The patient was initiated on treatment with pyridostigmine 60 mg PO four doses/day. Symptoms improved and no other treatment methods were considered at this stage.

These cases illustrate the occurrence of LRP4 antibody-related ocular and generalized myasthenia. Although rare in the pediatric population, further cases are likely to be reported through increased awareness of pediatric neurologists.

Reference:
1.Sardarzada, J., & Anlar, B. (2024). Lipoprotein Receptor-Related Protein 4 Antibody Positivity in the Youngest Patient in the Caucasus Region: A Case Report. Cureus, 16(9), e68961. https://doi.org/10.7759/cureus.68961

* Previously accepted and published in 2024

ABSTRACTS

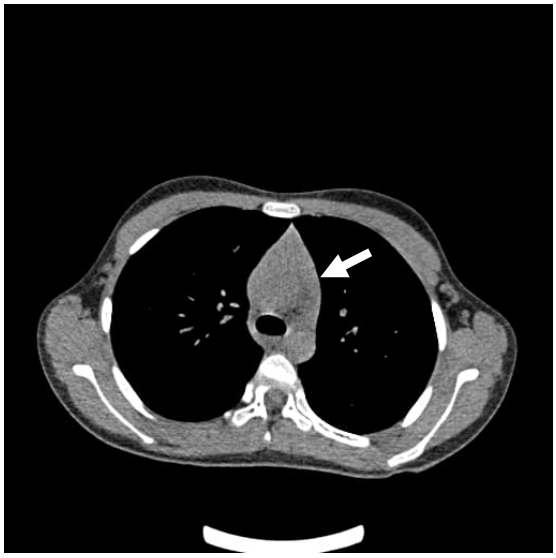

Figure 1: The chest CT scan in thymic hyperplasia

CT: computed tomography

ABSTRACTS

Topic: Neurogenetics

EPNS25_cr99 - Megalencephalic Leukoencephalopathy with Subcortical Cysts in a 21-Month-Old Boy: A Case Report

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Case report

Title: A Case Report of Megalencephalic Leukoencephalopathy with Subcortical Cysts in a 21-Month-Old Boy: Clinical Presentation, Diagnostic Workup, and Management

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Clinical case: We present a rare case of megalencephalic leukoencephalopathy with subcortical cysts (MLC) in a 21-month-old boy who presented with macrocephaly, developmental delay, recurrent tonic spasms, spasticity, and distinctive dysmorphic features, including protruding ears, epicanthic folds, and a high-arched palate. He exhibited global developmental delays, particularly in motor domains, along with mild axial hypertonia. Despite recurrent staring episodes, EEG findings were normal, including during sleep deprivation, ruling out epileptiform activity.

Neuroimaging demonstrated hallmark features of MLC, including extensive white matter abnormalities and subcortical cysts in the frontal and parietal regions. Genetic testing confirmed a mutation in the *MLC1* gene, establishing the diagnosis. Treatment included Baclofen for spasticity and Melatonin for sleep disturbances, along with regular physiotherapy, although the child remained unable to sit independently by 21 months.

MLC is a rare inherited neurodegenerative disorder characterized by macrocephaly, progressive white matter changes, and subcortical cyst formation. While seizures are common, this case was notable for the absence of epileptiform activity on EEG despite recurrent tonic spasms. Diagnosis requires a comprehensive clinical evaluation, neuroimaging, and genetic testing. MRI plays a critical role in identifying the characteristic white matter abnormalities and cystic changes.

Management is primarily supportive, focusing on pharmacological interventions for spasticity and sleep, along with intensive physiotherapy for motor delays.

Conclusion: This case highlights the importance of early diagnosis and multidisciplinary management in improving outcomes for pediatric patients with MLC. Clinicians should consider MLC in children with macrocephaly, motor delays, and neuroimaging findings of white matter changes and subcortical cysts. Genetic testing is crucial for a definitive diagnosis and understanding disease pathophysiology.

ABSTRACTS

Topic: Neuromuscular Disorders

EPNS25_cr100 - A rare mutation in the ALS2 gene causes hereditary spastic paraparesis

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Case report

Objectives: Hereditary spastic paraparesis (HSP) is a neurodegenerative disease of the corticospinal tract caused by a series of monogenic mutations. It is characterized by spasticity affecting the lower extremities, brisk deep tendon reflexes, pathological plantar skin reflexes, and a distinctive gait pattern due to upper motor neuron involvement. More than 70 genes have been implicated in causing the HSP phenotype. We present a case of infantile-onset HSP caused by an ALS2 (Alsin Rho Guanine Nucleotide Exchange Factor) gene mutation.

Methods: Whole exome sequencing (WES) was performed from the patient's serum sample.

Results: A 5-year-old girl was admitted to our outpatient pediatric neurology clinic due to her atypical gait that had been present since she was approximately two years old. She was born at term from consanguineous, healthy parents. Her developmental milestones were delayed compared to her peers. There was no other known neurological disease in her family history. Neurological examination revealed increased deep tendon reflexes, a positive Babinski sign, spasticity, and decreased muscle strength, especially in the lower extremities. Her speech was not fluent. There was no sensory deficit. She had a paraparesis gait pattern. Brain magnetic resonance imaging (MRI) revealed a hyperintense appearance in T2A and FLAIR (fluid-attenuated inversion recovery) series starting from the posterior peritrigonal and occipital horn surrounding white matter, extending to the centrum semiovale, which may be compatible with slow myelination, and dilated perivascular space structures extending parallel to the vascular trace in the vicinity of both anterior commissures, in the periventricular white matter around the occipital horn, in the corpus callosum, and at the centrum semiovale levels. Whole spinal MRI was normal. Metabolic work-up, including lysosomal diseases, was unremarkable. Electroneuromyography (ENMG) was normal in terms of polyneuropathy and myopathy. WES detected a likely pathogenic homizygous mutation of c.470G>A (p.Cys157Tyr) in the ALS2 gene.

Conclusions: Mutations in the ALS2 gene cause three known clinical conditions that may overlap: juvenile amniotrophic lateral sclerosis, primary lateral sclerosis, and infantile-onset HSP. Since there is no genotype-phenotype correlation, considering the patient's clinical and laboratory findings, the patient's diagnosis is compatible with infantile-onset HSP. When the literature is reviewed, our case is different in that the MRI findings are delayed myelination and perivascular spaces.

ABSTRACTS

Topic: Epilepsy: Medical and Surgical treatment

EPNS25_cr102 - Successful use of cannabidiol in Rett syndrome with severe drug resistant epilepsy

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Case report

Rett syndrome (RTT) is a severe, progressive, neurodevelopmental disorder which affects predominantly females. In most cases it's associated with pathogenic variants in MECP2 gene. RTT is characterized by developmental regression of spoken language and hand use. Affected individuals may present multiple other neurological impairments and comorbidities such as seizures. Epilepsy in Rett syndrome is often severe and drug resistant.

Cannabinoids are substances extracted from the cannabis plant, which are known for their medical properties and have been used for years in many pathologies . Among cannabinoids, cannabidiol (CBD) has anti-epileptic properties without a psycho-stimulant effect. The mechanisms of action of CBD are not fully understood but appear to result in a reduction of neuronal excitability through functional antagonism of GRP55 receptors, desensitization of TRPV1 receptors, and inhibition of adenosine transport Five randomized control trials pointed out the significant efficacy of adjunctive high-purified-CBD in comparison with placebo in patients suffering from Lennox-Gastaut syndrome (LGS)

Few data are actually published about use of hp-CBD in Rett syndrome

We describe a 14 years old femaleRett patient with a de novo pathogenic mutation of MECP2 affected by severe pharmacoresistant epilepsy . Multiple antiseizure medication were used since the seizures appeared, with frequent ER accesses. Also galenic cannabidiol was prescribed, with no benfit on seizure control. High purified CBD was started in add-on with lamotrigine and clobazam in october 2022. After more than 2 years of follow-up hp-CBD continues to mantain his antiseizure effect with a very good tolerance. No side effects appeared, liver enzymes are stillnormal. The behavioral scale RSBQ (Rett Syndrome Behavior Questionnaire®) a 45-item checklist developed to assess behavioral and emotional characteristics of RTT divided into eight subscales (General mood, Breathing abnormalities, Hand behaviors, Repetitive face movements, Body rocking and expressionless Face, night-time behavior, Fear/anxiety, and Walking/standing) demonstrated a decrease in the severity scores

We certainly need a more significant number of Rett patients treated with hp-CBD but we think that this ASM should be considered in the flow-chart of the management of severe epilepsy in MECP2 mutations.

ABSTRACTS

Topic: Epilepsy: Medical and Surgical treatment

EPNS25_cr104 - 3x1: One intervention, three problems solved

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Case report

Objectives: Ketogenic diet (KD) is an effective treatment for refractory childhood epilepsy. Beyond its anticonvulsant and neuroprotective benefits, several recent publications show the usefulness of KD in other pathologies such as obesity and diabetes (DM), improving glycemic and weight control.

Methods: Patient from Morocco, resident in Spain since he was 3 years old. History of idiopathic epilepsy and obesity with a body mass index (BMI) 32 in Morocco. He was diagnosed with tuberous sclerosis at 3 years of age when he arrived in Spain in the context of a hospital admission due to the onset of DM1. Two years after diagnosis he had episodes of partial seizures, for which antiepileptic treatment was started. He sequentially receives up to 5 antiepileptic drugs (AEDs) and everolimus with persistence of seizures, which become daily, and paroxysmal activity in serial electroencephalographic recordings.

Results: Given the refractoriness to treatment, low-glycemic index and then KD was started (in combination with AEDs and Everolimus), showing good adherence and improvement in seizure control. Secondly, he benefited from KD in the control of his DM1 with a decrease in insulin requirements and a clear decrease in his BMI to 26.

Conclusions: With adequate monitoring, KD can be an effective and safe concomitant treatment both for the treatment of refractory epilepsy and a promising treatment for obesity and DM.

ABSTRACTS

Topic: Cerebrovascular Disorders

EPNS25_cr105 - Acute spinal cord ischemia in a healthy adolescent: diagnostic challenges and therapeutic approach

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Case report
A 16-year-old male weightlifter with no history of recent trauma or family predisposition to cardiovascular or neurological diseases presented to emergency department with acute weakness and flaccidity in the lower limbs following a Valsalva maneuver, progressing to paraparesis. Clinical examination revealed a sensory level at T10, areflexia in the lower limbs, and limited active movement of the right leg. Urgent spinal MRI showed signal hyperintensity (STIR sequences) at T9-T10 and Schmorl's nodes at the same level. Thoraco-abdominal CT and angio-CT were unremarkable.

Due to the suspected inflammatory nature of the lesion, intravenous dexamethasone (0.12 mg/kg/day) was initiated, along with acetylsalicylic acid (1.5 mg/kg/day) for presumed acute spinal cord ischemia. Within 48 hours, MRI revealed signal changes at T10-T12 on ADC/DWI sequences, consistent with acute ischemic evolution. These findings suggested spinal cord ischemia, an uncommon cause of paraparesis at this age. The diagnosis was further supported 10 days later by normal brain and intracranial vessel imaging.

Extensive diagnostic workup, including cardiovascular, oncological, microbiological, and autoimmune evaluations, was inconclusive. Positive findings included recent Chlamydia pneumoniae infection and hyperhomocysteinemia. The final diagnosis was acute spinal cord ischemia caused by a fibrocartilaginous embolism, with genetic testing (NGS stroke panel) ongoing.

No further neurological events occurred during hospitalization. Treatment included subcutaneous enoxaparin, an indwelling urinary catheter, and a physiotherapy program, continued post-discharge at a specialized center.

After four months, significant recovery was noted: ambulation was possible with Canadian crutches and an ankle-foot orthosis for left leg spasticity, managed with botulinum toxin. Neurogenic bladder persisted, requiring six daily catheterizations.

Acute spinal cord ischemia is rare and diagnostically challenging in pediatrics. It may be idiopathic or secondary to factors such as hypotension, cardiovascular malformations, infections, trauma, or vasculitis. Targeted imaging is essential to characterize the lesion and determine the cause, including dissection, fibrocartilaginous embolism, or arteriovenous malformations. In our clinical case, a thorough screening of potential causes was performed, and therapy was promptly initiated, focusing on those etiologies that benefit from early intervention. Treatment includes addressing the underlying cause, such as anticoagulation for thromboembolism or steroids for myelitis, followed by intensive rehabilitation. Early intervention and rehabilitation are key to optimizing recovery in pediatric cases of acute spinal cord ischemia.

ABSTRACTS

Topic: Neurodevelopmental Disorders / Developmental Neuroscience

EPNS25_cr106 - Is it just Laryngomalcia? Unusual presentation of Jouberts Syndrome

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Case report

Joubert's syndrome is a rare autosomal recessive disorder which affects the brain. The cerebellar vermis and the brainstem are not fully developed during pregnancy, thus affecting control of posture and muscles, head and eye movements. Regulation of heartbeat, breathing and temperature control can also be affected. Its implications are in the form of a spectrum affecting breathing pattern, tone of the muscle, mobility, learning, cognition as well as causing visual difficulties and epilepsy. It can also be accompanied by ataxia, developmental delay, abnormal eye movements and neonatal breathing dysregulation. Specific MRI finding is the "molar tooth sign" where there is abnormal cerebellar vermis and brainstem.

A 2 months old female initially presented with laryngomalacia and squeaky noises when unsettled. She was reviewed by ENT. She was born by normal vaginal delivery with unremarkable antenatal scans. The mother had congenital cataract and she had a termination of pregnancy 1 year prior this pregnancy, at 15-16th weeks gestation, as fetus developed into cystic hygroma (there was no post-mortem and genetics were within normal limits).
At the age of 7 months old, the child had a squint and mild gross motor delay. She could not have solid foods. She was under ophthalmology, physiotherapists, and occupational therapists. She was then noted to have reduced tone, global developmental delay and large divergent squint. MRI was requested. On examination, she had soft, palpable anterior fontanelle with tendency to flop forward or sideways while sitting, at 11 months. She had a slightly anterior anus, high arched palate and slightly laxed knee joints. Her baseline haematological investigations, metabolic screen, TFT , developmental delay panel and genetic SPN array were normal.
Her MRI was reported as structural abnormality in the midbrain and cerebellum, along with dysgenesis of splenium of corpus callosum. The features are in keeping with Joubert's spectrum disorder.

Incidence of Joubert's syndrome is rare. It presents mostly as floppiness (hypotonia), unsteadiness (ataxia) and developmental delay. This case highlighted a complex initial presentation as laryngomalcia followed by large divergent squint and developmental delay.

References

1. https://rarediseases.org/rare-diseases/joubert-syndrome/ (accessed on 20/01/2025)

2. https://www.gosh.nhs.uk/conditions-and-treatments/conditions-we-treat/jouberts-syndrome/

3. Joubert syndrome and related disorders- Francesco Brancati, Bruno Dallapiccola, Enza Maria Valente 2010 10.1186/1750-1172-5-20. https://pubmed.ncbi.nlm.nih.gov/20615230/

ABSTRACTS

Topic: Epilepsy: Diagnosis and Investigations

EPNS25_cr107 - False Lateralization of Epileptic Activity in a 3-Month-Old with Sturge-Weber Syndrome: A Case Report

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Case report

Objectives: Sturge-Weber Syndrome (SWS) is a rare neurocutaneous disorder characterized by leptomeningeal angiomatosis, facial port-wine stains, and associated neurological manifestations, most notably epilepsy. Typically, epileptic activity correlates with structural abnormalities seen on imaging. We report a unique case of false lateralization, where electroencephalographic (EEG) findings contradicted expected lateralization based on neuroimaging and clinical presentation. This case underscores the complexities of epilepsy localization in SWS and the importance of multimodal diagnostic approaches.

Methods: This case describes a 3-month-old male presenting with dyskinetic movements of the left hand, leg, and facial muscles. Brain MRI revealed significant right hemisphere atrophy and leptomeningeal angiomatosis, consistent with the diagnosis of SWS. However, EEG demonstrated focal epileptiform discharges from the left temporo-parieto-occipital (TPO) region, a phenomenon known as false lateralization. A detailed clinical history, neuroimaging, and EEG findings were analyzed to guide management.

Results: The patient exhibited clinical signs suggestive of right hemispheric involvement, supported by MRI findings of right-sided cortical atrophy and leptomeningeal vascular malformations. Despite these structural abnormalities, EEG consistently showed epileptiform discharges localized to the left TPO region. This discrepancy between imaging and electrophysiological findings presented challenges in localizing the seizure onset zone. Antiepileptic therapy was initiated, resulting in partial seizure control. The case highlights the need for advanced diagnostic tools, including prolonged EEG monitoring and multimodal imaging, to refine diagnostic accuracy and optimize treatment strategies in SWS-associated epilepsy.

Conclusions: False lateralization of epileptic activity in SWS complicates the interpretation of EEG findings and has significant implications for diagnosis and management. This case highlights the need for integrating clinical, electrophysiological, and imaging findings to avoid misdiagnosis and ensure targeted treatment in SWS patients with epilepsy. Greater awareness of this rare phenomenon is essential for improving clinical outcomes in pediatric neurology.

ABSTRACTS

Topic: Epilepsy: Medical and Surgical treatment

EPNS25_cr108 - Psychosis Induced by Ethosuximide in a Pediatric Patient

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Case report

Background and objectives: Although there are many different methods of treating epilepsy, drug therapy is still the main method. Ethosuximide, a central nervous system agent used for absence epilepsy, commonly causes gastrointestinal side effects and may lead to drowsiness, lethargy, insomnia, and hiccups. Rarely, it has been associated with psychosis and suicidal ideation in adults. This report describes the case of an 8-year-old girl who developed visual hallucinations, psychotic symptoms, and suicidal ideation while on ethosuximide.

Case: This report describes an 8-year-old girl with a 10-month history of daily staring episodes lasting 5-10 seconds. EEG revealed several clinical and electrical seizures characterized by brief staring episodes associated with 3 Hz generalized spike-and-wave discharges. She was diagnosed with childhood absence epilepsy (CAE) and initially started on lamotrigine. However, as the seizures persisted, her treatment was switched to ethosuximide. Seven days after starting ethosuximide, the patient reported experiencing visual hallucinations, cursing at God, and having suicidal thoughts. Ethosuximide was subsequently discontinued, and her symptoms improved afterward.

Conclusions: This case highlights the importance of monitoring for psychiatric side effects, including psychosis and suicidal ideation, in patients receiving ethosuximide treatment, particularly children and adolescents. While ethosuximide is an effective treatment for CAE, rare but severe psychiatric adverse effects, including hallucinations, and suicidal ideation, necessitate careful observation. Clinicians should educate caregivers to recognize early psychiatric symptoms for timely management and improved safety. Further research is needed to elucidate the mechanisms of these rare adverse effects and to identify patients at higher risk.

ABSTRACTS

Topic: Infectious and Inflammatory Diseases/ Neuroimmunology

EPNS25_cr112 - Headache as a first sign of central nervous system echinococcosis in a 15-year-old boy, a case presentation

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Case report

A 15-year-old Turkish boy presented with a headache and visual problems. On clinical exam, he exhibited homonymous hemianopsia but no other neurological symptoms. An ophthalmologic examination revealed bilateral papilledema. Urgent computed tomography (CT) revealed a large cyst in the parieto-occipital region of the brain. Brain MRI showed an unilocular, fluid filled cyst without surrounding oedema or contrast enhancement, which was morphologically suspected to be an echinococcus cyst. Further imaging by CT showed multiple cysts in both liver and lungs. Biochemical analysis revealed marked eosinophilia and positive serology for *Echinococcus granulosus* antibodies using the ELISA method. He was started on systemic therapy with albendazole and praziquantel. The cyst was removed using the Dowling approach. Unfortunately, the cyst ruptured during removal, necessitating a hypertonic salt rinse as protoscolicidal treatment during the operation. Anatomical pathology examination of the cyst wall demonstrated the presence of protoscolices. PCR of the wall confirmed the diagnosis of an *Echinococcus granulosus* infection. Postoperatively, hemianopsia and headache completely resolved. Systemic anthelminthic treatment was continued and the patient was discharged from the hospital with an epinephrine auto-injector because of the risk of spontaneous rupture of cysts with possible anaphylaxis.

Cystic echinococcosis is a zoonotic disease caused by *Echinococcus granulosus*. Humans become intermediate host primarily through ingestion of parasite eggs, typically from contaminated food, water or soil. Once ingested, the parasite develops into its larval stage in the viscera and forms cystic lesions, most commonly in the liver and lungs. Echinococcosis can also infect the central nervous system (CNS) in 2% of the cases, usually presenting with symptoms of increased intracranial pressure. A literature search revealed that CNS-infection is more common in boys and mostly located in the parietal lobe. Diagnosis involves a combination of clinical suspicion, imaging, and serology. Treatment depends on the disease stage and drug availability. For symptomatic CNS infection with *Echinococcus granulosus*, surgical removal of the cyst is the treatment of choice. This is typically combined with anthelminthic therapy in cases of hydatid dissemination or intraoperative cyst rupture, to prevent recurrence.

We conclude that common neurological symptoms, such as headaches, can sometimes be caused by rare and exotic diagnoses. Clinicians must remain vigilant to the evolving landscape of parasitic infections, driven by international travel and climate change. Tropical infections may increasingly challenge healthcare systems in non-endemic areas in the future.

ABSTRACTS

Topic: Neurogenetics

EPNS25_cr113 - Ataxia, upward gaze palsy and delayed myelination: more clues to KIF1A-associated neurological disorder

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Case report

Objective

KIF1A-associated neurological disorder (KAND) is a group of ultrarare neurodegenerative conditions with a wide phenotypic spectrum associated with pathogenic variants in *KIF1A* gene. Signs and symptoms of KAND are heterogeneous, leading to delayed or misdiagnosis. They often include spasticity, neurodevelopmental delay, intellectual disability, autism, microcephaly, progressive spastic paraplegia, autonomic and peripheral neuropathy, optic nerve atrophy, cerebral and cerebellar atrophy, and seizures. Moreover, progression and severity of KAND varies by mutation, with recent genetic investigations further expanding the clinical phenotypes of heterozygous *KIF1A* variants.

Method

Herein we describe a 15-month-old boy of nonconsanguineous parents who was referred due to hypotonia and marginally delayed motor development. Clinical and neuroimaging clues led to further investigation with genetic testing that confirmed a diagnosis of KAND in our patient.

Results

On examination he demonstrated central hypotonia with normal tendon reflexes, he was able to weight bare but unable to walk independently. Moreover, ataxia, nystagmus, visual fixation abnormality and upward gaze palsy were noted. Brain imaging with MRI revealed delayed myelination. Ultimately, whole exome sequencing with trio revealed a heterozygous de novo mutation at c.470T>C (p.Leu157Pro) in the *KIF1A* gene, reported as likely pathogenic. During his 2-year and 10-month follow-up visit neurocognitive testing with WPPSI-III ^{GR} revealed Verbal IQ of 60, Performance IQ of 83 and a Full Scale IQ of 71.

Conclusion

Originally, changes in the *KIF1A* gene were associated with three main disorders: non-syndromic intellectual disability 9 (MRD9), currently known as NESCAV syndrome, hereditary sensory neuropathy type IIC (HSNIIC) and hereditary spastic paraplegia 30 (SPG30). The overall severity, clinical progression of symptoms and outcome can vary greatly. Ataxia and vertical gaze palsy in children with delay in myelination and motor development are further clues to *KIF1A*-associated neurological disorder (KAND).

ABSTRACTS

Topic: Neuromuscular Disorders

EPNS25_cr114 - Trappc pathways: bridging focal epilepsy and muscular distrophy

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Case report

Introduction

Limb-girdle muscular dystrophy type 18 (LGMD-R18) is a rare autosomal-recessive congenital disorder of glycosylation caused by pathogenic variants in the TRAPPC11 gene. It is associated with progressive muscle weakness, intellectual disability, hyperkinetic movements, ataxia, and, in some cases, seizures. Despite recent advances, the clinical and genetic spectrum of TRAPPC11-opathies remains incompletely understood.

This case highlights the complexity of TRAPPC11-related disorders and expands the clinical picture.

Methods

We present the case of an 11-year-old girl, previously diagnosed with LGMD-R18 caused by pathogenic TRAPPC11 variant and drug-resistant genetic focal epilepsy.

Results

The patient, born to nonconsanguineous parents, had decreased fetal movements and marked neonatal hypotonia, requiring intensive care interventions. Developmental milestones were significantly delayed despite physiotherapy. Genetic testing identified two pathogenic TRAPPC11 variants, confirming LGMD-R18. Clinical examination included microcephaly, dolichocephaly, kyphoscoliosis, dysmorphic features, absent deep tendon reflexes (DTR), truncal and limb ataxia and stereotypic masticatory and hand movements. Seizures began at age 4, initially as brief, daily episodes of palpebral myoclonus, evolving into episodes characterized by eye and head deviation to the left, masticatory automatisms, generalized tremor and dyskinetic movements, resistant to multiple treatments, including cannabidiol and ketogenic diet. Electroencephalogram (EEG) findings evolved into a pattern consistent with Lennox-Gastaut syndrome. Magnetic resonance imaging (MRI) revealed subarachnoid spaces enlargement, while electroneurographic and needle electromyographic studies were within normal limits.

Conclusions

This case underscores the multisystemic complexity of TRAPPC11-opathies and highlights the challenges of managing drug-resistant seizures. Moreover, it provides insights into genotype-phenotype relationship, as there are only a limited cases of TRAPPC11-opathies described. While microcephaly, dysmorphic features, abnormal movements and seizures are known features of TRAPPC11-opathies, the association with Lennox Gastaut syndrome is notably rare.

ABSTRACTS

Topic: Neurodevelopmental Disorders / Developmental Neuroscience

EPNS25_cr115 - Infantile Seizures: Thinking beyond a Febrile Aetiology

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Case Report

Variants at the PPFIBP1 are associated to a rare Neurodevelopmental disorder with seizures, microcephaly, and brain abnormalities. We report a case of an infant presenting to hospital with prolonged seizures from 8-weeks of life with a rare genetic diagnosis of PPFIBP1. The patient was born full term. Family history of PFO in both his father and Granfather, and both have previously had a stroke. His father was also diagnosed with epilepsy and is currently on treatment. There were some concerns regarding early development as he was not fixing or following. The infant initially presented with fever and a focal seizure. Initial investigations including neurometabolic testing, infection screening and CSF investigations were within normal range. A CT-head demonstrated intracranial calcifications and MRI-head did not identify any other intracranial abnormalities. EEG showed transient sharps noted over the temporal/occipital regions (Left>right). An echocardiogram identified a small PFO in keeping with gestational age. Subsequently whole genome sequencing showed a diagnosis of PPFIBP1 (Heterozygous for a likely pathogenic splice region variant and a pathogenic stop gain variant in PPFIBP1 gene). He presents with global developmental delay and developed several different seizure types by 6-months of age, requiring multiple anti-seizure medications. He continues under the care of a multidisciplinary team including paediatric neurology, community paediatrics, ophthalmology, audiology, cardiology, physiotherapy, occupational therapy and speech & language therapy to monitor his progress as he continues to develop.

There is limited information available on this genetic variant, making it difficult to comment on outcome and prognosis of the disorder to the family. Children in the literature have been described to have significant delay in their development, epilepsy which may be refractory to treatment, brain abnormalities, cardiac abnormalities, poor weight gain, short stature, ophthalmological and hearing difficulties. Whole genome sequencing allows an early diagnosis; however, further case reports are needed to establish the phenotype and prognosis of this condition.

ABSTRACTS

Topic: Infectious and Inflammatory Diseases/ Neuroimmunology

EPNS25_cr116 - Linear scleroderma of the “en coup de sabre” type in a child with central nervous system involvement

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Case report

Objectives: To present the clinical case of a 5-year-old female patient with linear scleroderma of the “en coup de sabre” type who developed a stroke-like episode 3 years after the onset of cutaneous manifestations in the form of acute left-sided hemiparesis and three focal epileptic seizures in the first week after the onset of hemiparesis.

Methods: We analyzed our own patient follow-up data and previously described clinical cases of nervous system involvement in linear scleroderma “en coup de sabre” in the PubMed database.

Results: Juvenile localized scleroderma (JLS) is a rare chronic inflammatory disease of the connective tissue, characterized by inflammation and fibrosis of the skin and underlying tissues, in some cases involving fascia, muscles, bones and central nervous system.

According to the literature, the incidence of neurological disorders amounts to no more than 3.8%. Neurological symptoms in JLS can either precede the dermatologic manifestation of the disease, or appear after the onset of skin manifestations. The most common appear to be seizures, migraine-type headache, less common are trigeminal neuralgia, hemiplegic migraine, positional nystagmus along with vertigo.

The article presents a clinical case report of a 5-year-old female patient having linear scleroderma of the “en coup de sabre” type, who 3 years after the onset of skin manifestations developed a stroke-like episode in the form of acute left-sided hemiparesis and three focal epileptic seizures in the first week after the appearance of hemiparesis. MRI scans revealed cystic lesions and white matter changes in the right hemisphere of the brain at the level of the basal ganglia and the frontal lobe. No changes appeared in the DWI mode. According to the EEG data, periodic rhythmic deceleration was recorded in the frontal-central-temporal leads of the right hemisphere. The neurological deficit regressed within three weeks. Epileptic seizures did not recur while taking levetiracetam at a dose of 20 mg/kg/day during the catamnestic follow-up period for a year.

Conclusions: To date, just a few observations of patients with localized scleroderma of the face and scalp involving the nervous system have been described, and there are no treatment recommendations. For improving diagnostic methods as well as selecting optimal treatment tactics, a further study of this problem is crucial.

ABSTRACTS

Topic: Neurometabolic Disorders

EPNS25_cr117 - NAXE deficiency: a niacin (vitamin B3) repairdefect with acute neurologic presentation

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Case report

NAXE (NAD(P)HX epimerase) deficiency is an ultra-rare, potentially lethal, autosomal recessive metabolic disorder. Since the first description in 2016, 40 cases have been described. As an epimerase, NAXE performs the first step in recycling an inactive, potentially toxic niacin metabolite (NAD(P)HX), that accumulates during fever or stress, to active Nicotinamide adenine phosphate dinucleotide (NAD(P)H), representing a key enzyme for the function of the mitochondrial respiratory chain. Affected patients usually present with acute neurologic deficits, triggered by fever or stress, and fulminant, often lethal progression. Due to variable MRI (magnetic resonance imaging) changes and the lack of a reliable biomarker, a rapid diagnosis is difficult.

We present the case of a 20-month-old girl with previously normal development. From the ninth day of a febrile illness, she developed generalized muscular hypotonia, nystagmus and coma. CSF (cerebrospinal fluid) cell count, protein and glucose were normal; CSF lactate was elevated to 3.2 mg/dl (<2), serum lactate was normal. MRI revealed bitemporal signal alterations as well as extended myelopathy without gadolinium enhancement. Metabolite screening for inborn errors of metabolism, infectious workup and antibody testing for autoimmune disorders were negative. The patient was started on high dose methylprednisone and intravenous immunoglobulins, followed by plasmapheresis over 10 days. Following initial clinical improvement, she relapsed after a few weeks without a clear trigger.

Rapid-whole-exome sequencing (WES) revealed two compound heterozygous mutations in the NAXE gene. Results of metabolomics and lipidomics analysis are pending. After immediate initiation of therapy with niacin (100-200mg/d), coenzyme Q10 and thiamine, there was an incomplete recovery with bilateral hearing loss, spastic paraparesis, feeding problems and a need for daily intermittent non-invasive respiratory support. Follow-up MRI showed supratentorial atrophy, reversibility of bitemporal T2 lesions, and improvement of her myelopathy.

In (sub)acute myelopathy or encephalopathy elevated lactate in CSF may be indicative of NAXE deficiency. MRI changes can be variable, but the absence of gadolinium enhancement and normal cell count may suggest a non-inflammatory etiology. Regarding the short treatment window, high-dose supplementation with niacin 2x100 mg/d should be considered until results of genetic testing are available.

ABSTRACTS

Topic: Infectious and Inflammatory Diseases/ Neuroimmunology

EPNS25_cr118 - Preliminary study of mitochondrial cocktail therapy and magnetic resonance spectroscopy in pediatric acute encephalopathy with excitotoxicity

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Case report

Introduction: Acute encephalopathy with biphasic seizures and late reduced diffusion (AESD) is a severe neurological condition associated with excitotoxicity. Excessive glutamate release during status epilepticus leads to intracellular calcium influx and mitochondrial dysfunction, triggering oxidative stress, apoptotic factors, and ultimately cellular necrosis. Additionally, some cases of mild encephalopathy that could not be classified previously also show transient increases in glutamine on MRS. This subgroup has been reported as a spectrum of excitotoxic encephalopathy similar to AESD, clinically referred to as mild encephalopathy associated with excitotoxicity (MEEX).

We previously reported that early administration of a mitochondrial cocktail therapy—comprising vitamins used for mitochondrial diseases—might prevent AESD onset, based on clinical data. In this report, we present patients who exhibited elevated glutamine levels on magnetic resonance spectroscopy (MRS), indicating excitotoxicity, but did not develop AESD following early mitochondrial cocktail therapy.

Methods: We retrospectively examined the medical records of four cases of children under six years old who were hospitalized due to status epilepticus associated with fever lasting for more than 30 minutes and subsequently diagnosed with acute encephalopathy. We focused on the administration of mitochondrial cocktail therapy, clinical course, and MRS findings.

Results: Mitochondrial cocktail therapy was administered in three cases. Among them, two cases treated within 12 hours exhibited milder manifestations consistent with MEEX, while one case treated after 12 hours and one case without treatment developed AESD. MRS findings on days 5–8 showed glutamine levels ranging from 3.19 to 8.26 mM with all cases showing an increase exceeding the age-specific normal range + 2SD, and the high value of 8.26 mM was observed in the untreated case.

Discussion: These cases may represent one of the earliest reports combining MRS findings and clinical outcomes following mitochondrial cocktail therapy for acute encephalopathy. Although the early treatment cases showed elevated glutamine levels, indicating excitotoxicity, they did not progress to AESD. It remains unclear whether these cases were originally MEEX or if they were on the path to AESD but remained as MEEX due to the mitochondrial cocktail therapy. The use of MRS provides valuable insights into the pathophysiology of excitotoxicity in acute encephalopathy. Future research may clarify the role of mitochondrial therapy in preventing AESD and deepen our understanding of its underlying mechanisms.

ABSTRACTS

Topic: Movement Disorders/ Cerebral Palsy

EPNS25_cr119 - COQ4 mutation - More than childhood-onset ataxia

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Case report

Objectives: Ataxia is a clinical feature of many disorders, even pure cerebellar ataxia without any other symtoms can be caused by many mutations in dominant and recessive genes. Some oft he mutations may be responsive to CoQ10 treatment.

Methods: We present a 13 year old girl. At age 4 she was seen by a pediatrician and early onset progressive ataxia was diagnosed. Genetic testing (whole exome sequenzing) was ordered and MED 1-2L gen mutation was found, not explaining the clinical phenotype. The girl started school with good performance. At age 13 the first stroke like episode occured and the patient detoriated dramatically in terms of her vigilance and ataxia. Further stroke like epiosodes followed. Genetic testing was repeated, triple exom analysis was performed.

Results: Triple exom analysis revealed COQ4: c.718C>T p.(Arg240Cys) and c.164 G>T p.(Gly55Val) mutation. These results suggest, that this certain mutations in COQ4 explain the clinical phenotype of our patient. CoQ10 treatment was started in the patient only 14 days ago, so follow up is too short for any conclusions regarding treatment at this time.

Conclusions: According to our patient we emphasize the significance of repeated genetic testing, exspecially if genotype and phenotype do not match. CoQ10 treatment was started recently. It will be interesting to see if clinical improvement of ataxia occurs.

ABSTRACTS

Topic: Neurodevelopmental Disorders / Developmental Neuroscience

EPNS25_cr122 - Stolerman Syndrome: KDM6B Mutation and Developmental Delay

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Case report

Our patient is a 20-month-old child referred by his pediatrician for global developmental delay. In the neurological examination at that time and developmentally in subsequent consultations, we found that the boy has difficulties in social interaction, communication, and language. He does not respond to his name, has limited eye contact, and engages in stereotypies such as flapping when he is happy. He associates poor language acquisition, delayed speech and difficulties in understanding orders. His parents describe him as a routine-oriented child, somewhat clumsy motorically and hypersensitive to textures. He presents an unspecific phenotype with a bulbous nose, flat nasal root, detached ears, syndactyly on both feet and widened hands. Neuroimaging and neurometabolic studies are normal. Whole exome sequencing was requested, revealing a pathogenic variant in heterozygosity in the KDM6B gene (variant Chr17:g.7846714C>T c.685C>T;p.(Arg229*)), associated with Stolerman neurodevelopmental syndrome. The cosegregation study of both parents was negative, and the variant was not found, leading to the conclusion that the variant originated de novo, although mosaicism in the germline cannot be excluded. De novo mutations in the KDM6B gene have been identified through whole exome sequencing in patients with neurodevelopmental delay, variable intellectual disability, and facial dysmorphisms. These cases are grouped under the name Stolerman syndrome. Most of the mutations described in the literature cause loss of function and have been associated with alterations in histone lysine methylation. Few cases with autosomal dominant inheritance and incomplete penetrance have been reported. Phenotypically, they present very variable and nonspecific dysmorphic facial features, which may include, as in our case, anteverted nares, depressed nasal bridge, widened hands, thick fingers, and toe syndactyly. Some patients also meet criteria for a diagnosis of Autism Spectrum Disorder, most of them showing improved developmental traits after starting therapy, as in our patient.

ABSTRACTS

Topic: Neurodevelopmental Disorders / Developmental Neuroscience

EPNS25_cr123 - A Case of CAMK2A-Associated Neurodevelopmental Disorder: Diagnostic Insights Through Whole Exome Sequencing

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Case report

Objectives: This case report presents a 10-year-old female patient with developmental delay, intellectual disability, and epilepsy, emphasizing the importance of gathering detailed clinical history in order to facilitate comprehensive genetic testing.

Methods:

The patient is a 10 year old girl, diagnosed with epilepsy and severe psychomotor delay.

Her prenatal, perinatal, or family history was unremarkable. The psychomotor development was delayed from infancy (sitting at 18 months, walking with assistance at 2 years). Epileptic seizures began at 19 months, initially occurring once a month. Antiepileptic treatment was introduced at 27 months, leading to a temporary seizure-free period of two months before seizures resumed at one per week. Adding levetiracetam improved seizure control but introduced brief episodes of upward eye deviation a few times per month. Phenobarbital and vigabatrin exacerbated seizure frequency and caused cognitive decline.

Subsequent treatment included valproic acid and levetiracetam, with the latter discontinued at age six. Since then, seizures have decreased to twice yearly, with none observed in the past two years. She is currently treated with valproic acid. When she was first referred to our hospital at 9 years old, her EEG showed no epileptiform activity and brain MRI findings were normal for her age.

In addition to receiving outpatient neurological care, she was also under the supervision of a clinical geneticist. Karyotype, microarray, testing MECP2 and FOXG1 genes as well as epileptic encephalopathies NGS panel (containing 49 genes) were non-diagnostic.

The examination revealed facial dysmorphia, hypotonia and delayed psychomotor development (patient is non-verbal, walks a few steps with assistance). Whole exome sequencing (WES) was subsequently pursued given the chronology of developmental delay preceding seizures.

Results: WES identified a heterozygous in-frame deletion in the *CAMK2A* gene: c.874_876del, p.(Lys292del). This variant has been classified as likely pathogenic. Literature review associates *CAMK2A* variants with autosomal dominant intellectual developmental disorder (ID) 53. The identified variant aligns with previously reported phenotypes, including intellectual disability, hypotonia, speech and motor delays, behavioral abnormalities and epilepsy.

Conclusions: This case underscores the utility of WES over targeted panels in complex clinical presentations, particularly when initial genetic testing is non-diagnostic. Detailed phenotypic assessment and careful history-taking facilitated the decision to employ WES rather than broader epileptic encephalopathy NGS panel, which led to a definitive diagnosis. This case emphasizes the critical role of integrative clinical and genetic approaches in diagnosing rare neurodevelopmental disorders, enhancing personalized patient care and family guidance.

ABSTRACTS

Topic: Neurological Emergencies

EPNS25_cr124 - CACNA1A gene mutation leading to reversible coma responding to verapamil

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Case report

Objectives

Mutations in the CACNA1A gene (encoding the a1 subunit of the neuronal voltage-gated P/Q-type channels) may cause a wide variety of neurological disorders with no strict genotype-phenotype correlation. CACNA1A mutations are associated with familial hemiplegic migraine type 1, episodic ataxia type 2, and spinocerebellar ataxia type 6 with a clinical overlap between these three allelic disorders. We report on a young boy with three episodes of loss of consciousness after minor head trauma, associated with a CACNA1A gene mutation.

Case report

A four-month-old male has presented to the emergency department with central hypotonia and paroxysmal tonic upward gaze. Brain MRI, EEG and CSF neurotransmitter analysis were non-informative. Genetic testing (WES) revealed a de novo gain of function mutation in the CACNA1A gene (c.4043G>A p.R1348Q). Intensive daily physical, occupational and speech therapy was initiated at 6 months of age. At 16 months, acetazolamide was started but discontinued after a few weeks as it clearly worsened symptoms. At 18 months, ataxic features and global developmental delay were evident. At 19 months, daily oral verapamil (3mg/kg/day) was initiated to prevent coma associated with head trauma. At the age of 4.5 years, he experienced an episode of severe coma with dense left hemiplegia and diffuse right cerebral oedema after head trauma. Intravenous verapamil was initiated 10 hours after trauma with no immediate clinical improvement. After a week, he showed progressive clinical improvement, returning to his prior clinical status one month afterward. Two months, and also two years later, he had two episodes of head trauma of similar intensity with mild drowsiness and subtle unilateral arm weakness. Intravenous verapamil was initiated at 2 hours and at 20 minutes after the trauma, respectively, with striking improvement and discharge of the patient the very next day without any clinical sequelae. Today, at the age of nine, he stands with support, demonstrating a clear improvement in speech and cognition while he visits a regular school.

Conclusions

CACNA1A mutations should be suspected in childhood coma, especially in children with previous neurological features, as it seems to respond to intravenous verapamil, demonstrating clinical and neuroradiological recovery. Oral daily administration of verapamil could be associated with reduced risk of coma after head trauma, and this needs to be assessed in prospective studies.

ABSTRACTS

Topic: Neurogenetics

EPNS25_cr125 - Epilepsy, psychomotor regression and white matter abnormalities complicated by acute lymphoblastic leukaemia in a patient with WDR37 variant

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Case report

Objective

The WDR37 protein belongs to the WD repeat protein family, involved in the human proteasome. Members of this family are involved in a variety of cellular processes, including cell cycle progression, signal transduction, apoptosis, and gene regulation. De novo variants in *WDR37* are associated with epilepsy, colobomas, dysmorphism, developmental delay, intellectual disability, and cerebellar hypoplasia.

Method

Herein we report a case of a 9 years-old boy who presented with epilepsy, psychomotor regression, acquired movement and ocular abnormalities further complicated by the occurrence of acute lymphoblastic leukemia. Genetic testing identified a de novo missense variant in the *WDR37* gene.

Results

The patient initially presented with two episodes of generalized tonic-clonic seizures with spontaneous resolution and one episode of status epilepticus. On evaluation psychomotor regression and gait abnormality were noted, while a scleral exudate in the madula was found on ophthalmological examination. Lumbar puncture and EEG were normal, however MRI brain imaging revealed white matter and basal ganglia involvement as well as mild cerebral atrophy, therefore whole exome sequencing (WES) was requested. While still under investigation, the patient developed fever with negative screening for infection. Persistent leukopenia appeared to be preexisting on previous tests, with normal findings from the peripheral blood smear and immunophenotype. In addition, hepatosplenomegaly with significant fatty infiltration was detected and a subsequent myelogram established the diagnosis of acute lymphoblastic leukemia. Both antiepileptic medication and chemotherapy was initiated. A few months later, leukemia was in remission and the boy remained seizure-free. WES revealed a de novo heterozygous c.347G>T (p.Ser116Ile) mutation in the *WDR37* gene. His follow-up brain MRI showed improvement of white matter changes, while at the same time a clinical improvement was observed in both cognitive and motor function.

Conclusion

While genetic causes are known for many syndromes involving developmental anomalies, many individuals with overlapping phenotypes remain undiagnosed. De novo mutations in the *WDR37* gene have been associated with severe multisystemic manifestations, mainly epilepsy, developmental ocular anomalies, intellectual disability, craniofacial dysmorphism, variable skeletal, genitourinary and cardiac defects, increased risk for malignancy and in most cases leukodystrophic findings on brain MRI. The above constellation of findings should pinpoint to WDR37 gene mutations prompting for detailed genetic investigations.

ABSTRACTS

Topic: Movement Disorders/ Cerebral Palsy

EPNS25_cr128 - Atypical Inheritance and Genetic Complexity in Myoclonus-Dystonia Syndrome: A Case Report with double variants in SGCE and ANO3 Genes

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Case Report

Objectives: Myoclonus-dystonia syndrome is a rare neurogenetic disorder characterized by the association of myoclonus and dystonia. Mutations in the *SGCE* gene are a primary cause, with most cases resulting from paternal inheritance due to maternal imprinting. This report describes two cases from the same family with a novel *SGCE* pathogenetic variant (c.335G>C, p.Gly112Ala) exhibiting an atypical inheritance pattern and an unexpected additional variant in the ANO3 gene.

Methods: A 13-year-old male presented with myoclonus affecting the right arm and lower limbs, accompanied by dystonic features. Given the clinical presentation, genetic testing of the *SCGE* gene was performed, identifying a novel mutation (c.335G>C, p.Gly112Ala). The patient's mother had a history of cervical and cranial dystonia since childhood. Genetic analysis confirmed that she carried the same *SCGE* mutation as her son. Additionally, trio exome sequencing revealed a mutation in the *ANO3* gene (c.1391C>T, p.Thr464Ile), inherited from the mother and classified as a variant of uncertain significance.

Results: This study reports two members of the same family carrying dual mutations in the *SCGE* and *ANO3* genes, presenting with variable clinical phenotypes. The clinical significance of these variants remains uncertain and warrants further investigation. The *SCGE* variant, despite being recognized as pathogenic, poses interpretative challenges due to its typically paternal inheritance, necessitating an evaluation of potential uniparental disomy. Conversely, the *ANO3* variant, currently classified as of uncertain significance, requires functional studies to establish its pathogenicity. While further research is needed to determine if a single variant accounts for the observed phenotype, the possibility that the two mutations play distinct causal roles in each family member merits exploration. Such a scenario could provide a plausible explanation for the differing clinical presentations observed in these cases.

Conclusions: With this case report we wanted to emphasize the importance of a comprehensive clinical evaluation and genetic investigation in patients with suspected myoclonus-dystonia syndrome. Indeed, these findings have implications for genetic counselling and may inform future therapeutic strategies for this complex neurological disorder.

ABSTRACTS

Topic: Neurodevelopmental Disorders / Developmental Neuroscience

EPNS25_cr130 - Riboflavin Transporter Deficiency: A Rare Cause of Transfusion-Dependent Anaemia and Neurodevelopmental Regression

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Case report

Objectives:
To report a rare case of riboflavin transporter deficiency presenting with transfusion-dependent anaemia and developmental regression, highlighting diagnostic challenges and response to treatment.

Methods:

Riboflavin transporter deficiency, also known as Brown-Vialetto-Van Laere syndrome, is a rare neurological disorder characterised by pontobulbar palsy, bilateral sensorineural hearing loss, and involvement of lower motor cranial nerves VII–XII. Age at onset ranges from infancy to the third decade. BVVL is progressive, but the progression rate is variable. However, the presentation with haematological manifestations is quite rare and so far, only 13 cases have been reported. Here we present a case of 3 years old born to consanguineous parents at term via caesarean section due to foetal bradycardia. He was found to have anaemia during neonatal period necessitating recurrent packed red cell transfusions and multiple investigations, including bone marrow aspirate, revealed no morphological cause. He was initially thought to be pure red cell aplasia. He also had failure to thrive, height and weight on 2nd and 0.4th centile respectively, multiple admissions due to recurrent lower tract infections. He was under a neurodevelopmental paediatrician due developmental delay with only able to sit around 16 months and single words at around 20 months of life. He had an agnostic rapid whole genome sequence which was negative. He was referred to tertiary neurology with bilateral upbeat nystagmus. MRI and subsequent clinical examination revealed bilateral optic atrophy with normal parenchyma. At 23 months he presented with developmental regression. Repeat MRI was normal, and EEG raised suspicion of ESES for which sodium valproate was commenced. Clinical examination showed areflexia and tongue fasciculations. Riboflavin was commenced in view of a suspicion of BVVL The whole genome sequence was revisited, and a variant of unknown significance was identified in SLC52A2p. (Phe196Ile). Subsequent protein modelling predicted the variant to be severely destablising resulting in reduced SLC52A2 activity. Eight months since starting riboflavin treatment he showed improvement with his developmental skills and has not needed any further red cells transfusion since.

Results:
Riboflavin therapy led to improved developmental milestones, cessation of red cell transfusions, and clinical stabilisation over eight months.

Conclusions:
This case highlights a unique presentation of BVVL with transfusion-dependent anaemia. It underscores the importance of considering riboflavin transporter deficiency in children with unexplained anaemia and neurodevelopmental regression as timely treatment can significantly improve outcomes. Genetic testing and advanced protein modelling are invaluable tools in diagnosing rare conditions and guiding management.

ABSTRACTS

Topic: Neurogenetics

EPNS25_cr132 - Hyperekplexia - Story of two genes

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Case Report

We describe two cases of hyperekplexia with distinct genetic alterations varying in severity, clinical manifestations and available therapies. In both cases, there was no known consanguinity of the parents.
Baby SK was born at term via a normal vaginal delivery in another country. She had no notable family history of hyperekplexia and a negligible neonatal course. At 3 months of age, she was noted to have an accelerated startle reflex mainly in response to loud noises and tactile sounds. Upon inspection, it was observed that she exhibited some hypertonic posture. She was started on clonazepam from an early age. Her genetics showed a homozygous mutation in GLAR1 gene. It has been linked to delay in speech acquisition and mild intellectual disability. Our case did have speech difficulty, anxiety but no learning concerns. She was followed up till she was a teenager, and her startle reflex was well controlled.
Baby AS was born at term via a normal vaginal delivery. He was admitted from birth for an abnormal suck reflex, difficulty feeding and hypertonia in all four limbs. During his NICU stay, he was noticed to have significant startle reflexes. He had CFAM, EEG and MRI done which was reported to be unremarkable. Over the next several months, there were substantial concerns about faltering growth, frequent paediatric hospitalisations, global developmental delay, hazardous swallowing, and feed intolerance that necessitated PEG insertion. He also developed a see-saw nystagmus.The daily frequency of startles increased with numerous desaturation episodes, not responding to vigevano manoeuvre. He was on clonazepam, levetiracetam, oxcarbazepine and gabapentin. Sodium valproate, phenobarbitone and clobazam were tried and were unsuccessful in managing the episodes. His genetic analysis revealed a heterozygous mutation for a maternally inherited pathogenic GLRB Spice site variation and a paternally inherited GLRB likely pathogenic missense variant, resulting in biallelic pathogenic GLRB variant Hyperekplexia.
To summarise, early detection of hyperekplexia and molecular genetic investigation of all patients is critical for guiding therapeutic options and evaluating clinical severity. The majority of the mutations occur in GLRA1, which exhibits the classical type, responding well to treatment and having minor learning difficulties. Our second instance, involving a rarer biallelic GLRB pathogenic variation, has taken a considerably more dramatic trajectory, impairing many systems and quality of life while also proving to be more medication resistant. More long-term research to understand varied clinical manifestations are warranted.

ABSTRACTS

Topic: Neurogenetics

EPNS25_cr133 - Neuroimaging findings in a 16-year-old girl with an ACTA2 gene mutation: A case report

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Case report

Background: Smooth muscle dysfunction syndrome (SMDYS) is caused by a heterozygous mutation, predominantly de novo, in the actin protein encoded by the ACTA2 gene on chromosome 10q23. *Arg179His* variants in ACTA2 are associated with a neurovascular phenotype. This report describes a 16-year-old girl who presented with vertigo and stenosis of the internal carotid arteries (ICA).

Case presentation**:** A 16-year-old girl presented with intermittent dizziness and vertigo for the past 3 months. Her medical history includes patent ductus arteriosus (PDA) closure in the neonatal period, valve surgery one year ago for aneurysmal aortic dilatation, and it was noted that she had fixed dilated pupils at the age of 3.5 years. Brain magnetic resonance imaging (MRI) showed that both the internal carotid arter (ICA) and the intracranial vascular structures followed a straight course, with fusiform enlargement of both the cavernous and petrous segments of the ICAs and narrowing at the supraclinoid level. Based on these findings, an ACTA2 gene analysis was performed, which identified a heterozygous *Arg179His* variant in ACTA2.

Conclusions: One of the striking features of SMDYS is the presence of a patent ductus arteriosus (PDA) requiring repair in infancy and also characterised by a wide spectrum of vascular disease due to smooth muscle cell dysfunction in the cerebral vessels, pupils and heart. The Arg179His variant is known to be associated with a straight course of the intracranial arteries, absence of basal Moyamoya collaterals, dilation of the proximal internal carotid arteries and occlusive disease of the terminal internal carotid arteries. As shown in this case, although the MRI raised a high index of suspicion for the diagnosis, the patient's history and genetic analysis provide a clear path to the correct diagnosis.

ABSTRACTS

Topic: Neurogenetics

EPNS25_cr134 - Pontocerebellar hypoplasia type 10: A rare case complicated with coexistence of spinal musclular atrophy phenotype and genotype in neonatal screening test

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Case report

Introduction: Pontocerebellar hypoplasia type 10 (PCH10) is a rare autosomal recessive disorder due to CLP1 gene variants, characterized by cerebellar atrophy and neurodevelopmental delay. Howewer, spinal muscular atrophy (SMA) is neuromuscular disorder caused by *SMN1* gene mutations. We present a patient with a late diagnosis PCH10 complicated with SMA phenotype with *SMN1* gene mutation.

Case Presentation: A female infant was referred at 15 days of life with a perinatal SMA genetic screening test, showing homozygous deletion in *SMN1* exon 7 ,and four copies of *SMN2* exon 7.

At her first visit, her head circumference was 36 cm (56th percentile, 0.17 SDS), with normal muscle tone and reflexes. Born at 40 weeks via cesarean section (breech presentation), her parents were first-degree cousins of Syrian descent, with a family history of SMA.

At one month, early intrathecal nusinersen treatment was applied. However, at three months, she exhibited neurodevelopmental regression, with worsening axial hypotonia, hyperactive deep tendon reflexes, no head control, and absent social smiling. Her DTRs were hyperactive, which is atypical for SMA. Microcephaly (37 cm, -2.7 SDS) was noted. Electromyography showed normal nerve conduction velocities. Brain MRI revealed thin corpus callosum, prompting further genetic analysis.

Whole Exome Sequencing (WES) identified a homozygous c.419G>A variant in the *CLP1* gene, associated with pontocerebellar hypoplasia type 10. The ClinVar database classified this variant as pathogenic. The patient was diagnosed with PCH10 associated with SMN1 genetic variants.

Discussion: This case highlights the importance of further genetic testing when clinical findings do not align with the expected phenotype. The coexistence of SMA and PCH10 complicates disease progression and treatment. While nusinersen is effective for SMA, there is currently no targeted therapy for PCH10.

Conclusion: This case presentation emphasizes the need for further genetic tests in patients do not macth the expected clinical course in follow-up.

ABSTRACTS

Topic: Neurogenetics

EPNS25_cr136 - KINSSHIP Syndrome: A Case Report With Clinical And Molecular Evaluation

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Case report

KINSSHIP syndrome is a rare genetic disease characterized by cognitive, behavioral and physical examination abnormalities. This syndrome can cause patients to have developmental delays.

An 11-year-old girl was admitted to the pediatric neurology clinic with complaints of neuromotor developmental delay, delayed language development and learning difficulties. The patient's medical history included an uneventful pregnancy and delivery process, but there were significant delays in reaching developmental milestones. She sat without support at the age of 1.5, walked at the age of 2.5 and spoke at the age of 3.5. Although there was no similar disease in the family history, it was learned that there was no consanguineous marriage between the parents. On physical examination, thin upper lip, long nose, low columella, short philtrum, strabismus in both eyes, upslanting palpebral fissures, clinodactyly in bilateral 3rd, 4th, and 5th fingers of the hands, widening of proximal interphalangeal joints, pes equinovarus in both feet, overlapping fingers on the right, bilateral hearing loss, and an operation scar on the lip due to cleft palate were present. The patient's neuromotor developmental stages were retarded. The patient's brain magnetic resonance images were normal. In the genetic analysis, a heterozygous deletion in the AFF3 gene was detected as a result of microarray examination and the diagnosis of KINSSHIP syndrome was confirmed.

The patient was recommended speech therapy, special education support, and behavioral therapy with a multidisciplinary approach. The family was given genetic counseling and informed about the nature of the syndrome and possible prognosis.

KINSSHIP syndrome is a rare syndrome that is difficult to diagnose and is usually diagnosed with clinical symptoms and genetic tests. In this presentation, the importance of early intervention is emphasized by drawing attention to the clinical findings of the syndrome. Increasing awareness of this rare syndrome can improve earlier diagnosis and management processes.

ABSTRACTS

Topic: Infectious and Inflammatory Diseases/ Neuroimmunology

EPNS25_cr138 - Clinical presentation in familial aquaporin 4-positive NMOSD

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Case report

Objectives: Neuromyelitis optica spectrum disorder (NMOSD) is a rare inflammatory disease of the central nervous system with severe immune-mediated demyelinating and axonal damage of the spinal cord and optic nerve. Serum autoantibodies targeting the water channel aquaporin-4-immunglobuline G (AQP4-IgG) are associated with NMOSD. AQP4-IgG-serumpositive NMOSD is usually sporadic, only few familiar cases have been described so far.

Methods: We present demographic status, clinical course, laboratory findings, treatment and neuroimaging of two affected family members (mother and daughter) with the diagnosis of AQP4 positive NMO spectrum disorder. The family is of Turkish descent.

Results: Initial presentation of the mother was at the age of 38 years with cervicothoracic longitudinally extensive transverse myelitis and sensorimotor spinal cord symptoms and positive AQP4-antibody titre. High dose methylprednisolone resulted in incomplete remission, therefore Rituximab was initiated after two further relapses involving the spinal cord. Due to severe hypogammaglobulinemia as a side effect of long-term Rituximab-therapy and an urgent suspicion of common variable immune defect (CVID), therapy was switched to azathioprine (AZA). Unfortunately, AZA had to be withdrawn after seven months due to leukopenia and cytomegalovirus sepsis. Consequently, treatment with Satralizumab was given over the period of the last three years. Her last clinical relapse was at the age of 48 years, which was completely resolved with two steroid pulses (Expanded Disability Status Scale, EDSS-Score 0).

The daughter's first symptom was right-sided optic neuritis (ON) at the age of 14 years. Initial AQP4-antibody titre was positive. Magnetic resonance imaging of the spinal cord did not show any spinal lesions. Her symptoms persisted after high dose methylprednisolone, therefore 5 cycles of plasmapheresis were started, resulting in a rapid improvement. Subsequently, therapy with AZA with a slow tapering of oral steroids was initiated. At the 4-month post-diagnosis follow-up, the EDSS score was 0.

Conclusions:

Our two cases of familiar NMOSD demonstrate that the clinical presentation can be very variable in terms of the initial neurological symptoms as well as the age of onset. The results for human leukocyte antigens (HLA) alleles are pending, as specific HLA haplotypes are shared among familial cases. Careful examination of the family history is essential for an early diagnosis and tailored therapy in the cohort of pediatric patients with initial presentation as isolated ON.

ABSTRACTS

Topic: Neurogenetics

EPNS25_cr140 - A Case Report of a De Novo TAOK1 Variant Associated with Childhood-Onset Action Tremor

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Case report

Objectives:

The aim of this study was to investigate the potential genetic basis of childhood-onset tremor in a 15-year old patient.

Methods:

We conducted a comprehensive clinical and genetic evaluation of a 15-year-old male with a history of bilateral upper limb tremor. The patient was assessed through detailed neurological examination, including motor function assessment, electromyography (EMG), and magnetic resonance imaging (MRI). Trio exome sequencing (ES) was performed on the patient and his parents to identify potential genetic variants. The identified variant was further analyzed using available genomic databases, including GnomAD and ClinVar.

Results:

The patient presented with a bilateral upper limb postural and kinetic tremor, initially observed in early childhood and progressively worsening with age. The tremor was exacerbated by stress and emotions, impairing motor tasks such as writing, eating, and holding objects. Neurological examination revealed no other significant findings. EMG confirmed a kinetic tremor with a frequency of 6–7 Hz. Exome sequencing identified a de novo heterozygous frameshift variant in *TAOK1* (NM_020791.4: c.952del, p.Gln318Argfs*9), classified as likely pathogenic based on ACMG criteria. This variant was absent in both GnomAD and ClinVar databases, with no additional pathogenic variants detected. The patient's tremor significantly improved with propranolol treatment.

Conclusions:

This case supports the association between *TAOK1* mutations and tremor, specifically childhood-onset, bilateral action tremor, even in the absence of other neurodevelopmental symptoms. The findings suggest that *TAOK1* variants should be considered in patients with a family history of tremor, particularly those with early-onset action tremor that worsens with stress. Further studies involving larger patient cohorts are needed to explore the frequency of *TAOK1* mutations in hereditary ET and to evaluate the long-term progression and potential development of additional neurological symptoms

ABSTRACTS

Topic: Neurogenetics

EPNS25_cr142 - AHDS: A Rare Disorder Not To Be Forgotten

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Case report

Introduction:

Allan-Herndon-Dudley syndrome (AHDS or MCT8 Deficiency) is a rare X-linked disorder and presents with significant hypotonia, feeding difficulties in infancy, developmental delay, intellectual disability and abnormal thyroid function tests. We present a rare case mimicking a neuromuscular presentation in an infant.

Case summary:

A 10-month-old male with an unremarkable birth history presented with profound hypotonia, delayed development, and abnormal thyroid function tests (low free T4, elevated TSH). He had significant motor delay including head lag, inability to sit unsupported, and feeding difficulties. MR brain showed a small pituitary gland and levothyroxine was commenced. Despite therapy adjustments, his developmental progress remained severely impaired and concerns were raised about an alternate diagnosis. Metabolic and genetic testing including microarray and specific panels (Prader-Willi, SMN1, congenital myotonic dystrophy) were normal. Over time, feeding challenges led to failure to thrive requiring gastrostomy feeding. At two years, whole-genome sequencing identified a hemizygous missense variant in SLC16A2, confirming a diagnosis of AHDS. He has commenced Tiratricol (TRIAC), with notable improvements in head control, limb movements, and energy levels.

Discussion:

MCT8 is crucial for the transport of thyroid hormones particularly T3 from the blood into tissues, including the brain. In our case, his profound hypotonia, developmental delay, and feeding difficulties prompted further investigations including metabolic and neuromuscular genetic testing. MR findings of a thin corpus callosum and small pituitary gland supported the hypothesis of a central disorder, but normal anterior pituitary function and an inadequate response to levothyroxine suggested an alternative aetiology. Whole-genome sequencing confirmed the diagnosis of AHDS, emphasising the critical role of comprehensive genetic testing in identifying rare disorders. Treatment with Tiratricol (TRIAC), a thyroid hormone analogue bypassing the defective MCT8 transporter, has shown early benefits, consistent with emerging evidence of its potential efficacy in AHDS management. However, long-term outcomes remain uncertain.

Conclusion:

AHDS should be considered in a male infant presenting with profound hypotonia, severe developmental delay, feeding difficulties and abnormal thyroid function with negative results on routine genetic/metabolic investigations.

ABSTRACTS

Topic: Movement Disorders/ Cerebral Palsy

EPNS25_cr143 - Pelizaeus-Merzbacher Disease in a Young Girl

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Case report

Background: Pelizaeus-Merzbacher disease (PMD) is a rare X-linked recessive demyelinating leukodystrophy affecting the central nervous system (CNS). Carrier females with the submicroscopic duplication in the PLP gene that causes PMD are usually asymptomatic.

Methods: Observational study

Results: A girl who was born in 2014 in term, but had delays in fetal development starting at 27 weeks, had neurological examinations when she was 9 years old. At that age, she could hold her head, turn, and sit with support, but she could not stand on all fours, crawl, or walk. She also had stigmas of dysembryogenesis, including hypertelorism, strabismus, prognathism, a Gothic sky, and a hydrocephalic head shape. At an early age, she was diagnosed with cerebral palsy.

An MRI of the brain showed signs of diffuse focal lesions in the white matter, atrophic changes in the brain tissue, hypogenesis of the corpus callosum, and internal hydrocephalus, as interpreted by a radiologist in Kazakhstan. However, due to hypomyelination, a Dried Blood Spot (DBS) test was performed for whole exome sequencing, which revealed a mutation in the PLP1 gene associated with X-linked Pelizaeus-Merzbacher disease, which is heterozygous in NC_000023.10: g.(?_84258919)(119297693_)dup (GRCh37), with a minimum size of 35.0 Mb.

Discussion:

Literature suggests that PMD predominantly affects males due to its X-linked inheritance pattern. This inherent gender bias may have contributed to the initial misdiagnosis in the female patient.

This case highlights the importance of considering rare differential diagnoses, even when a seemingly straightforward diagnosis like cerebral palsy is initially suspected. The initial misdiagnosis underscores the need for a comprehensive diagnostic approach, including careful clinical assessment, neuroimaging studies, and genetic testing, especially in cases with atypical presentations. Early and accurate diagnosis of PMD is crucial for appropriate management, genetic counseling, and family planning.

Conclusion:

This case study emphasizes the importance of a thorough diagnostic workup, including genetic testing and neuroimaging, in patients with suspected neurodevelopmental disorders, even when an initial diagnosis appears straightforward. Early and accurate diagnosis of PMD is crucial for appropriate management and genetic counseling.

ABSTRACTS

Topic: Neurogenetics

EPNS25_cr144 - Oculomotor apraxia as nuclear sign in a new description of a tctn1-related disorder

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Case report

Introduction

Mutations in tectonic gene TCTN1 have been recently associated with autosomal recessive Joubert Syndrome type 13 in a few patients, a hereditary ciliopathy classically characterized by developmental delay, hypotonia and a pathognomonic cerebellar and brain stem malformation finding on MRI called the molar tooth sign (MTS). These can be accompanied by abnormal breathing pattern and/or oculomotor apraxia. Additional non-classical features include retinal dystrophy, ocular colobomas, renal disease, hepatic fibrosis, polydactyly or oral hamartomas, deriving in clinical subtypes or related disorders, all of them sharing the distinctive MTS, including known variants in TCTN1 to date.

Case report

Two sisters, 5- and 2-year-old, both born to consanguineous (cousins) healthy parents and with no relevant perinatal history, none of them requiring postnatal assistance or respiratory support. The first child was assessed at 6 months old presenting oculomotor apraxia as an exclusive symptom, showing a normal psychomotor development that persists throughout time. An MRI was performed at this moment and was reported to be normal, with no signs of MTS. Shortly after, her sister was born and also manifested oculomotor apraxia phenotype, but contrary to her sibling, she demonstrated evidence of hypotonia and global developmental delay. Imaging in this infant is still pending, therefore the absence of the MTS is yet to be proven. Exome sequencing and familial segregation analysis was performed in both patients, a homozygous variant of uncertain significance was identified in the TCTN1 gene (NM_001082438.2) c.620A>G p.(Tyr207Cys), confirming autosomal recessive inheritance.

Discussion

A new variant of TCTN1 gene is being exposed, displaying manifestations that differ from those known thus far. It is certain that in one of the subjects it is only expressed as oculomotor apraxia, for this reason, in the absence of classical clinical features, especially the MTS, it cannot be framed within the term ´Joubert Syndrome and related disorders´. Furthermore, oculomotor apraxia hasn´t been described before in association with variants in TCTN1. Intrafamilial phenotypic heterogeneity is remarkable as well.

Conclusion

This new description of an oculomotor apraxia phenotype related to TCTN1- disorder could widden or modify classic diagnostic criteria for Joubert Syndrome and expand the phenotype.

ABSTRACTS

Topic: Epilepsy: Diagnosis and Investigations

EPNS25_cr146 - A case of FIRES: acute treatment and early neuropsychological outcome

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Case report

Febrile-infection-related epilepsy syndrome (FIRES) is a rare and challenging entity, with an acute presentation of refractory status epilepticus following/during a febrile illness. The outcome of FIRES is poor with significant morbidity, including refractory epilepsy and neurocognitive sequelae.
We present a 9-year-old boy, previously healthy, with normal development, family history significant with a first cousin with a GLUT1 deficiency. He was admitted to the emergency department with depression of consciousness. He started fever and a mild headache 60 hours before, followed by 24 hours of apyrexia. Initial laboratory workup, brain CT and lumbar puncture were normal. Aciclovir and ceftriaxone were initiated.
On day 2 he was confused and agitated, followed by multiple focal seizures on day 4, some of them with secondary generalization, with progression to status epilepticus. Levetiracetam, phenytoin, midazolam and methylprednisolone (1g/day) were started in the ICU. The status epilepticus evolved to super refractory, despite the multiple antiepileptic and anesthetic drugs and immunoglobulin (2g/kg). Brain MRI, extensive blood and CSF workup didn't reveal infectious, toxic, autoimmune, paraneoplastic and metabolic causes. Ketogenic diet was started on day 23 and anakinra (3 mg/kg/day) on day 25 (after treating ventilator-associated pneumonia). There was a good response to the treatment, with fewer clinical and electrographic seizures, which allowed a progressive discontinuation of antiepileptic drugs. The initial cognitive improvement was progressive and substantial.
Three months later, he remains treated with anakinra 7.5 mg/day, perampanel 12 mg/day, clobazam 20 mg/day, ketogenic diet and cenobamate (in titration). He has on average one short focal seizure a day. Neuropsychological testing revealed a normal IQ score, but significant impairment in processing speed, verbal working memory, reading (fluency, accuracy and comprehension), writing and arithmetic skills. He started a rehabilitation program and returned to school, with an individual education plan.
This case highlights the challenges of FIRES. Cognitive deficits have a broad spectrum and are considered to be multifactorial. They are related to acute or chronic phase factors, such as longer use of anesthetic drugs and duration of refractory status epilepticus, number and side effects of antiepileptic therapy, and ongoing seizure activity in the chronic phase. Despite the severity and refractoriness of the super refractory acute status epileptic, our patient had a satisfactory outcome.

ABSTRACTS

Topic: Neuromuscular Disorders

EPNS25_cr147 - A Case of DYNC1H1-Related Neuromuscular Disorder: Clinical Features and Genetic Insights

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Case report

Objectives

DYNC1H1-related disorders exhibit a broad spectrum of phenotypes, including various neuromuscular presentations, congenital malformations, developmental delay, and epilepsy. This case highlights a rare presentation of a DYNC1H1-related neuromuscular disorder (NMD), contributing to the expanding phenotypic spectrum of this condition.

Methods

A retrospective review of the patient's history, medical records, genetic testing results (NGS), and video documentation was conducted.

Results

A 5-year-old boy presented with gait disturbance and pes deformity. Clinical examination revealed leg muscle atrophy, moderate muscular hypotonia, pes cavus, and diminished knee reflexes. His motor milestones were normal, with no history of fatigue. Cognitive development was appropriate for his age.

Electromyography did not demonstrate neurogenic changes. Creatine kinase (CK) levels and brain and spine MRI findings were unremarkable. The boy’s mother also exhibited an unusual gait. Whole-exome sequencing identified a heterozygous missense mutation in the DYNC1H1 gene (c.1792C>T), with parental testing confirming the same mutation in the mother. The revised clinical presentation and obtained data supported a diagnosis of spinal muscular atrophy with lower extremity predominance (SMA-LED).

Conclusion

This report highlights a rare presentation of a DYNC1H1-related NMD, contributing to the expanding phenotypic spectrum of this condition. Genetic testing is crucial in identifying underlying mutations in atypical neuromuscular presentations, which is essential for early diagnosis and management.

ABSTRACTS

Topic: Epilepsy: Diagnosis and Investigations

EPNS25_cr149 - Recurrent focal status epilepticus in a form of small vessel vasculitis: brain biopsy as a key element in diagnosis and treatment.

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Case report

Objectives: Small vessel vasculitis (SVV) of the central nervous system (CNS) have a highly variable clinical presentation. Isolated and recurrent involvement of a single brain region is rarely described, as is status epilepticus. The diagnosis is based on histopathological findings. The aim is to describe an atypical presentation of SVV of CNS, to highlight the crucial role of brain biopsy in the diagnosis and treatment.

Methods: Neurological examination, Neuropsychological assessment, Ictal and Interictal video EEG recordings, Magnetoencephalography, brain MRI and PET, brain biopsy.

Results: A 17-year-old male patient experienced epilepsy onset at 12 years. The course was characterized by recurrent focal aphasic status epilepticus (SE), associated with slow and epileptiform activity over the parieto-temporal region of the left hemisphere on EEG. The SE were refractory to ASM (carbamazepine, lacosamide), whereas they stopped after steroid or IVIG treatments. During SE, brain MRI showed hyperintense signal alteration in T2 sequences in the left parietal area, that suggested the presence of focal cortical dysplasia. However, this hypothesis was challenged by the disappearance of the signal abnormality after steroid therapy, and by the finding of inter-ictal left parieto-temporal hypometabolism at PET scan. At SE recurrences, we observed the reappearance of the hyperintense left parietal signal alteration together with the appearance of PET hypermetabolism of left temporo-parietal and insular areas. Neurological examination was normal in the interictal period, although neuropsychological evaluation revealed persistent language difficulties, especially in verbal fluency. Extensive immunological and genetic diagnostics were unrevealing. Brain biopsy showed inflammatory infiltrates pointing to the diagnosis of small vessel vasculitis. Systemic involvement and/or involvement of other organs were excluded. After the diagnosis of vasculitis, the patient received a cycle of cyclophosphamide, followed by mycophenolate.

Conclusions: The case is an example of atypical clinical and neuroradiological presentation of primary CNS vasculitis, with recurrent SE and recurrent isolated involvement of a single brain region. In this case, clinical, neurophysiological and radiological data oriented towards a focal brain involvement and the biopsy was extremely important to drive the diagnosis and direct treatment.

ABSTRACTS

Topic: Miscellaneous

EPNS25_cr151 - Case Report: Nitric Oxide induced subacute combined degeneration of the spinal cord in a 14 year old

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Case report

Traditionally developed as an analgesic, Nitric oxide(NO) has been used recreationally since the early 17th century when it was noted to provide a 'high' with feelings of euphoria. Subacute degeneration of the spinal cord secondary to Nitric oxide inhalation was first documented in the 1970s. The abuse of inhaled NO has increased in the UK, making it a public health concern.

A 14-year old boy presented to his local hospital with a history of an ascending sensory loss starting at his feet and rising to the mid-calf, alongside an unstable gait. He had a history of dropping things and reduced sensation in his fingers. He proffered a history of regular (at least once weekly) use of recreational NO inhalation over the preceding 4 to 5 months.

On examination, he had sensorimotor deficits in his lower limbs, with weakness at knees, ankles and feet, including foot drop and loss of touch and proprioception, particularly below the knees. Power testing at the hips was normal.

Electromyography demonstrated moderate and generalised large fibre axonal type polyneuropathy. MRI brain and spine were unremarkable. Ophthalmological assessment was normal. Vitamin-B12 levels were normal, however he had raised methylmalonic acid levels, suggesting functional Vitamin-B12 deficiency. It was concluded that he had neurological sequelae (demyelination) of functional vitamin-B12 deficiency secondary to NO inhalation.

Treatment with intramuscular vitamin-B12 was initiated over a 4-week period alongside physiotherapy input. He had mild improvement of his symptoms acutely. The vitamin-B12 was continued for a further 3 months and was associated with further gradual improvement over the next year.

At 21months post exposure, he has mild residual weakness with 4/5 power in dorsiflexion and plantar flexion of feet with normal power elsewhere. He has ongoing proprioception difficulties of his toes but normal at the ankle. He is unable to walk on his heels. He has reduced touch sensation in the bottom third of both legs and feet with hyperaesthesia of feet, particularly on the plantar aspect.

Demyelination of the spinal cord secondary to NO inhalation has been well documented in the adult population. There has been a rise in the number of adult cases[2], leading to development of a guideline by the British association of neurologists. We present the case of a 14year old with subacute combined demyelination of the spinal cord secondary to nitric oxide inhalation, in the hope to increase understanding and recognition in the paediatric population.

ABSTRACTS

Topic: Neuromuscular Disorders

EPNS25_cr154 - Successful Treatment of MuSK Antibody–Positive Myasthenia Gravis with Rituximab

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Introduction

Myasthenia gravis (MG) is a neuromuscular junction condition resulting from autoantibodies targeting proteins critical for synaptic transmission, chiefly the acetylcholine receptor (AChR) or, less frequently, muscle-specific tyrosine kinase (MuSK). This article analyses the clinical course and therapy of MuSK-MG in a 16-year-old patient, thereby augmenting the scarce data on pediatric instances.

Case Report

A 16-year-old male patient presented with speech and swallowing difficulties and drooping eyelids that started two weeks ago. The patient had left semi-ptosis. Bilateral orbicularis oculi muscles were weak, neck extensor muscle strength was 4/5. Nasone speech was present. Ice and fatigue tests were performed with a preliminary diagnosis of MG. No significant response was obtained. Neostigmine test was performed; ophthalmoparesis and partial improvement in speech were observed. The patient was given high-dose IV methylprednisolone treatment for 5 days. Improvement was observed in his complaints. Single fiber EMG performed on the left frontalis and extensor digitorum muscles of the patient showed an increase in the mean of consecutive differences (MCD) and conduction block in three pairs. The patient's acetylcholine receptor (AchR) antibody was negative. Anti-MuSK antibody titer was >12.0 U/mL (N<0.4 U/mL). The patient was diagnosed with Anti-MuSK antibody positive MG and pyridostigmine hydrobromide and oral methylprednisolone were started. Pyridostigmine treatment was stopped because there was no adequate response to the treatment. Ophthalmoparesis and speech completely improved in the first week of oral methylprednisolone treatment. Attack symptoms developed again during the drug tapering period 2 months later. Rituximab treatment was started in addition to low-dose steroid treatment. Rituximab was given in 2 doses of 2x375mg/m^2/day at 2-week intervals. Low-dose steroid treatment was completed in 6 months and stopped. No attacks were observed in the patient's 1-year outpatient clinic follow-ups. Side effects of steroid treatment included a moonface, widespread acne, weight gain and striae. No attack symptoms were observed.

Conclusion

This case report demonstrates that rituximab may be an effective and tolerable treatment for MuSK antibody-positive myasthenia gravis compared to the side effects of steroid therapy.

ABSTRACTS

Topic: Neurogenetics

EPNS25_cr155 - Refractory Epilepsy in Siblings with Knobloch Syndrome: Case Report

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Knobloch and Layer described congenital encephalocele, vitreoretinal degeneration, and high myopia symptoms in five siblings from a family with consanguineous marriage. The disease, now known as Knobloch Syndrome (KS), is caused by mutations in the COL18A1 gene, which encodes collagen XVIII. Knobloch Syndrome type 1 (KS, OMIM #267750) is one of the rare hereditary syndromes, with an incidence of less than one case per million. Diagnosing KS can be challenging due to its varied clinical features and rarity. We present the case of two male siblings of Iraqi origin, born to consanguineous parents and followed for intractable epilepsy, who exhibited occipital encephalocele, high myopia, global developmental delay, intellectual disability, and widespread polymicrogyria.

Both cases showed developmental delay and intellectual disability, with tonic, myoclonic, and atonic seizures, high myopia, nystagmus, and strabismus. Case 2 also had a dislocation lens in the left eye. Case 1 was diagnosed with hypothyroidism at the age of seven. The patients had undergone surgery for occipital encephalocele in the neonatal period, resulting in scars in the occipital region. Magnetic resonance imaging (MRI) revealed agenesis of the inferior cerebellar vermis, hypoplasia of the pons and medulla, and widespread polymicrogyric changes in the bilateral frontal and anterior temporoparietal regions. Electroencephalography (EEG) findings indicated generalized epileptiform activity, and intractable seizures responded to clobazam treatment. These siblings extend the epileptology of KS to include Lennox-Gastaut Syndrome, characterized by tonic-atonic seizures, slow spike-wave discharges, and paroxysmal fast activity. This emphasizes the need to consider KS in cases of intractable epilepsy, cortical development malformations, and early-onset ocular abnormalities. A comprehensive report on the phenotypic, clinical, and electrographic characteristics of each genetically validated case will contribute significant data to the literature.

ABSTRACTS

Topic: Neurogenetics

EPNS25_cr156 - Atypical Neuronal Ceroid Lipofuscinosis Type 2 - presentation of two siblings

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Case report

Background: Neuronal Ceroid Lipofuscinosis Type 2 (CLN2) is the only treatable subtype among neurodegenerative lipofuscinoses. The hallmark of typical CLN2 include seizures, language delay, ataxia and visual loss. Atypical cases with late-onset symptoms are increasingly diagnosed.

Aim: To raise awareness of atypical CLN2 presentation and underscore the importance of early intervention.
Methods: Phenotypic, genetic, laboratory and imaging findings of two siblings with atypical CLN2 are presented.

Results: Patients are a 14.5year-old male and his 12.5years-old sister. Their early neurodevelopment was normal. The boy was noticed with tip-toes walking since the age of 6. He was first evaluated at the age of 11 years-old, when ataxia, tremor and dysarthria were gradually added to his symptoms. Magnetic Resonance Imaging (MRI) showed cerebellar atrophy. Whole exome sequencing revealed two likely pathogenic novel mutations in *TPP1*- gene (c.889C>T and c.1012C>T). TPP1 enzyme activity in leukocytes was low (8.5nmoles/mg protein/h). Currently, he presents with dysarthria, tremor, cerebellar ataxia, abnormal saccades and nystagmus. Cognition is mildly impaired and vision is normal. Generalized epilepsy on levetiracetam has recently presented. Interestingly, electroencephalogram(EEG) is normal and intermittent photic stimulations elicit no paroxysmal response in low frequencies. His sister, carrying the same *TPP1*-mutation, remains completely asymptomatic. Brain MRI shows cerebellar atrophy. TPP1 enzyme activity in leukocytes is also low (8.1nmoles/mg protein/h).
Conclusion: *TPP1*-mutations may result in atypical CLN2 despite substantial low enzyme activity. Phenotype includes late-onset movement disorders, dysarthria and epilepsy. Typical EEG findings, visual and cognition impairment may lack. Treatment with cerliponase alfa may benefit these atypical CLN2 patients.

ABSTRACTS

Topic: Neuromuscular Disorders

EPNS25_cr157 - Challenges in treating and preventing recurrence of Miller Fisher variant of Guillain-Barré syndrome in children in limited-resource setting: A case report

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Case report

Diagnosing and managing children with Guillain-Barré syndrome (GBS) in Indonesia has many challenges, even in tertiary care hospitals. Recurrency of Miller-Fisher variant of GBS is relatively more common than other variants. We herein report a case of a 10-year-old girl who came to our emergency unit with the chief complaint of worsening paralysis in all of her limbs since 1 week prior to admission. Her earliest symptom was double vision accompanied by dizziness 10 days before admission. She was taken to a clinic and was misdiagnosed with vertigo. Three days later she experienced weakness in both of her legs and the weakness ascended to her arms. Physical examination revealed oculomotor and trochlear nerve paresis, and hyporeflexia. Cerebrospinal fluid examination showed albumin-cytological dissociation. Nerve conduction study reported axonal motoric polyradiculoneuropathy in all extremities. Based on these findings, the patient was diagnosed with GBS with Miller Fisher variant. Plasmapheresis was only done in two sessions instead of the recommended five sessions due to limited resources. Immunotherapy with azathioprine was given to compensate the inadequate treatment and prevent recurrence. In the second monitoring outpatient visit one month after discharge, she was able to walk for 10 meters without help. She no longer experienced dizziness nor double vision. The GBS Disability Score was 2. To the best of our knowledge, this is the first case report which addresses challenges in managing and preventing GBS with Miller Fisher variant in a developing country. Studies of treatments to treat and prevent GBS recurrency in children are still much needed since providing current adequate definitive treatments remains a challenge.

ABSTRACTS

Topic: Epilepsy: Diagnosis and Investigations

EPNS25_cr160 - Eating epilepsy as initial symptom in five children with pathogenic PRRT2 variants

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Case report

Introduction

Pathogenic variants in the proline-rich transmembrane protein 2 (*PRRT2*) gene are typically associated with paroxysmal kinesigenic dyskinesia or self-limited (familial) infantile epilepsy (SeLIE). SeLIE is an autosomal-dominant (AD) epileptic disorder with typical seizure onset during the first 12 months of life and a good response to certain antiseizure medications, especially sodium channel blockers. The prognosis regarding the epilepsy is favorable with typical remission before the age of two years.

Case series

We retrospectively analyzed the data of five infants with pathogenic AD *PRRT2* mutations who were admitted to our tertiary center because of frequent focal motor seizures. All patients were in between four and six months of age. They had no family history of seizures and interictal EEG and MRI were unremarkable. During their hospitalization we could observe, that in the initial phase of epilepsy all seizures occurred during or shortly after feeding. Levetiracetam (LEV) did not reduce seizure frequency in any of the five patients. Therefore, four patients were switched to carbamazepine (CBZ), two following receipt of the genetic testing, and two due to clinical suspicion of PRRT2 related epilepsy. One patient was switched to sodium valproate (VPA). After changing antiseizure medication all patients were immediately seizure free. Due to electroclinical and genetic findings, all patients were classified as SeLIE and further disease course was uncomplicated in all five cases.

Conclusion

Pathogenic *PRRT2* mutations are usually associated with a benign, self-limited infantile epilepsy. Because of its early presentation and high seizure burden at onset the initial differentiation of a developmental epileptic encephalopathy (DEE) can be challenging. In our case series, we report the presence of eating epilepsy as an indicator for a benign *PRRT2*-associated condition and suggest genetic testing as well as early consideration of sodium channel blockers.

ABSTRACTS

Topic: Neuromuscular Disorders

EPNS25_cr161 - Immune-mediated necrotizing myopathy in Duchenne muscular dystrophy carrier: A case report

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Case report

Objective
To describe a case of immune-mediated necrotizing myopathy in a Duchenne muscular dystrophy (DMD) carrier, highlighting the importance of recognizing atypical manifestations by the combination of investigation methods.

Methods
This study reports a case of a 6-year-old female patient with coexisting immune-mediated necrotizing myopathy and DMD carrier status. The diagnosis was established through a combination of clinical evaluation, laboratory testing, imaging studies, genetic analysis, and muscle biopsy findings.

Results
The patient initially presented with ptosis and dysarthria, followed by progressive axial and proximal muscle weakness. Physical examination revealed a negative Gower's sign. Laboratory studies showed markedly elevated creatine kinase levels and borderline elevated PM-Scl75 antibodies on myositis profile. Imaging findings demonstrated generalized muscle atrophy with hyperintense myositis on MRI muscle and reduced extraocular muscle size on MRI orbit. Muscle biopsy revealed scattered necrotic fibers with myophagocytosis, with dystrophin staining showing reduced N-terminal expression in non-necrotic sarcoplasmic membranes. Genetic analysis revealed negative for heterozygous DMD with non-randomized X-linked inactivation. RNA analysis from muscle pathology further supported the diagnosis. Treatment included monthly intravenous immunoglobulin, corticosteroids, and methotrexate, resulting in improved muscle strength over time.

Conclusion
This case underscores the potential coexistence of DMD and immune-mediated necrotizing myopathy. Early recognition and diagnostic precision, utilizing myositis profiling and genetic testing, are crucial to guide timely and appropriate therapeutic interventions, which can significantly improve patient outcomes.

ABSTRACTS

Topic: Neuromuscular Disorders

EPNS25_cr162 - Could Late-Onset Isolated Ocular Symptoms Indicate Congenital Myasthenic Syndrome? A Case Report

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Case report

Objective: Congenital myasthenic syndromes (CMS) are a group of neuromuscular disorders characterized by impaired neuromuscular transmission, exhibiting both genotypic and phenotypic heterogeneity. CMS neuromuscular junction diseases range from minor signs in infancy to severe clinical manifestations impacting essential functions from neonatal onward. CMS may occur presynaptic, synaptic, or postsynaptic based on clinical, laboratory, and electrophysiological findings, allowing specialized therapeutic choices. However, delayed or inappropriate treatment may exacerbate the clinical course. A CMS patient with an isolated ocular presentation including a CHRNB1 mutation discovered by next-generation sequencing (NGS) is presented.

Method: A 15-year-old male patient presented to the pediatric neurology outpatient clinic with complaints of bilateral ptosis. His antenatal/postnatal history was unremarkable, and he had a three-year history of progressive bilateral ptosis. The patient had no family history of similar symptoms, and his parents were non-consanguineous. Although his neuromotor development was age-appropriate, a detailed history revealed mild movement slowness and increased fatigability compared to peers.

Results: Neurological examination indicated bilateral ptosis, ophthalmoplegia, and limited inward and outward gazing. Bilateral muscle strength was 4/5, and deep tendon reflexes were normal. Laboratory tests for isolated ocular myasthenia included muscle enzymes, anti-AChR/MuSK/LRP4 antibodies, metabolic screening, and thoracic and brain imaging, which were normal. Electromyography with a repetitive nerve stimulation (RNS) test did not show a significant decremental response. Although the findings suggested isolated ocular myasthenia, CMS could not be ruled out; thus, an NGS myasthenia panel was conducted. A repeated electrophysiological study with low-frequency RNS showed a decremental response and a repetitive M-wave, suggesting a congenital myasthenic syndrome involving prolonged endplate potential duration, such as slow-channel syndrome or acetylcholinesterase deficiency. Genetic analysis identified a heterozygous variant of uncertain significance in the CHRNB1 gene (c.938T>C; p.(Met313Thr)). As autosomal dominant CHRNB1 mutations are linked to CMS type 2A, a slow-channel syndrome, fluoxetine was started. A family segregation study was planned. The patient showed moderate clinical improvement at one month, but not a complete response.

Discussion: Autosomal dominant slow-channel CMS is a progressive postsynaptic neuromuscular junction disease. Pyridotigmine worsens CHRNB1-associated slow-channel CMS clinically. Fluoxetine, quinidine, and adrenergic medications have shown significant improvement. Genetic diagnosis is essential for CMS outcomes and therapy option.

ABSTRACTS

Topic: Neurogenetics

EPNS25_cr165 - Atypical Presentation of Riboflavin Transporter Deficiency in an Infant: Importance of Early Genetic Testing in Unexplained Neuropathy

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Case report

Objectives

We present the case of a previously healthy 15-month-old girl with slowly progressive bilateral upper limb weakness following a recent respiratory infection. Initial investigations, including brain and spinal MRI, were normal. Cerebrospinal fluid (CSF) analysis revealed mild pleocytosis, while all other findings, including neuroimmunological testing, were unremarkable. Given the suspected postinfectious or immune-mediated etiology, empirical treatment with intravenous immunoglobulins (IVIG) and high-dose corticosteroids was initiated, but no significant improvement was observed.

Methods

For further clarification, nerve conduction studies (NCS) were performed, revealing axonal and demyelinating changes in both upper limbs. Given the atypical course and persistent weakness, early genetic evaluation using trio clinical exome sequencing (ES) was initiated to investigate a potential hereditary neuropathy.

Results

Genetic testing identified bi-allelic pathogenic variants of the *SLC52A2* gene (a maternally inherited missense variant NM_024531.5:c.401C>T p.(Pro134Leu) and a *de novo* contiguous gene deletion on 8q24.3, encompassing the complete *SLC25A2* gene on the paternal chromosome), compatible with riboflavin transporter deficiency (RTD). RTD is a rare neurometabolic disorder that mainly affects motor neurons and cranial nerve nuclei, leading to progressive weakness, cranial nerve dysfunction, and, if untreated, respiratory failure. It is part of the Brown-Vialetto-Van Laere syndrome (BVVLS) spectrum and often manifests with sensorineural hearing loss, vision loss, and bulbar dysfunction. In our patient, immediate initiation of riboflavin and coenzyme Q10 supplementation led to a gradual improvement in upper limb strength. Her presentation was atypical, as she did not show cranial nerve involvement, hearing impairment, or vision loss. We hypothesize that the early age at diagnosis (15 months) may have contributed to this incomplete phenotype. At the three-month follow-up, the patient demonstrated continued improvement under riboflavin therapy.

Conclusions

This case highlights the importance of early genetic testing in unexplained neuropathy, particularly when empirical immunotherapies fail. Identifying treatable causes such as *SLC52A2*-associated RTD is essential for timely intervention and improved outcomes. Furthermore, our case demonstrates the phenotypic variability of BVVL syndrome, emphasizing that an underlying riboflavin transporter deficiency should be considered even in the absence of cranial nerve involvement.

ABSTRACTS

Topic: Movement Disorders/ Cerebral Palsy

EPNS25_cr166 - HADDT- syndrome: a rare cause of a hypotonic ataxic movement disorder with possible secondary mitochondrial involvement

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Case report

Objective: The C-terminal Binding Protein (CTBP1) is an important transcriptional regulatory protein which plays an important role in the development of the nervous system. It is abundant on neuronal synapses. Mutations in the CTBP1 gene lead to an intellectual disability, hypotonia, ataxia, developmental delay, failure to thrive, and tooth enamel defects (HADDTS) phenotype. To date, 17 patients have been described in the literature. In two patients, muscle biopsy revealed signs of a secondary mitochondrial disorder.

Case and Methods: We report on a 3-year-old boy who presented with motor development delay and delayed speech. He was able to sit, crawl and walk with a walker. The clinical examination revealed muscular hypotonia and weak deep tendon reflexes. Genetic testing for SMA was negative. Extensive laboratory diagnostics showed normal values for lactate, ammonia and CK. Analysis of the amino acids revealed elevated values for proline. The cMRI showed cerebellar atrophy. Nerve conduction velocity of the tibial and peroneal nerve were normal. In the standardized developmental examination using the Mental Bayley Scales of Infant Development, the patient achieved a mental developmental index of 60.

Results: Trio-exome sequencing revealed a heterozygous missense mutation in the CTBP1 gene (c.991C T, p.Arg342Trp). This finding, in context with the clinical signs and symptoms, led to the diagnosis of a HADDT syndrome as the cause of the developmental disorder with hypotonic ataxic movement disorder. The laboratory tests did not reveal any evidence of a mitochondrial disorder, nevertheless we started a supplementation with coenzyme Q10 and carnitine.

Conclusions: HADDT is a rare syndrome characterized by a hypotonic ataxic movement disorder. It is caused by mutations in the CTBP1 gene, which is involved in neural development and the regulation of mitochondria. Therefore, patients could potentially benefit from treatment with carnitine and coenzyme Q10.

ABSTRACTS

Topic: Neurometabolic Disorders

EPNS25_cr169 - Subacute degeneration of spinal cord in a child with normal Vitamin B12 levels

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Case report

Introduction: Subacute combined degeneration (SACD) is a condition caused by Vitamin B12 or Folate deficiency. It is more prevalent in the elderly and infrequently seen in children.

Case History:

We describe a 16-year-old boy with autism spectrum disorder who exhibited demand avoidance and difficult behaviours. He had historically always had a very restrictive diet which had only exacerbated recently with significant weight loss. His diet mainly comprised of fish fingers, crisps and drinking Dr. Pepper. His estimated calorie intake was around 1300 calories. He presented with deterioration in his mobility and being immobile for a significant period of time over the last few months. He presented to us in a wheelchair ,had ataxia and could only able to go up a few stairs. On assessment, he was noted to have a mild tremor in his upper limbs, normal tone and power with brisk reflexes. In his lower limbs, he had increased tone, brisk reflexes and no antigravity movements, no clonus and plantar flexion with normal sensation.

Investigations: He had investigations which showed a normal Hb with a slightly elevated MCV, Vitamin D 11 (deficient), Vitamin B12 320 ng/l (normal), Folate 2.3 pmol/L (low), Homocysteine 56.6 (Elevated). He had an MRI head and spine which showed extensive abnormal paracentral T2 hyperintense signal throughout the dorsal columns of the spinal cord typical of subacute combined degeneration.

Treatment: He received intramuscular cyanocobalamin three times per week for one month before switching to weekly thereafter. He is continued on daily Folic acid therapy. He is still undergoing treatment.

Conclusion: Although very rare in developed countries, in children with significant food avoidance behaviour, one should have a high index of suspicion for vitamin deficiency disorders when encountered with new onset gait disturbances, especially as SACD is a treatable disorder if identified and treated early in the course of the disease. If there is a suspicion of vitamin B12 insufficiency despite normal B12 levels, clinicians should test patients' homocysteine levels, especially if the B12 level is borderline low-normal. This insufficiency can affect people of all ages and cause neurologic abnormalities on tests and imaging, which can become permanent if left untreated. The "normal" vitamin B12 assays could be attributable to the prevalence of high percentages of false negative results.

ABSTRACTS

Topic: Cerebrovascular Disorders

EPNS25_cr170 - Acute Spinal Cord Infarction: Etiology and Management

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Case report

Introduction: Acute spinal cord infarction (ASCI) in children is extremely rare and difficult to diagnose because of the wide range of clinical and radiological findings. Energy drinks (EDs) are sweetened beverages containing caffeine or guarana with side effects on the cardiovascular system, such as arterial hypertension, cardiac arrhythmias, and myocardial ischaemia.

Methods: An adolescent patient with ASCI is presented.

Results: A previously healthy 17-years-old male patient was transfered to our intensive care unit (ICU) from another center. He initally presented with acute weakness and breathing difficulty following a history of cough, diarrhoea and hoarseness for the last 3 days, and he had syncope once. His vital signs showed hypertension and his Glasgow Coma Scale was 6. He had flasc quadriparesis, he was intubated and was admittted to the ICU. He presumed diagnosis of postinfectious demyelinating disease and received intravenous immunoglobulin, methylprednisolone and plasma exchange. These treatments resulted in no improvement and he was transferred to our centre on 3rd day. On admission, neurological examination revealed flaccid quadriparesis, sensory examination was intact. History revealed that he had 2 litres of ED before the onset of acute weakness. Spinal MRI showed myelopathy secondary to acute cervical spinal infarction. Computed tomography angiography revealed vascular irregularity in the left vertebral artery. He was started on low molecular weight heparin. Additionally, he was administered mesenchymal stem cells, both intravenously and intrathecally on 20th day and on 35th day, respectively. The patient was discharged on the 60th day with tracheostomy, he was able to walk with support. At final follow up at 6th months, tracheostomy was closed and he was able to walk independently.

Conclusion: ASCI is a neurological emergency associated with long-term sequelae impacting patient's quality of life. Vasculopathies, systemic hypotension, cardiac surgery, cardioembolic disease, tumors, trauma, embolism, and radiotherapy are the most common etiological causes. EDs have significant cardiovascular side effects, and may also be one of the causes of ASCI. Mesenchymal stem cell administration emerges as an option to improve neurologic outcome for patients with ASCI.

ABSTRACTS

Topic: Neurogenetics

EPNS25_cr173 - A Novel Mutation in a Collagen Encoding Gene is Associated with Pediatric Ischemic Strokes

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Case report

Aim: Pediatric ischemic strokes are rare but it is critical to understand their origins due to their potential long-term impacts. The genetic contribution in these cases is an area of growing interest, particularly in variants of the COL4A1 gene. Pathogenic variants in COL4A1 have been implicated in cerebrovascular abnormalities, including small vessel disease and hemorrhagic strokes.

Case: 10-year-old female patient admitted to emergency with right hemiparesis, right hypoglossal paralysis, central facial paralysis, dysarthria, and ataxia. Magnetic Resonance Angiography showed ischemia detected in the left basal ganglia and caudate nucleus. Low Molecular Weight Heparin and Prednisolon treatment was started.

Whole Exome Sequencing of the patient indicated a heterozygous variant in the COL4A1 gene(p.G1580A). COL4A1 gene encodes a critical architectural component of the typeIV collagen fiber that forms essential physical contacts with the basement membrane blood vessels.

Discussion: Mutation in COL4A1 protein(p.G1580A), meaning the Glycine residue in position 1580 is mutated into Alanine. A different mutation in this same position was diagnosed with brain small vessel disease 1 in the literature(Phenotype OMIM#175780). The sequences of human COL4A1 and COL4A2, retrieved from UniProt(IDs=P02462andP08572, respectively) were used to generate the hexamer models via AlphaFold3 server. Visualization of these models using PyMOL revealed that the mutated glycine residue is located on the outer surfaces of the patient's COL4A1 proteins. Potential protein binding partners were identified using the STRING protein interaction database. One of these partners is GP6, platelet membrane glycoproteinVI that is essential for the activation and aggregation of platelets triggered by collagen.

When endothelial lining is lost and arterial wall is damaged, subendothelial matrix becomes exposed to blood circulation, leading to platelet accumulation. Therefore, we proposed that GP6 protein might interact with COL4A1 hexamer structure in mutations such as p.G1580A and affect vascular function. To gain more precise insights, we conducted a protein three-dimensional structure analysis using the AlphaFold3 server to further explore the biochemical relationship between GP6 protein and COL4A1 hexamer structure. This complex revealed that the disease-associated COL4A1 mutation is located at the GP6 binding interface. Our findings suggest that this mutation may disrupt the interaction of the hexamer region with other signaling pathways.

In conclusion, we argue that the COL4A1 variant in this study should be cataloged among the genetic causes of pediatric ischemic strokes. This case is a rare but novel finding that indicates variants in other genes also encoding components of BM could lead to the same disease phenotype.

ABSTRACTS

Topic: Neurometabolic Disorders

EPNS25_cr175 - Infant being irritable, a diagnostic challenge

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Case report:

INTRODUCTION:

Thiamine is a water-soluble vitamin cofactor in energy metabolism. Mutations in SLC19A3 cause a deficiency of its transporter, leading to Thiamine-Responsive Basal Ganglia Disease. There are three forms of presentation depending on the age of onset. It presents with encephalopathy and varied neurological symptoms such as extrapyramidal symptoms, ophthalmoplegia, or seizures, with bilateral involvement of the basal ganglia being characteristic. Early initiation of treatment with thiamine and biotin is essential.

CLINICAL CASE:

A 4-month-old infant with a one-and-a-half-month history of irritability, leading to several pediatric consultations without identifying an apparent cause. Progressively associates weight and height stagnation, cervical-axial hypotonia, and extrapyramidal symptoms. The analytical study shows a slight elevation of serum lactate, which is normal in CSF. Brain MRI shows bilateral and symmetrical signal alteration with hyperintensity in T2 and FLAIR in lenticular nuclei, thalami, cerebellar hemispheres, and caudate nuclei. Administration of thiamine and biotin is initiated. Subsequently, low thiamine levels in CSF and two heterozygous variants in the SLC19A3 gene are identified.

CONCLUSIONS:

This entity is a neurometabolic disease, and in the presence of suspicion, a patient with unexplained encephalopathy and bilateral basal ganglia lesions, treatment should be initiated without waiting for diagnostic confirmation. Early administration of thiamine can improve clinical symptoms, reverse radiological abnormalities, and prevent progression. Remembering the possibility of early-onset forms, with more nonspecific and difficult-to-interpret symptoms is important.

ABSTRACTS

Topic: Infectious and Inflammatory Diseases/ Neuroimmunology

EPNS25_cr177 - Case of a 17month- old- boy with acute necrotizing encephalitis and dbr1 gene mutation

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Case report

Background
Acute necrotizing encephalitis (ANE) is a rare but distinctive form of acute encephalopathy, typically triggered by a virus-associated febrile illness. It is characterized by symmetric multifocal brain lesions involving the thalami and both supra- and infratentorial regions. While most cases are sporadic, genetic forms have been identified in association with mutations in the *RANBP2* gene.
The lariat-debranching enzyme DBR1 mediates the turnover of branched RNA intermediates from pre-mRNA splicing. Bi-allelic *DBR1* mutations are linked to brainstem infections caused by HSV-1, influenza, norovirus and SARS-CoV-2. Enhanced viral susceptibility has been demonstrated in DBR1-deficient fibroblasts, supporting the hypothesis that DBR1 deficiency contributes to brainstem viral infections in humans by disrupting tissue-specific and cell-intrinsic antiviral immunity.
We present an infant with ANE in the context of Human Herpesvirus 6 (HHV-6) infection, in whom a homozygous mutation in the *DBR1* gene was identified.

Case presentation
17-month-old boy born to consanguineous parents with a previous history of prematurity and normal psychomotor development. He developed status epilepticus and acute encephalopathy, requiring intubation and mechanical ventilation, two days after an upper respiratory tract infection. WBCs was 16640/μl and CRP 166mg/L. Cerebrospinal fluid disclosed 8 WBC, 342mg/dl protein and 81mgdl glucose. Brain MRI revealed symmetric thalamic and brainstem lesions consistent with ANE. Infectious, immunological and metabolic screening were conducted. HHV-6 was identified in blood, and not in CSF. He was managed with standard of care treatment together with high-dose methylprednisolone and intravenous immunoglobulin. He had a favorable clinical response and he was weaned off mechanical ventilation 6 days later. By the 7th day, he was alert, tracked and focused visually, he showed left upper and lower limb weakness, mild action dystonia and tremor of the upper limbs and bilateral Babinski sign signs more pronounced on the left. He continued to improve and a brain MRI 3 months after the onset of his disease showed subtle residual lesions.
Due to the history of parental consanguinity genetic testing was performed, revealing a homozygous mutation in the *DBR1* gene (NM_016216.4:c.442A>G, p.(Arg1486Gly)

Conclusions
This is the first report of a patient with genetic form of ANE in the context of HHV-6 infection and a homozygous mutation in the *DBR1* gene.

ABSTRACTS

Topic: Neuromuscular Disorders

EPNS25_cr178 - Juvenile Amyotrophic Lateral Sclerosis: The Identification of P525L FUS Pathogenic Variant Redirects Care

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Case report

Juvenile amyotrophic lateral sclerosis (JALS) is a group of degenerative motor neuron disorders affecting both upper and lower motor neurons, presenting within the first 25 years of life. JALS is extremely rare, with an estimated incidence of 1 per million worldwide. Genetic associations are identified in up to 40% of cases. We present a case of JALS linked with fused in sarcoma (*FUS*) pathogenic variant in a 13-year-old boy. P525L *FUS* pathogenic variant is increasingly reported as associated with an aggressive clinical deterioration and early death.

The patient first experienced symptoms of left arm flaccid paralysis, worsening over six weeks in March 2024. Prior to this, he'd experienced a febrile "flu-like," illness. Ten months later, his condition progressed to affect all four limbs. Neurological examination by then elicited profound muscle weakness to all four limbs, present and symmetrical deep tendon reflexes, scapular winging and hand muscle wasting. Sensation and swallowing function were preserved. Forced vital capacity was 50% of predicted, indicating respiratory dysfunction. Initial neurometabolic, infectious, autoimmune and cerebrospinal fluid investigation results were within normal range. Magnetic resonance imaging with contrast of his brain, spine and left brachial plexus were normal. The investigative net was widened with bone marrow aspiration and neurotransmitter assay to look for paraneoplastic and other inflammatory causes. He had three serial electromyography (EMG) and nerve conduction studies (NCS). Initial studies identified pure motor neuropathy of anterior horn cell level pathology. Subsequent EMG and NCS suggested severe, progressive pure motor axonal loss at three regions (lumbo-sacral, thoracic and cervical) indicative of motor neuron disease. Whole genome sequencing (WGS) identified a de novo pathogenic P525L *FUS* variant, confirming the diagnosis of JALS. He was supported by a multidisciplinary team including; physiotherapy, occupational therapy, speech and language therapy, dietetics, paediatric neurology and the paediatric respiratory and clinical genetics teams.

After extensive investigation, JALS was confirmed by WGS. Although advances in genetic testing have identified *FUS*-JALS as the most common pathogenic variant, JALS remains incredibly rare in the paediatric population. Diagnosis allowed the family to finally be given an approximate prognosis. Efforts were reorientated towards the monitoring of, and interventions for the prognosticated rapid deterioration of his mobility and respiratory function. When faced with an extremely rare and rapidly progressing presentation of paediatric motor neurone disorder, identifying a causative variant earlier can give the answers needed to redirect care.

ABSTRACTS

Topic: Neurometabolic Disorders

EPNS25_cr179 - Neurological perspectives in fucosidosis: case report

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Case report

NEUROLOGICAL PERSPECTIVES IN FUCOSIDOSIS: CASE REPORT

Background. Fucosidosis is a rare autosomal recessive lysosomal storage disorder caused by a mutation in the FUCA1 gene, leading to α-L-fucosidase deficiency and the accumulation of fucose-containing compounds in multiple organ systems, particularly in the central nervous system. The aim of this presentation is to highlight the neurological implications of pediatric fucosidosis.

Methods. Anamnesis and clinical examination were performed at the Neurology Unit of the Mother and Child Institute in Chisinau. Paraclinical data were retrieved from medical databases. The patient underwent electroencephalography (EEG), brain magnetic resonance imaging (MRI), and genetic testing - conducted abroad. A review of the literature on similar cases was also performed.

Results. A 3-year-old child, who had normal development until the age of one, presents at the age of three with severe neurological delay. The child does not speak, does not walk, cannot sit independently, and exhibits strabismus and kyphosis. EEG findings revealed sharp waves in the right frontal-central-temporal leads, with a low index, along with periodic slow-wave activity in the left frontal region. The formation of the main rhythmic waves showed a delayed pattern. Brain MRI findings demonstrated significant hyperintense changes in both cerebral hemispheres, particularly in the periventricular and subcortical white matter, on T2-weighted and FLAIR sequences. On T1-weighted sequences, the white matter signal intensity appeared similar to that of the cortex, suggesting a possible delay or stagnation of myelination. Genetic testing revealed a p.T135R missense mutation in the FUCA1 gene, in a homozygous state. The findings were suggestive of fucosidosis.

Conclusion. This case highlights the severe and progressive neurological decline in pediatric fucosidosis, with characteristic clinical, EEG, and MRI findings confirming its neurodegenerative course. Genetic testing identified a pathogenic FUCA1 mutation, establishing the diagnosis. Given the lack of curative treatment, early recognition is crucial for supportive management, genetic counseling, and exploring emerging therapeutic strategies such as enzyme replacement and gene therapy to improve patient outcomes.

ABSTRACTS

Topic: Epilepsy: Medical and Surgical treatment

EPNS25_cr181 - DEPDC5-related epilepsy spectrum: report of a new family with a focus on neonatal or early infancy onset seizures

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Case report

Introduction: DEPDC5 mutations are associated with a broad spectrum of focal epilepsies, often linked to cortical malformations such as focal cortical dysplasia (FCD). Epileptic spasms are increasingly recognized as a feature of DEPDC5-related mTORopathies, yet their occurrence in early infancy and resistance to standard neonatal status epilepticus protocols remain poorly characterized. We describe a mother-infant pair with DEPDC5-related epilepsy, highlighting distinct clinical features.

Case report: A six-week-old female infant, presented with focal seizures followed by clusters of epileptic spasms. Sporadic episodes were reported as starting around 4 weeks. EEG monitoring revealed focal seizures with a right fronto-temporal focus followed by a burst-suppression pattern. Established status epilepticus treatments, including phenobarbital and phenytoin, and a trial with pyridoxine failed to control seizures. Brain MRI showed an extensive cortical malformation involving the left frontal region, including the anterior, superior, and mesial aspects of the gyrus cinguli. The introduction of vigabatrin led to sustained remission of spasms and focal seizures. Suspecting a MTORpathy a NGS panel was urgently requested showing a a heterozygous DEPDC5 nonsense variant (c.1264C>T; p.Arg422*), inherited from the mother. Five months later, she was readmitted with recurrent focal seizures, which resolved after increasing the vigabatrin dosage. To date the patients present un unremarkable neurological examination with normal development.

Her mother, carrying the same genetic variant, experienced the onset of focal epilepsy during pregnancy, with episodes suggestive of temporal lobe involvement. MRI revealed subtle right temporal cortical alterations, possibly indicating dysplasia, and subcortical hyperintensities in the temporo-parietal region.
Her seizures were fully controlled by levetiracetam monotherapy.

Conclusions: DEPDC5-related epilepsy, encompasses different manifestations even in carriers of the same mutation. Epileptic spasms are incresingly observed in a small but significant subset of DEPDC5 mutation carriers and vigabatrin proved to be a valuable therapeutic option. Surgical interventions, including cases with somatic mutations, have shown promising outcomes. These findings support individualized treatment strategies and further research into pharmacological and subsequent surgical approaches for DEPDC5-related epilepsies.

ABSTRACTS

Topic: Cerebrovascular Disorders

EPNS25_cr182 - Cerebral venous sinus thrombosis in a pediatric patient with sars-COV-2 infection: a case report

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Case report

Objectives. To assess the clinical and imaging features of a pediatric patient with cerebral venous sinus thrombosis (CVST) during acute SARS-CoV-2 infection.

Methods. This is the report of a 3-year-old boy who was admitted to the pediatric intensive care unit of the Institute of Mother and Child. Patient data collected included general status, clinical symptoms, laboratory tests (PCR SARS-CoV-2; inflammatory and coagulation parameters), neuroimaging: computed tomography (CT), and magnetic resonance angiogram (MRA). Statistical analysis was performed using SPSS Statistics 26.0 software; continuous data were expressed as means and ranges, and categorical data were presented as counts and percentages.

Results. The patient showed impaired consciousness, vomiting, and severe headache; the symptoms started eight days before with fever and odynophagia, followed by headache. On physical examination, he had a Glasgow Come Scale score of 13, bradypsychia, and no focal neurologic deficit or meningeal signs. The child had no known genetic or acquired risk factors other than SARS-CoV-2 infection. PCR for SARS-CoV-2 by oropharyngeal swab was positive. In the beginning laboratory tests reported inflammatory parameters as mild leukocytosis (13,90 per mm3), increase of C-reactive protein 40 mg/L (0-15), erythrocyte sedimentation rate 25 mm/h (0–10), and abnormal coagulation parameters: platelet count of 63,000 per mm3, prothrombin index of 50% (70–130), fibrinogen of 2,0 g/L, and D-dimer of 27.74 mg/L (0–0.5). Proteins C and S, homocysteine, antithrombin III, and anti-Xa were normal; the autoimmune panel for lupus and antiphospholipid syndrome was negative. A Head CT scan revealed right occipital intracerebral. MRA showed bilateral transverse sinus thrombosis with extension to the right sigmoid sinus.

Conclusions. Our patient with SARS-CoV-2 developed severe coagulopathy, but despite the known associated poor prognosis and the severity of the CVST, the child was discharged with good clinical outcome, asymptomatic and without neurologic sequelae after 22 days of admission. The results of our case report suggest that you need to consider the possibility of CVST associated with SARS-CoV-2 with severe headache and other neurologic symptoms, even in pediatric patients.

ABSTRACTS

Topic: Neuromuscular Disorders

EPNS25_cr184 - Hereditary Axonal Neuropathy Mimicking Guillain-Barré Syndrome: IGHMBP2-associated Charcot-Marie-Tooth Disease Type 2S

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Objectives: Hereditary neuropathies represent a diverse group of genetic disorders characterized by phenotypic and genotypic variability. While progressive weakness and muscle atrophy are hallmarks, atypical presentations can challenge differentiation between hereditary vs acquired conditions, such as inflammatory neuropathies. Our aim is to report two siblings who presented with progressive muscle weakness following a respiratory infection with considerable intrafamilial variability who were initially managed as immune-mediated polyneuropathy.

Case report: A 13-year-old girl, with an onset of abnormal gait pattern from the age of 7 years, presented with progressive muscle weakness and deterioration after a respiratory infection at the age of 11 years. There was no consanguinity between parents. At the exact same time period, during the course of a similar infection running in the family, her 11-year-old brother also experienced acute onset weakness, inability to get up from the floor and frequent falls. The neurological examination of both siblings revealed distal predominant lower extremity weakness, absence of DTRs, steppage gait and the older sister also having bilateral pes cavus deformity. There was no sensory involvement. The brother was hospitalized with a preliminary diagnosis of Guillain-Barré syndrome (GBS). CSF protein level was increased (111 mg/dL). Spinal MRI showed contrast enhancement in cauda equina. EMG revealed acute-subacute axonal polyneuropathic involvement in both sensory and motor fibers suggestive of AMSAN. Given the clinical presentation and initial work-up IVIG therapy was initiated for both of the siblings. Although the sister had marked clinical response to initial treatment, there was no clinical improvement during monthly IVIG prophylaxis for 18 months. Follow-up EMG studies remained stable in both patients. Whole exome sequencing analysis identified two novel, likely pathogenic variants in the IGHMBP2 gene: c.747C>G (p.Asp249Glu) in exon 6 and c.1129T>C (p.Cys377Arg) in exon 8. Both variants are present in a compound heterozygous state in the two siblings, and are located within the helicase domain of the protein.

Conclusions: These siblings with acute onset deterioration with intrafamilial variability in terms of presentation and initial response to immunomodulatory treatment highlight the importance of considering hereditary neuropathies in the differential diagnosis of immune-mediated neuropathies. *IGHMBP2*-associated disorders include To our knowledge, none of the patients so far reported with *IGHMBP2* causative variants presented within the spectrum of acute demyelinating polyradiculopathy.

ABSTRACTS

Topic: Neurogenetics

EPNS25_cr185 - A rare case report of protocadherin 12 gene mutation accompanied by renal agenesis

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Case report

INTRODUCTION: Protocadherins represent a group of cell surface proteins, with over 70 members, that form part of the cadherin family.Protocadherin 12 (PCDH12) encodes a protocadherin that is associated with membrane stability, adhesion and maintenance of vascular structure. The presence of bi-allelic pathogenic variants in the PCDH12 gene has been observed to be associated with microcephaly, seizures, and spasticity with brain calcification. For the first time, homozygous mutations in the PCDH12 gene were identified in 10 patients from 4 consanguineous families with peritalamic hyperechogenicity, progressive microcephaly with hypothalamic-midbrain dysplasia, early-onset intractable epilepsy and psychomotor retardation in the prenatal period. The objective of this study was to present a patient with microcephaly, epilepsy and psychomotor retardation in whom a homozygous mutation in the PCDH12 gene was identified through further genetic examination.

CASE: An 8-year-old female patient with a history of term birth was admitted for the first time at the age of 1 month due to myoclonic seizure and was found to have microcephaly (34 cm). Serologic tests normal results. On physical examination at the last follow-up visit, the patient exhibited microcephaly (44.7 cm -4.97 SDS) and axial hypotonism, absence of head control, no deep tendon reflexes and spasticity in the upper and lower extremities. Brain MRI imaging revealed dysgenetic changes in the brainstem, corpus callosum and basal nuclei. The patient's current electroencephalography (EEG) was evaluated as epileptic. The patient also had left renal agenesis. Further genetic examination of the patient with the present findings revealed a mutation in the PCDH12 gene.

Discussion: Bi-allelic mutations in the protocadherin-12 (PCDH12) gene have been observed to present with progressive microcephaly, craniofacial dysmorphism, psychomotor retardation, refractory epilepsy and axial hypotonia. Notably, our case exhibited left renal agenesis, a condition that has not been previously documented in the literature. The diagnosis of patients with congenital TORCH infections is often facilitated by the presence of microcephaly and intracranial calcifications.

Conclusion: In the absence of serologic evidence of congenital infection, and in the presence of a family history, it is recommended that further genetic examination for mutations in the PCDH12 gene be considered.

ABSTRACTS

Topic: Neurogenetics

EPNS25_cr186 - IRF2BPL-Related Disorder: A Rare Pediatric Case of Neurodevelopmental Regression, Abnormal Movements, Loss of Speech, and Seizures (NEDAMSS)

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Case report

Introduction: IRF2BPL-related disorder is a severe neurodevelopmental condition that presents with a broad spectrum of clinical features, including varying degrees of developmental delay, often accompanied by regression in many cases. This mutation is associated with the *Neurodevelopmental Regression, Abnormal Movements, Loss of Speech, and Seizures (NEDAMSS)* phenotype, which includes neurodevelopmental regression, abnormal movements, and seizures. Affected individuals commonly experience intellectual disability and a range of seizure types. Neuroimaging, particularly brain MRI, may reveal cortical and/or subcortical atrophy, cerebellar atrophy, brainstem atrophy, and corpus callosum abnormalities.

Case Presentation: An 8-year-old female child, born to consanguineous parents, presented with delayed developmental milestones. The patient had reached appropriate developmental milestones for the first 18 months but then exhibited sudden developmental regression, including the loss of speech, motor skills, and social interaction. Parents noted abnormal movements, such as dystonia and stereotypic hand-wringing. The child developed frequent seizures, which were difficult to control with antiepileptic medications. She had bilateral vision loss. The patient's neuroimaging, especially brain MRI, showed cortical and/or subcortical atrophy, cerebellar atrophy, and corpus callosum hypoplasia. The patient was started on oral Baclofen treatment due to dystonia. Speech was absent, and social engagement was minimal. Genetic testing revealed autosomal dominant, heterozygote, a likely pathogenic variant in the IRF2BPL gene (c.336_343delinsACAGAAAT), confirming the diagnosis of IRF2BPL-related disorder. In contrast, no pathogenic variants were detected in family screening.

Discussion: Clinically, NEDAMSS, affected children exhibit a combination of regression, seizures, and abnormal movements. The loss of speech is one of the most striking features and often precedes the development of seizures. The age of onset varies widely, ranging from the first year of life to the sixth decade, and the disorder's progression may be either progressive or debilitating in some individuals.

Conclusion: IRF2BPL-related disorder is a rare but severe neurodevelopmental condition that can present with early regression, seizures, abnormal movements, and speech loss. Early diagnosis through genetic testing can aid in management and provide families with valuable information for future planning. Further research into the pathophysiology and treatment of this condition is needed to improve outcomes for affected individuals.

ABSTRACTS

Topic: Movement Disorders/ Cerebral Palsy

EPNS25_cr187 - A Rare Cause of Early-Onset Generalized Dystonia: VPS16 Gene Mutation

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Case report

Dystonia is a heterogeneous neurological movement disorder that affects various body regions, including the face, neck and other areas. The disorder is characterised by involuntary muscle contractions accompanied by abnormal postures, which may manifest in childhood, adolescence or adulthood. The Vacuolar Protein Sorting (VPS16) gene encodes a common subunit of two protein complexes, namely the Homotypic Fusion Protein Sorting (HOPS) and the Class C Core Vacuole/Endosome Tethering (CORVET) complexes. These are crucial for the fusion of endosomal and lysosomal vesicles. Mutations in this gene have been linked to early-onset generalized dystonia, which presents with prominent involvement of the oromandibular, bulbar, cervical, and upper extremity muscles. In addition to dystonia, patients may present with intellectual disability and neuropsychiatric symptoms. This case report presents a rare instance of early-onset dystonia with a similar family history and a mutation in the VPS16 gene.

CASE: A 22-year-old man with a history of normal perinatal birth and development presented with speech difficulty and hoarseness at the age of 5 years. He had facial dystonia involving the lips and tongue, which caused speech and swallowing difficulties. During the follow-up of the patient, craniocervical dystonia developed at the age of 10. Later, gait disturbances due to trunk dystonia appeared. The patient had no cognitive delay or psychiatric symptoms. She used biperiden hydrochloride, trihexyphenidyl, carbidopa and levodopa, and clonazepam to reduce the severity of her symptoms but did not benefit. The patient underwent intramuscular botulinum toxin injection at the age of 14 due to a significant exacerbation of her symptoms. During the follow-up period, deep brain stimulation was partially beneficial. A decrease in the frequency of dystonic attacks was observed. It was learned that the patient's mother had similar symptoms since the age of 20. Physical examination revealed torticollis and dystonic movements when head position was corrected. The patient was unable to walk distances longer than a few meters without assistance. The patient had dystonia involving the face, craniocervical region and trunk. A mutation in the VPS16 gene (ENST00000380443.5:n.759-2A>G) was identified. The patient is being monitored for early onset generalized dystonia and is being treated with clonazepam.

CONCLUSION: A VPS16 mutation is linked to early-onset generalized dystonia, with approximately one-third of patients exhibiting cognitive impairment and neuropsychiatric symptoms, while approximately half have a positive family history. Individuals with childhood-onset and progressive dystonia should be screened for mutations in the VPS16 gene.

ABSTRACTS

Topic: Movement Disorders/ Cerebral Palsy

EPNS25_cr188 - Neurodevelopmental Disorder with Hyperkinetic Movements and Dyskinesia; Two Independent Patients, One Treatment

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Case report

Introduction:ADCY5-related dyskinesia is a rare disorder associated with mutations in the Adenylate Cyclase 5 (ADCY5) gene. ADCY5 is the primary isoform found in the heart and brain, particularly in the striatum and nucleus accumbens, where it controls the dopaminergic pathway. The clinical picture is characterized by early-onset paroxysmal chorea, dystonia, and myoclonus. In this report, we present two separate cases of ADCY5-related dyskinesia.

Case 1:A 9-year-old girl born at term with a birth weight of 3500 grams had the first symptoms of choreiform movements in her hands at 9 months of age. During follow-up, she experienced involuntary contractions while walking. At 18 months of age, she was followed up with a prediagnosis of movement disorder. On physical examination, she had involuntary choreiform movements in the upper extremities, sudden contractions of the jaw and her speech was significantly delayed compared to her peers. Acetazolamide and carbamazepine treatment was initiated and partially beneficial. However, the patient's symptoms worsened over time. Whole exome sequencing revealed a mutation in the ADCY5 gene and a diagnosis of ADCY5-related dyskinesia was made. Oral caffeine treatment was given. After caffeine treatment, the patient's choreiform movements and jaw contractions significantly decreased and she started to speak.

Case 2: A 5 years and 6 months old female patient with no prenatal and postnatal significant history was admitted with the complaints of inability to control her head and inability to sit up at the age of 7 months and was followed up with a prediagnosis of hypotonic infant. At 1 year and 8 months of age, when she started to sit without support, sudden involuntary contractions in the whole body were noticed. Physical examination revealed movement disorder that recurred several times a day and did not affect consciousness, choreiform movements in the arms and legs, proximal muscle weakness and myoclonus-like spasms lasting 1 second in the whole body and head. The patient was initially started on clonazepam but only partially benefited from the treatment. Genetic analysis for movement disorders revealed a mutation in the ADCY5 gene and a diagnosis of ADCY5-related dyskinesia was made. Therefore, oral caffeine treatment was started and the patient started walking in the first week of treatment.

Conclusion:Early detection of ADCY5 mutations can provide significant improvements in developmental delay. Clobazam, acetazolamide, and carbazemepine may be beneficial. Caffeine was observed to have significant benefits in both of our patients.

ABSTRACTS

Topic: Neurogenetics

EPNS25_cr189 - A novel JARID2 mutation in a Korean family with developmental delay with intellectual disability, dysmorphic face, and infantile spasm

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Case report

Infantile spasms (IS) are an epileptic disorder characterized by spasms occurring in infancy, hypsarrhythmia on the electroencephalography (EEG) and a strong association with developmental delay or regression. Variants in *JARID2* gene (MIM*601594) were reported to be associated with developmental delay with variable intellectual disability and dysmorphic facies (DIDDF, MIM#620098) that consisted of neurodevelopmental delay, cognitive impairment, hypotonia, and dysmorphic facial features. Here, we described the first Korean family of DIDDF with infantile spasms due to a mutation in *JARID2.*

The proband is a 6-month-old girl, born at 34weeks 3days of gestation by normal vaginal delivery weighing 2430g to a 20 year old vietnamese mother. She admitted to the Neonatal Intensive Care Unit with transient tachypnea and preterm care for 3 weeks. At 6 months of age, she was admitted to our pediatric developmental clinic with developmental delay, hypotonia, and exotropia. At that time, she had no eye contact or social smile. Her father also had developmental delay, intellectual disability, and a dysmorphic face. She showed head lag on pull to sit test and had been unable to lift her head on prone position. Biochemical investigation, metabolic work up, peripheral blood karyotyping and chromosomal microarray were performed, and no abnormalities were identified. Brain magnetic resonance imaging was normal. She had no overt seizure until then, but prominent hypsarrhythmia and burst suppression pattern was noticed in electroencephalography. She had spasms at (?) months old. We conducted WES and identified a heterozygous missense mutation, c.1945+1G>A in *JARID2*, categorized as a likely pathogenic variant, which has not been reported in population databases. Her father has the same variant.

To our knowledge, this is a novel mutation in *JARID2* which has not been reported previously in the literature and the first infantile spasms in a patient with a *JARID2* variant. In patients with unexplained developmental delay and additional atypical presentations, a detailed medical history, physical examination, family history, and appropriate genetic testing are helpful in diagnosis of the etiology.

ABSTRACTS

Topic: Neuromuscular Disorders

EPNS25_cr193 - Newborn apnea syndrome. A case of mutation in the GLE1 gene

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Case report

Objectives:

Arthrogryposis with anterior horn neuron disease is associated with mutations in the GLE1 gene, leading to perinatal death. Most affected children die within the first hours or days after birth. Only a few cases of survival beyond the perinatal period have been reported. This report presents a case of a child with a GLE1 mutation who survived beyond this critical period.

Methods:

From January to May 2024, approximately 100 newborns with neurological pathologies were examined in a maternity hospital. One case of progressive apnea of unknown etiology was identified.

Results:

A female newborn, born at 37 weeks, 2700 g, showed respiratory failure and apnea episodes (4–6 times daily) on day 4 of life, with an oxygen saturation drop to 50%. Neurological examination revealed lethargy, absent sucking and swallowing reflexes, hypotonia, no response to pain, and contracture of the third fingers on both hands.

The family history included three stillbirths and one neonatal death of unknown cause. Due to the unclear etiology and complicated family history, whole-exome sequencing was performed, confirming a homozygous GLE1 mutation (NM_001003722.2:c.1750>T), associated with congenital arthrogryposis with anterior horn neuron disease. Unfortunately, no treatment currently exists.

Conclusion:

This clinical case is one of the rarest worldwide and the first reported in Kazakhstan. The disease is diagnosed due to perinatal mortality and is mainly identified postmortem through autopsy findings of anterior horn cell loss.

A GLE1 mutation causes one of the most severe forms of motor neuron disease, which manifests in utero. This may explain the lethal outcome of the patient’s sibling and the mother’s history of fetal losses, depending on the mutation’s pathogenicity.

Scientific publications do not describe management strategies for these patients, as the disease is extremely rare, and children do not survive beyond the perinatal period. However, this disease is considered a prototype of spinal muscular atrophy (SMA). A multidisciplinary team decided to manage the patient following SMA protocols, recommending: Joint stretching up to five times per week to prevent contractures, proper positioning and non-invasive ventilation (NIV).

Early diagnosis of this disease can help prevent fatal outcomes, and multidisciplinary management can improve quality of life.

ABSTRACTS

Topic: Infectious and Inflammatory Diseases/ Neuroimmunology

EPNS25_cr199 - Mycoplasma Encephalitis in a Pediatric Patient: A Case Report and Review of Treatment Challenges

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Case report

Background: Mycoplasma pneumoniae is a common cause of upper and lower respiratory tract infections. Among its extrapulmonary manifestations, involvement of the nervous system is well-documented. Neurological complications include encephalitis, transverse myelitis, acute disseminated encephalomyelitis (ADEM), Guillain-Barré syndrome, and thromboembolic stroke.

Methods: Case report.

Results: A previously healthy 15-year-old boy was admitted to the pediatric infectious disease intensive care unit with impaired consciousness, headache, seizures, fever, and dry cough. His illness began a week prior with a cough. Cerebrospinal fluid (CSF) analysis revealed a pleocytosis of 245 cells/µL (70% neutrophils, 30% lymphocytes) and a protein level of 0.43 g/L. Viral and other bacterial etiologies were excluded, while IgM enzyme immunoassay (EIA) for Mycoplasma pneumoniae was positive. Chest X-ray findings indicated interstitial pneumonia. The patient received azithromycin therapy with clinical improvement; however, he didn't take full course of antibiotics, but it showed emotional lability, bradyphrenia, bradylalia, bradykinesia, and tremor persisted. On day 8, brain MRI (T2-weighted) showed hyperintense lesions in the bilateral basal ganglia, specifically in the globus pallidus and the right caudate nucleus. Given the psycho-neurological deficits and MRI findings, intravenous immunoglobulin (IVIG) therapy was recommended. However, due to the absence of standardized treatment protocols for mycoplasma encephalitis, there were challenges in accessing IVIG. Ultimately, IVIG was administered at 0.4 g/kg/day for two days, leading to gradual clinical improvement.

Discussion: Three main hypotheses exist regarding the pathogenesis of mycoplasma-associated neurological manifestations: direct bacterial invasion, immune-mediated mechanisms, and vascular dysfunction. These uncertainties contribute to the lack of a standardized treatment approach, with IVIG use remaining controversial. Given our experience with an incomplete IVIG course, it is difficult to draw definitive conclusions regarding its efficacy in mycoplasma encephalitis. Further studies are needed to establish standardized treatment protocols.
Conclusion: The present case highlights the necessity of investigating the efficacy of mycoplasma encephalitis treatment protocols, specifically comparing those incorporating immunotherapy with those that do not, with the ultimate goal of establishing standardized treatment guidelines.

ABSTRACTS

Topic: Neuro-Oncology

EPNS25_cr201 - Unveiling the Pathophysiology of Mutism Due to a Small Focal Brainstem Lesion: A Case Report

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Case report

Objectives: Acquired mutism, including akinetic mutism (AM) and pediatric post-operative cerebellar mutism syndrome (ppCMS), arises from damage to specific brain regions and is characterized by an inability to produce verbal communication. We seek to further elucidate the pathophysiology of these entities thought to be driven by disruptions of specific neurocircuits.

Methods: We report a case of a 12-year-old patient who developed mutism due to a focal ischemic lesion in the mesencephalon following resection of a suprasellar craniopharyngioma.

Results: Immediately post-resection there was an impaired vigilance. This prompted radiological evaluation on which a linear T2 FLAIR hyperintensity with restricted diffusion was found paramedian in the left mesencephalon involving the nucleus rubor and extending into the periaqueductal gray. There was spontaneous clinical improvement within 48 hours. A few days later however, the patient experienced progressive neurological decline, including a loss of voluntary motor functions and speech, culminating in akinesia and mutism. Awareness and memory seemed unaffected. There was no radiological progression and the lesion showed normal evolution of ischemia in further radiological follow up. In the absence of spontaneous recovery, treatment with methylphenidate was initiated. Afterwards, the patient demonstrated gradual improvement, regaining speech and showed continued recovery of motor deficits up to six months after the ischemic event.

Conclusions: This case shows an overlap between AM (loss of involuntary movements) and ppCMS (delayed onset with progression within days). For both conditions, involvement of neurocircuits that contain the ventral tegmental area have been described. We hypothesize that these conditions may represent a disease spectrum and that neurocircuit dysfunction at the level of the mesencephalon may underlie the development of mutism in this case. These findings underscore the need for further exploration of the neurocircuitry involved in AM and ppCMS to better understand their shared pathophysiology and therapeutic targets.

ABSTRACTS

Topic: Neuromuscular Disorders

EPNS25_cr204 - Phenotypic and genotypic correlation at myotonic syndrome in children with CLCN1 gene mutation

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Case report

Myotonia congenita(MC), also known as congenital myotonia, is a rare genetic disorder that affects the skeletal muscles.

Unfortunately, in Kazakhstan myotonic syndrome is misdiagnosed and the second reason is that hypotension is usually characterized as myotonic syndrome, so it is important to make clear how it looks like clinical symptoms.

Methods: During the period of 2022-2024, over 300 patients who were in the rehabilitation center were examined, among whom 2 patients with myotonic syndrome, but only one of them was genetically confirmed.

Results: The patient 14-year-old child complains of stiffness and slow relaxation of muscles at the beginning of successive movements. According to his mother, the above complaints have been bothering him since he was 3 years old. Family history: 1 child is proband; 2 child is a girl with similar symptoms. The father has hypertrophy of the calf muscles, and the father's brother also has similar symptoms.

Neurological examination: Hypertrophy of the calf muscles, moderate tenar hypotrophy. Muscle percussion creates a "muscle roll" that disappears after a few seconds. The "fist" symptom is positive.The muscles of the face and eyes are not affected.

A complete exomic sequencing was also performed to make the diagnosis, which confirmed the diagnosis of congenital myotonia. The result of the analysis, Genotype: c.1931-2A>G; c.2680C>T in a heterozygous state in the CLCN1 gene.

Discussion: This clinical case illustrates the typical manifestations of myotonic syndrome (MS). Taking into account the patient's phenotype and genotype, currently there is no specific targeted therapy to correct this mutation. It is recommended to limit physical activity, avoid hypothermia, and limit the consumption of potassium-containing foods such as bananas, nuts, and meat. Membrane-stabilizing drugs such as mexilitine or carbamazepine at a dose of 200 mg per day were prescribed as drug therapy in order to reduce the manifestations of myotonic syndrome.

Rehabilitation facilities often accept patients who have no need for rehabilitation, due to incorrect diagnosis, often myotonic syndrome is misinterpreted as hypotension. Timely confirmation of the presence of myotonia makes it possible to start therapy with membrane protectors that reduce the manifestations of myotonic syndrome and prolong the life of myocytes.

Conclusion: Early diagnosis and genetic counseling are crucial for MC management. Treatment focuses on symptomatic relief, including membrane-stabilizing drugs.

ABSTRACTS

Topic: Epilepsy: Diagnosis and Investigations

EPNS25_cr206 - Late onset drug resistance epilepsy as an only manifestation of celiac disease

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Case report

Objective:

In the current era of genomic medicine, the development of genetic diagnostic tests has led to significant progress in the treatment of epilepsy. However, drug-resistant epilepsy still exists, with a prevalence of about 30%. The etiology of epilepsy is key to treatment in most cases. We present a case of drug-resistant epilepsy in a 15-year-old boy, where celiac disease was an incidental finding. After starting a gluten-free diet, his epilepsy dramatically improved.

Methods:

A 15 -year-old male with mild learning disabilities was evaluated for new-onset epilepsy. The patient had normal perinatal history and developmental milestones. Seizures began at age 15 years. Patient experienced frequent tonic-clonic seizures, often occurring upon awakening and in clusters.

Results :

The physical and neurologic exam were within normal limits. The patient's BMI was 34.5 kg/m² (104%, overweight). EEG findings revealed frequent interictal bilateral spike-and-slow wave complexes, predominantly in the frontal areas. Ictal EEG showed abrupt generalized, high-amplitude rhythmic 10-Hz activity, followed by rhythmic spike-wave discharges.

Genetic testing via an epilepsy panel was performed, with negative results. A brain MRI showed no abnormalities, and a brain CT also showed no calcifications. The patient was treated with antiepileptic drugs (AEDs), including valproic acid (1500 mg/day), levetiracetam (2000 mg/day), and topiramate (200 mg/day), but without significant effect.

The patient has a family history of celiac disease, with relatives on both the paternal and maternal sides diagnosed with the condition (without any history of seizures). Test results were positive for celiac disease, as indicated by the following: Immunoglobulin A (IgA): 1.18 g/L (normal range: 0.47–2.49 g/L); Transglutaminase Ab (IgA): >128 U/mL; Endomysial Ab (IgA): 1:2560 (normal <1:10)

The patient was placed on a gluten-free diet, and since then, his seizures have dramatically improved, with no further episodes reported. He is now off all antiepileptic medications, and his EEG is normal. Additionally, his academic performance has significantly improved. A follow-up test for Transglutaminase Ab (IgA) showed a significant decrease in levels, with the value now at 38 U/mL.

Conclusions:

Autoimmune diseases, such as celiac disease, should be considered in cases of drug-resistant epilepsy when the etiology remains unknown. This case underscores the importance of exploring underlying autoimmune causes in epilepsy, even when classic symptoms are absent.

ABSTRACTS

Topic: Infectious and Inflammatory Diseases/ Neuroimmunology

EPNS25_cr208 - Dorsal midbrain syndrome and multiple cranial nerve palsies: A case of antiglycine-receptor antibody-related disease

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Case report

Objective:
We describe the clinical course, diagnostic challenges, and successful treatment of a 4-year-old girl with a subacute onset of cranial nerve palsies ultimately diagnosed with anti-glycine receptor (GlyR) related disease. This rare pediatric autoimmune disease targets the GlyR alpha-1 subunit, a key chloride channel in inhibitory neurotransmission. It typically presents with epilepsy, progressive encephalomyelitis with rigidity and myoclonus (PERM), transverse myelitis, cerebellar ataxia, or acute disseminated encephalomyelitis (ADEM) and is usually non-paraneoplastic.

Methods:
We examined the previously healthy girl presenting with facial palsy, hypoglossal paresis, asymmetric vocal cord closure, and bilateral ptosis. Initial symptoms were hiccups and swallowing problems, which progressively worsened over the last three days. Neuroophthalmological studies revealed dorsal midbrain syndrome, which includes bilateral ptosis and central oculomotor disturbances. Initial investigations, including cranial MRI and nerve conduction studies, were normal. Cerebrospinal fluid (CSF) analysis revealed mild pleocytosis and slightly elevated glucose and protein. Infectious causes were ruled out. Anticholinergic and ganglioside antibodies were negative. Intravenous antibiotics and immunoglobulin therapy were initiated with slow improvement. After several days, anti-GlyR antibodies were detected in both CSF and blood, confirming the diagnosis.

Results:
Identifying anti-GlyR antibodies in the CSF and blood led to a diagnosis of anti-GlyR-related disease. It prompted the initiation of a course of oral steroids, which resulted in a rapid and full recovery of all neurological symptoms.

Conclusion:
This case highlights the broad spectrum of clinical manifestations of GlyR-related diseases in children. Moreover, it underlines the importance of early consideration of antibody-related disease in the differential diagnosis of pediatric patients presenting with acute neurological symptoms, as timely detection of specific antibodies and prompt initiation of immunosuppressive therapy can facilitate complete recovery, especially in GlyR-related diseases.

ABSTRACTS

Topic: Neuro-Oncology

EPNS25_cr211 - Methotrexate-Induced Myelopathy in a child with acute lymphoblastic leukemia: A Rare Presentation

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Case report

Introduction: Methotrexate-induced encephalopathy is a recognised complication of intrathecal methotrexate in acute lymphoblastic leukaemia (ALL), often presenting with seizures, encephalopathy, and motor deficits. However, methotrexate-induced myelopathy is rare and less well reported. We describe an unusual case with an atypical presentation of hemiplegia and radiological findings resembling transverse myelitis.

Case: A 4-year-old boy with low-risk B-cell ALL in remission, without CNS involvement, developed left-sided limb weakness hours after intrathecal (IT) methotrexate. He had received high-dose intravenous methotrexate 24 hours earlier in consolidation phase 3 and underwent IT methotrexate uneventfully under general anaesthesia. Post-procedure, he developed left-sided hemiparesis without facial weakness, speech or visual disturbances, or bladder and bowel dysfunction. Pain was a predominant symptom. The weakness later progressed to all four limbs, more severe on the left. He was afebrile, haemodynamically stable, and had unremarkable laboratory and cerebrospinal fluid (CSF) findings, including normal methotrexate clearance. CT and MRI of the head, including MR angiography, were normal. However, spinal MRI revealed extensive abnormalities in the cervical, thoracic, and lumbar spinal cord, involving both grey and white matter—an atypical pattern. Notably, myelin oligodendrocyte glycoprotein and aquaporin-4 antibodies were negative, and CSF studies showed no malignancy. Management included high-dose prednisolone with tapering, folinic acid rescue, and intravenous immunoglobulin, initiated within 12 hours of symptom onset. The child showed significant improvement and was discharged ambulant, with mild residual left-sided weakness after six weeks.

Discussion: Methotrexate-induced myelopathy typically presents with dorsal spinal cord T2-prolongation, affecting the posterior funiculi. Here, extensive longitudinal spinal cord involvement with both grey and white matter abnormalities resembled transverse myelitis. Such findings broaden the spectrum of methotrexate-related neurotoxicity.

Conclusion: Methotrexate-induced myelopathy is a rare complication with distinct radiological features. The early diagnosis in our case led to early intervention with immunomodulatory therapies and satisfactory recovery. Awareness of such presentations is critical for timely diagnosis and management, which can lead to favourable outcomes.

ABSTRACTS

Topic: Neurogenetics

EPNS25_cr212 - Exploring a Novel 1p36.33p36.32 Copy Number Variant: Unraveling Clinical Features, Diagnostic Methods, and Genetic Counseling Implications

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Case report

Objectives

The clinical features related to the duplication of 1p36.33 can vary based on the size of the duplication. This chromosomal region is susceptible to copy number variants, which can lead to a range of phenotypic characteristics. This study unveils a newly identified copy number variant affecting 1p36.33p36.32, presenting with developmental delay and facial dysmorphism.

Methods

Utilizing whole-genome Oligo-Array CGH, the causative copy number variant was identified and subsequently validated through real-time PCR. In silico analysis guided by ACMG criteria provided insights into the interpretation of the CNV. An extensive diagnostic approach, including MRI, EEG, and echocardiogram, was employed to investigate our patient with tonic seizures and neurodevelopmental delay.

Results

Assessment of a child with tonic seizures, developmental delay, and dysmorphic facial traits revealed a 2.236 MB gain in the 1p36.33p36.32 region (nucleotide 834101 to 3070599) through array CGH. Following ACMG guidelines, this copy number variant was classified as pathogenic. The MRI detected left ventriculomegaly.

Conclusions

This study significantly contributes to understanding 1p36.33 CNVs, offering a comprehensive phenotype associated with the newly identified copy number variant. The implications of these findings extend to genetic diagnosis and counseling, particularly in comparable conditions.

ABSTRACTS

Topic: Infectious and Inflammatory Diseases/ Neuroimmunology

EPNS25_cr213 - A Case Series of Subacute Sclerosing Panencephalitis in Children

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Case report

Objective: Subacute sclerosing panencephalitis (SSPE) is a rare condition that primarily affects children and is caused by a dormant measles virus in the central nervous system, leading to an inflammatory reaction. The prognosis of these cases is always fatal, therefore, early recognition of the condition is crucial. We aimed to present our case series of patients with SSPE. **Method**: A retrospective observational case series was conducted utilizing medical records of children diagnosed with SSPE. **Results**: Two patients were identified. The first patient, female, a 7 year old female, presented with involuntary jerking movement from two months before admission. History of measles infection was unknown. She was diagnosed with SSPE based on Dykens criteria and Jabbour's clinical stages IIA. EEG revealed an abnormal baseline rhythm with epileptiform waves in the right and left frontopolar region. A measles IgG ELISA examination from cerebrospinal fluid (CSF) showed a level of 7.89 IU/mL (negative <0.02 IU/mL), supporting the diagnosis of SSPE. She was treated with isoprinosine and supportive therapies and remains under long-term monitoring. The second patient,a 6 years old male, presented with recurrent tonic and myoclonic seizures one month before admission. During observation, he developed spasticity and loss of consciousness. MRI revealed only mesial sclerosis. Lumbar puncture examination showed a positive measles IgG ELISA result of 6.6 IU/mL (negative <0.02 IU/mL). He was diagnosed with SSPE at Jabbour's clinical stage IIC. He was treated with isoprinosine and supportive therapies and is being monitored for potential neurological deterioration. **Conclusion**: In every patient with worsening involuntary jerking movements and motor regression who does not respond to standard treatment, SSPE should be suspected. It is also important to assess the history of measles infection. Immunomodulatory and supportive therapies may provide benefits for patients with SSPE, however, there is still no consensus on its treatment.

ABSTRACTS

Topic: Infectious and Inflammatory Diseases/ Neuroimmunology

EPNS25_cr214 - Unraveling Sudden Weakness: A Mysterious Case of Ascending Paralysis in a 12-Year-Old

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Case report

This case report describes a 12-year-old female who presented with pain and weakness of the limbs. Her antenatal and perinatal history was unremarkable, and she attained developmental milestones age appropriately. She is currently in the 7th grade with good scholastic performance. A family history of unspecified intellectual disability was noted in her elder sibling.

On examination, the patient was conscious, with normal speech and memory. Cranial nerve examination was unremarkable. Motor system examination revealed decreased tone in both lower limbs, with significant weakness predominantly affecting the lower limbs. Upper limb strength was relatively preserved, though bilateral handgrip was weak. Deep tendon reflexes were absent in both upper and lower limbs, and plantar reflexes were bilaterally flexor.

Initial blood investigations, cerebrospinal fluid (CSF) analysis, and nerve conduction studies (NCS) were non-contributory. A provisional diagnosis of Acute Inflammatory Demyelinating Polyneuropathy (AIDP) was made, and the child was started on intravenous immunoglobulin (IVIG).

On day 10 of illness, she developed holocranial headache and was found to have bilateral papilledema. MRI brain revealed periorbital T2 flaring, tortuous optic nerves, and stenosis of the right transverse sinus, suggestive of raised intracranial pressure. A diagnosis of secondary Idiopathic Intracranial Hypertension (IIH) associated with Guillain-Barré Syndrome (GBS) was made. She was initiated on acetazolamide, following which she showed clinical improvement.

The patient was discharged on day 14 of hospitalization with significant neurological recovery.

ABSTRACTS

Topic: Neuropsychiatric Disorders / Functional Neurological Disorders

EPNS25_cr215 - A twist in time perception: tachysensia as a manifestation of Alice In Wonderland Syndrome

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Case report:

Alice In Wonderland Syndrome (AIWS) is a rare neurological disorder characterised by distortions in somatosensory perception (vision, auditory, time perception). Well-described symptoms include aschematia, macro-/micropsia, tele-/pelopsia, derealisation, lilliputianism, aberration in judgement of time, having a tendency to appear in an episodic way, with significant variability in frequency, intensity and duration of the episodes.

Our aim is to describe a case of a pre-adolescent boy with AIWS and elaborate on diagnostic and management challenges.

We reviewed the electronic patient record and collected all relevant clinical information and results of investigations.

Our patient is a 12-year old boy previously fit and healthy with a history of low-grade fever two days ago who was brought by his parents to the Emergency Department due to the sudden onset of multiple episodes of unusual sensory experiences. The initial episode was a complex visual hallucination, while subsequent episodes included symptoms of teleopsia (objects appearing to be farther), pelopsia (objects appearing closer) and mainly episodes of tachysensia during which he described that “everything was speeding up” (movements, speech, sounds). These episodes lasted 5-10 minutes. He was completely aware of these episodes and able to describe them and to carry on his activity during them. History was negative for any substance use and no symptoms compatible with psychosis were present. A number of investigations were performed with normal findings: MRI head imaging with contrast, long awake and sleep EEG with fixation on/off & provocation tests, CSF studies, antibodies for immune-mediated encephalitis in serum & CSF, copper/ceruloplasmin, ANA, anti-dsDNA. As a goitre was found on clinical examination, thyroid function tests and anti-thyroid antibodies were requested revealing euthyroid autoimmune thyroiditis and treatment with thyroxin was started. Diagnosis of AIWS was discussed with the patient and his parents and meditation techniques were taught. The episodes carried on for 1 week and then self-resolved (prior to the onset of treatment with thyroxin). To the best of our knowledge, co-existence of AIWS and autoimmune thyroiditis has not been described before, although a definite causal relationship cannot be concluded from a single case.

Our case highlights the importance of considering and recognising AIWS in pediatric patients with unusual sensory experiences. The lack of established diagnostic criteria poses challenges in managing this condition. Appropriate management requires a comprehensive approach for the identification of underlying comorbidities, while prospective studies are needed to shed light on the natural history and pathophysiological mechanisms.

ABSTRACTS

Topic: Neurogenetics

EPNS25_cr218 - The Role of HEPCAM in Jcobsen Syndrome: A Pediatric Case Report Hilighting White Matter Abnormalities

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Case Report

Objectives

Jacobsen Syndrome (JS) is a rare contiguous gene deletion disorder characterized by a deletion at the terminal end of the long arm of chromosome 11. JS has various phenotypic features, such as neurodevelopmental delays and congenital heart defects. Furthermore, deletion mutations in the long arm of chromosome 11 can also give rise to Megalocephalic Leukoencephalopathy (MLC), affecting the HEPCAM gene. The following case report presents a 9-year-old girl with JS and remarkable white matter abnormalities (WMA).

Methods

We performed a chromosomal analysis due to the obvious genetic nature of her symptoms. Furthermore, extensive diagnostic approaches, including a brain magnetic resonance imaging scan and metabolic tests were employed to investigate neurodevelopmental delay, strabismus, and hearing loss.

Results

Physical examination revealed distinct craniofacial anomalies and skeletal deformities, including a flat nasal bridge, retrognathia, bilateral clinodactyly, and syndactyly. chromosomal analysis confirmed a karyotype of 46(XX) and deletion at 11q23.3. Additionally, the patient's initial MRI revealed involvement of the periventricular white matter, primarily in the posterior regions, with subcortical changes in the high parietal areas and mild cerebral and cerebellar atrophy. Despite the complex clinical presentation with craniofacial anomalies and limb malformations, there were slow partial improvements in the WMAs over time as evidenced by sequential MRI findings.

Conclusions

This case adds to the previously documented literature on the topic of white matter abnormalities in the context of Jacobsen syndrome and showcases these changes after several years.

ABSTRACTS

Topic: Neuromuscular Disorders

EPNS25_cr219 - Delandistrogene moxeparvovec in Duchenne Muscular Dystrophy: One centre experience from the United Arab Emirates

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Case report

Background

Duchenne muscular dystrophy (DMD) is a progressive neuromuscular disease caused by mutations in the dystrophin gene that abolish dystrophin production in muscle. Delandistrogene moxeparvovec is the first adeno-associated virus-based gene therapy approved by the US Food and Drug Administration in 2023 for patients with DMD aged 4 years and above, excluding patients with a deletion in exon eight and/or exon 9.

Method

We present a case series of four patients who received delandistrogene moxeparvovec in our centre in the United Arab Emirates. The multidisciplinary team assessed all these children. These children were fully vaccinated. All these patients had anti-AAVrh74 antibody titres of <1:400 and were considered eligible for the therapy. Baseline functional motor assessments, like North Star ambulatory assessment (NSAA), and timed function tests were performed in all these children.

Prednisolone was started in all these patients before the infusion. Delandistrogene moxeparvovec with a dose of 1.33×10^{14} vector genomes (vg)/kg was administered intravenously over one hour. The parents were given information on the possible side effects, such as acute liver injury, myocarditis and myositis. All were observed inpatient for 24 hours.

They had weekly blood tests, including full blood count, liver function tests, and troponin-i. The same dose of prednisolone was continued for the first two months. They had monthly functional motor assessments.

Result

None of them had any immediate or late side effects following the infusion. A minimum two-point increase in the NSAA scores was noted within three months after the therapy. The initial drop in CK levels was seen in all the children. After around eight weeks, it started rising in almost all the children without any clinical signs of immune-mediated myositis or rhabdomyolysis. Parents reported improvement in their endurance and strength.

Conclusion

Delandistrogene moxeparvovec was well tolerated in all the children. Improvement in functional motor scores was seen as early as after three months. However, long-term monitoring and data are needed to assess the safety and efficacy of it.

ABSTRACTS

Topic: Neurometabolic Disorders

EPNS25_cr222 - A case of HADHA gene mutation causing the neuromyopathic phenotype in mitochondrial trifunctional protein deficiency

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Case report

Background:

Long-chain 3-hydroxyacyl-CoA dehydrogenase (LCHAD) and Mitochondrial trifunctional protein (MTP) deficiency are very rare disorders, and even rare is the neuromyopathic phenotype. LCHAD/MTP deficiencies are autosomal recessive disorder affecting the long-chain fatty-acid oxidation pathway exhibiting in non-specific symptoms, making diagnosis of the condition difficult. Three known clinical phenotypes include: 1). Severe, fatal neonatal form presenting in cardiomyopathy 2). Intermediate form characterized by recurrent hypoketotic hypoglycaemia and 3). Mild, attenuated form with peripheral neuropathy and recurrent rhabdomyolysis. Early dietary interventions remain key management strategy to prevent future complications associated with this condition.

Clinical case:

We report a 5 year old female who presented with long term and progressive gross motor difficulties; peripheral neuropathy and absent patellar reflexes with previous hospital admissions secondary to infections. Neurophysiological studies showed generalized neuropathy affecting predominantly the sensory fibres. Genetic studies identified two heterozygous variants in HADHA genes, which encodes the alpha subunit of the MTP, using whole genomic sequencing: c.2098G>T p.(Gly700Ter) and c.707C>A p.(Thr236Lys). Referral was made to tertiary neurology and metabolic centre for ongoing specialist management and family education.

Conclusion:

This presentation aims to highlight the importance of early recognition of MTP deficiencies. Even though this can present in atypical symptoms, MTP deficiencies should be included as a differential diagnosis in patients who present with neuromyopathy of unknown cause and episodic exacerbation of symptoms related to exercise/fasting/infections. Although clinical diagnosis may be difficult, genetic testing can aid and confirm diagnosis. There may also be a potential role of screening of MTP deficiencies in Newborn blood spot screening programme.

The importance of early intervention is key to prevent long term, irreversible complications related to MTP deficiencies. This includes a patient-centred approach: tailoring patient's diet, creating an emergency regime plan if required and having an MDT approach to managing patients and their families. Another key learning point is that diagnosis can also help family planning in future pregnancies.

ABSTRACTS

Topic: Neurometabolic Disorders

EPNS25_cr224 - Cavitating encephalopathy in a child with methylmalonic acidemia with homocysteinemia

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Case report

Introduction: Combined methylmalonic aciduria and homocystinuria, cblD type (MAHCD), is a rare disorder of vitamin B12 (cobalamin) metabolism. It is characterized by decreased levels of the coenzymes adenosylcobalamin (AdoCbl) and methylcobalamin (MeCbl), and an extremely variable clinical presentation. MAHCD is an autosomal recessive disorder caused by mutations in the MMADHC gene.
Methods: We present the case of a 5-year-old boy of Roma ethnic origin with a normal premorbid history, who presented with subacute encephalopathy, including dementia syndrome (developmental regression and behavioral abnormalities), increased drowsiness, and ataxia.
Results: Cerebrospinal fluid (CSF) analysis was normal, including negative anti-morbillous antibodies. Electroencephalography (EEG) revealed impaired baseline activity and generalized paroxysmal manifestations. Magnetic resonance imaging (MRI) showed bilateral cavitating leukoencephalopathy. No abnormalities were observed in the blood count, kidney function, pancreas, or heart. Metabolic screening revealed significantly elevated levels of methylmalonic acid, ethylmalonic acid, and methyl citrate, while the acylcarnitine profile showed increased propionylcarnitine. Homocysteine levels were also markedly elevated at 59.9 µmol/L. Vitamin B12, folic acid, lactate, and ammonia levels were normal. Genetic analysis identified a homozygous mutation in the MMADHC gene (c.748C>T; Arg250*). Therapy was initiated with high-dose parenteral vitamin B12 (1000 mcg weekly), L-carnitine (1000 mg twice daily), folic acid (400 mcg twice daily), levetiracetam, risperidone, and a low-protein diet. Speech development improved following therapy, although behavioral abnormalities persisted. Control homocysteine levels ranged between 45-54 µmol/L. The differential diagnosis included progressive cavitating leukoencephalopathy, Canavan disease, vanishing white matter disease, mitochondrial leukoencephalopathy, primary and secondary CNS vasculitis, subacute sclerosing panencephalitis, and HIV encephalopathy.
Conclusion: Disorders related to cobalamin deficiency should be included in the differential diagnosis of acute or subacute behavioral disorders, neuropathy, developmental retardation or regression, and cavitating leukoencephalopathy. The absence of hematological abnormalities does not exclude the diagnosis. Rapid diagnosis requires precise metabolic testing and the increasingly common use of genetic panels.

ABSTRACTS

Topic: Infectious and Inflammatory Diseases/ Neuroimmunology

EPNS25_cr225 - An unusual presentation of MOG positive Acute Disseminated Encephalomyelitis

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Objectives:

Acute disseminated encephalomyelitis (ADEM) presents predominantly in early childhood and is characterized by encephalopathy, polyfocal neurological deficits and typical magnetic resonance imaging (MRI) abnormalities. The significance of MOG-positive ADEM in children lies in its distinct clinical and radiological features, challenging diagnostic landscape, and implications for treatment and prognosis. Here we discuss the case of an infant who presented with limb weakness and progressive drowsiness. This case was unusual due to the very young age of presentation.

Methods:

This is a retrospective case note review of an infant who presented with encephalopathy and weakness and diagnosed with MOG positive ADEM.

Results:

A 9-month-old female infant with a family history of epilepsy presented with drowsiness and weakness involving both lower limbs, and left upper limb following a recent minor head injury. On presentation, she had difficulty feeding through a bottle and required nasogastric tube feeding, she was unable to sit unsupported, or pull to stand and had a fluctuating GCS (8-12/15). She was started on triple therapy (ceftriaxone, clarithromycin and acyclovir). CT head showed right sided frontotemporal and basal ganglia hypo densities. She was transferred to a tertiary center where an MRI, MRV, MRA confirmed the diagnosis of ADEM. She underwent a lumbar puncture and antibody investigations. Her examination revealed a right lateral gaze, loss of head holding, truncal ataxia, reduced power of 3/5 in her left upper limb and 4/5 in bilateral lower limbs with hyporeflexia. She was commenced on a 3-day course of IV Methylprednisolone followed by a weaning regimen of oral prednisolone and a trial of biotin in view of the atypical presentation. When there was no clinical improvement with steroids, she underwent 5 cycles of plasma exchange, as well as received 2g/kg of intravenous immunoglobulin. Following this she showed significant clinical improvement. She was now able to drink milk through a bottle, sit with support and had anti-gravity movements in all limbs. She continued to improve at follow-up 6 weeks later.

Conclusion:

MOG antibodies are an important cause of ADEM in childhood. MOG related ADEM should remain on the differential list even in infants presenting with encephalopathy and weakness. Timely and appropriate treatment can significantly improve the outcome and long-term prognosis.

ABSTRACTS

Topic: Neurodevelopmental Disorders / Developmental Neuroscience

EPNS25_cr227 - THE DIAGNOSTIC JOURNEY OF INFANTILE GM1 GANGLIOSIDOSIS

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Case report

INTRODUCTION

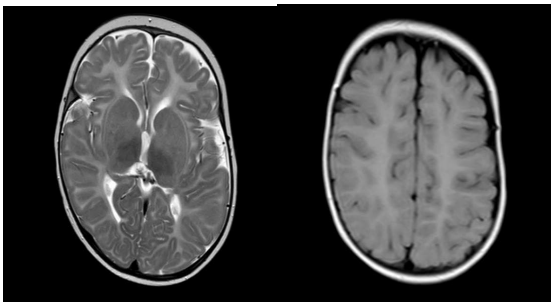
GM1 gangliosidosis a rare neurodegenerative disorder causes accumulation of GM1 ganglioside (glycosphingolipid) is due to a deficiency of betagalactosidase.GLB1 gene is located on chromosome 3(1)This case study focuses on the progression of symptoms and how clinical examination and diagnostic tools helped establish a definitive diagnosis.

CASE DESCRIPTION

Baby boy born at term was fine till 3-4 months of age parents noticed that he was unable to sit with support and had not yet begun to roll. These concerns intensified as he continued to struggle with key developmental milestones.He was admitted for cellulitis a few months back. Examination then revealed hypotonia,nystagmus and cherry red spots on fundoscopic examination. Workup for cherry red spots was planned. Blood lysosomal enzyme screen showed marked deficiency of beta galactosidase,urine mucopolysaccharidoses screen revealed trace of keratan sulphate and oligosaccharide chromatography results were all consistent with the diagnosis of GM1 gangliosidosis. MRI Brain revealed absent corpus callosum and abnormal white matter myelination.Genetic testing revealed two variants in the GLB1 gene.

DISCUSSION

The infantile form of GM1 gangliosidosis(type I) is the most severe,manifests in the first 6 months of life with generalized CNS involvement,hypotonia,delay in neuropsychomotor development,weak sucking,subnormal weight gain,hepatosplenomegaly,facial dysmorphism,macular cherry-red spot,skeletal dysplasia,repeated respiratory infections and early death. Cardiomyopathy and cardiac hypertrophy are less frequent findings(1,2)
Only half of the patients with gangliosidosis have a cherry red spot at macula(3,4,5)Though this finding may not be found due to regression of lesion with time. In our case this finding significantly aided in establishing the diagnosis as this is indicative of a limited number of diseases which can be validated through biochemical testing.Neuroimaging findings in infantile GM1 gangliosidosis includes delayed myelination and abnormal appearance of the subcortical white matter,internal capsule and basal ganglia(6)Thalamic hyperdensity on CT scans and hypointense signal of the thalami on T2-weighted MR images have also been reported(7)
Unfortunately there is no effective treatment for GM1 gangliosidosis. Substrate reduction therapy,enzyme enhancement therapy,enzyme replacement therapy,stem cell transplantation,gene therapy have been explored but none is approved for clinical application. Timely diagnosis of the disease is crucial as the current method of prevention relies solely on genetic counseling.



ABSTRACTS

CONCLUSION

This report aims to meticulously analyze and correlate the intricate details of the patients condition.Early diagnosis is only then possible which can aid in timely intervention if possible.

ACKNOWLEDGEMENT

For our mentor Dr Kafil Shadani

ABSTRACTS

Topic: Fetal and Neonatal Neurology

EPNS25_cr228 - Laryngeal spasm as a clinical presentation of neonatal epileptic encephalopathy due to KCNQ2 mutation

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Case report

Introduction: Mutations in KCNQ2 present a broad clinical spectrum, ranging from self-limited familial neonatal epilepsy (SLFNE) to neonatal-onset development epileptic encephalopathy disorders. The most common clinical presentations in the neonatal period are tonic/clonic seizures.

Clinical Case: A term neonate with no prenatal history. Vaginal delivery at term in an other hospital. At 24 hours of life, the baby presents with an episode of hypertonia in our limbs followed by clonic movements of the right upper limb. Initial first-line investigations for neonatal seizures (NS) show no abnormalities, and treatment with phenobarbital is started. Due to suspicion of neonatal seizures, the baby is transferred to our center for continuous monitoring with an amplitude-integrated EEG (aEEG). The episodes of generalized hypertonia persist, along with severe laryngeal spasm requiring respiratory support, with no correlation on the aEEG. Further complementary tests are conducted, including cranial MRI and a full metabolic study (blood/urine/CSF), all of which show no abnormalities. The anti-seizure treatment is escalated (levetiracetam and vitamins), but no clinical improvement is observed. On clinical examination, signs of cerebral hyperexcitability are evident (exhausting jaw jerk reflex) and generalized hypertonia, suggesting neonatal hyperekplexia, so treatment with clonazepam is initiated. This results in improvement of the hypertonia but does not resolve the episodes of laryngeal spasm. Continuous dual monitoring (aEEG/vEEG) is implemented to categorize the episodes, with a clinical-electrical correlation found on vEEG. Therefore, a sodium channel blocker (oxcarbazepine) is added, leading to complete resolution of the symptoms. Genetic testing (Cinical Exome) reveals a pathogenic mutation in KCNQ2 (NM_001382235.1): c.608T>C (p. Leu203Pro).

Conclusions: Laryngeal spasm is a rare clinical presentation of development epileptic encephalopathies due to KCNQ2 mutation. Differential diagnosis in these cases includes neonatal hyperekplexia (no clinical-electrical correlation). vEEG remains the gold standard test for diagnosing neonatal seizures.

ABSTRACTS

Topic: Infectious and Inflammatory Diseases/ Neuroimmunology

EPNS25_cr229 - Multiphasic disseminated encephalomyelitis mimicking multiple sclerosis and management

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Case report

Introduction: Differentiating multiphasic disseminated encephalomyelitis (MDEM) from multiple sclerosis (MS) is challenging. We report a case of MDEM presenting as MS in a 14-year-old female.

Case: She visited our clinic with right-sided extraocular muscle palsy, ptosis, and diplopia. Brain MRI revealed T2 high-signal lesions in the right temporal lobe, right parietal lobe, left midbrain, and thalamus. Magnetic resonance spectroscopy did not show any tumors or metabolic diseases. Cerebrospinal fluid (CSF) analysis was normal, with no pleocytosis, elevated protein, or decreased glucose levels. The oligoclonal band was negative, and both anti-aquaporin 4 and MOG antibodies were negative in serum.

She underwent four days of pulse therapy but discontinued it due to chest discomfort and headache. She was then treated with intravenous immunoglobulin (2 g/kg, divided over four days) and a tapered dose of prednisolone (2 mg/kg/day for one week), followed by a maintenance dose (1 mg/kg/day) for four weeks. A follow-up brain MRI, two weeks later, showed resolution of the lesions. The patient experienced a prodromal symptom resembling palpitations in the left chest and flank area, followed by hemiplegia, associated with a new lesion in the right parietal lobe. Laboratory tests, including repeat CSF analysis, showed no abnormalities, consistent with the initial findings. She received a second round of pulse therapy for five days and continued prednisolone for four weeks, recovering from hemiplegia and MRI abnormalities. However, she had two additional relapses with similar symptoms at 30–45 day intervals. Her genetic study using NGS for mitochondrial and metabolic diseases was negative. Given the clinical presentation resembling MS, she was started on interferon beta-1b every other day and has remained symptom-free since.

Conclusions: We suggest that cases of MDEM presenting as MS be managed as MS.

Key words: multiphasic disseminated encephalomyelitis, multiple sclerosis, interferon beta-1b

ABSTRACTS

Topic: Infectious and Inflammatory Diseases/ Neuroimmunology

EPNS25_cr231 - Anti-NMDAR Encephalitis, isolated with chorea and aphasia

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Case report

Background and Objectives
Anti-N-methyl-D-aspartate receptor (anti-NMDAR) encephalitis is a rare but potentially life-threatening autoimmune disorder that typically presents with a combination of psychiatric, cognitive, and movement abnormalities. This case report describes an atypical presentation of anti-NMDAR encephalitis in a young child, initially manifesting with isolated, severe chorea, aphasia, and significant weight loss. The diagnosis was confirmed, and the child was treated with aggressive immunosuppressive therapy. The disease resolved following rituximab administration, which was initiated 19 months after disease onset.

Methods
A 4-year-old boy was admitted to the emergency room with acute-onset movement disorders (chorea) and speech impairment (aphasia). He did not have fever, a significant family history, or any prior noteworthy medical conditions.

Results

His initial assessment included: Neurological examination: Conscious and alert, but unable to speak, only able to produce rudimentary words. but no focal neurological signs. Hypotonia was noted, with no spasticity or rigidity.

- **CSF analysis**: Normal protein (0.2 g/L), normal glucose (3 mmol/L), cytosis (3 cells).
- **Anti-NMDAR antibodies**: Positive at a titer of 1:64.
- **MRI**: No significant findings.
- **EEG**: Burst of rhythmic delta waves during sleep
- **ANCA**- N
- **ANA**-N

From December 2022 to May 2024, the patient underwent multiple treatments, including pulse therapy with Methylprednisolone (no significant improvement was observed), intravenous immunoglobulin(with no notable effect), Cyclophosphamide, with no significant improvement and Rituximab. After Rituximab, the hyperkinetic movements resolved completely, speech was fully restored, and he is now completely asymptomatic.

Discussion
This case highlights the possibility of anti-NMDAR encephalitis presenting with isolated chorea and speech disorders, which can complicate the initial diagnosis. Additionally, this case emphasizes the need for an aggressive, stepwise treatment approach. Despite limited response to initial therapies, the patient's full recovery following rituximab illustrates the necessity of continuing aggressive interventions, until the desired clinical outcomes are achieved. Prompt and comprehensive treatment is critical to prevent lasting neurological deficits and to maximize recovery.

ABSTRACTS

Topic: Infectious and Inflammatory Diseases/ Neuroimmunology

EPNS25_cr232 - The use of tocilizumab in a pediatric patient with acute necrotizing encephalopathy and covid-19

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Case report

Introduction: Genetic acute necrotizing encephalopathy (ANE1) is a rare infection–associated disease that occurs in patients with a genetic predisposition resulting from a missense mutation in the *RANBP2* gene. The outcome varies; however, most surviving patients experience persisting neurologic deficits. Several targeted immunotherapies have been used lately in the acute phase and are related to better outcomes. However, data on children is limited. Our goal was to present the clinical manifestation, neuroimaging data, treatment, and outcome of an infant with ANE1.

Methods: A 10-month-old girl presented to the emergency department with alternating mental status and a febrile upper respiratory tract infection due to SARS-CoV-2. A CT scan was performed, revealing hypodense areas at the level of the thalami. Cerebrospinal fluid analysis showed an increased protein level (1080 mg/dl) without pleocytosis while the culture was sterile. Inductive treatment with acyclovir, remdesivir, and ceftriaxone was initiated upon admission. Due to progressive deterioration, she was intubated and transferred to the ICU. Brain MRI showed symmetric bilateral T2 hyperintensities in the thalami, leading to the diagnosis of acute necrotizing encephalitis.

Results: The infant received two doses of intravenous immunoglobulin (2 g/kg) and high doses of methylprednisolone (30 mg/kg for 5 days with subsequent tapering). Additionally, she received two doses of tocilizumab (12 mg/kg and 8 mg/kg) on the second and third days of hospitalization. A follow-up brain MRI revealed residual lesions confined to the medial and lateral thalamic nuclei one week later, indicating significant improvement after treatment. The infant was extubated after 16 days. Her initial neurological assessment indicated truncal hypotonia, reduced muscle strength, a positive Babinski sign on the right side, and irregular limb movements. She was discharged with oral prednisolone in a tapering dose over 10 weeks. Genetic testing (WES) identified a pathogenic variant in *RANB2*. The infant was evaluated one and three months after treatment; no neurological deficits were noted, except for new-onset sleep disturbances. Neurodevelopment was normal for her age.

Conclusions: ANE1 is a rare and often devastating acute encephalopathy. The timing of immunomodulatory therapy may be critical, as patients treated within 24 hours of symptom onset tend to have better outcomes. The early addition of tocilizumab to other immunomodulatory agents enhances prognosis, resulting in significant reduction and containment of the thalamic lesion and complete clinical recovery without neurological sequelae. However, whether these patients could benefit from preventive maintenance therapy remains uncertain.

ABSTRACTS

Topic: Movement Disorders/ Cerebral Palsy

EPNS25_cr233 - Long term follow-up of bilateral Globus Pallidus Internus Deep Brain Stimulation (GPi-DBS) following bilateral Simultaneous Magnetic Resonance-Guided Focused Ultrasound (MRgFUS) pallidotomy for a Life-Threatening Status Dystonicus in a pediatric patient with pantothenate kinase-associated neurodegeneration (PKAN)

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Case report

Background: Invasive treatments, such as radiofrequency stereotactic lesioning or deep brain stimulation (DBS) of the globus pallidus internus (GPi), are effective in managing drug-resistant status dystonicus (SD). However, these open procedures are not always feasible, particularly in patients with severe comorbidities.

Objective: This report aims to show the safety and efficacy of bilateral simultaneous transcranial magnetic resonance-guided focused ultrasound (MRgFUS) pallidotomy, followed by programmed GPi-DBS, in treating life-threatening SD in a pediatric patient with pantothenate kinase-associated neurodegeneration (PKAN).

Methods: A young patient with PKAN and medically refractory SD underwent bilateral MRgFUS pallidotomy under general anesthesia. This approach was chosen due to severe comorbidities that contraindicated open surgery. Following stabilization, programmed GPi-DBS was performed.

Results: SD resolved within 4 days after MRgFUS, with mild and transient intraoperative hypothermia as the only adverse event. Eight weeks later, GPi-DBS was performed. One year post-DBS, the patient remained stable, with good control of dystonic episodes.

Conclusion: Bilateral simultaneous MRgFUS pallidotomy under general anesthesia is a safe and potentially effective alternative therapeutic option for fragile patients with SD. This approach also facilitates the subsequent safe implantation of GPi-DBS, with reduced perioperative risks.

ABSTRACTS

Topic: Neuromuscular Disorders

EPNS25_cr234 - Heart transplant (HTx) in a patient with Fukutin-related-protein Limb-Girdle-Muscular-Dystrophy (LGMD R9) and severe cardiomyopathy – a case study

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Case report

Objective: Limb-Girdle-Muscular-Dystrophy R9 (LGMD R9) is caused by autosomal recessive mutations of the Fukutin-related protein (FKRP) that causes defective glycosylation of Alpha-dystroglycan. Patiens with compound heterozygote mutations have a more severe course as with homozygote mutations. Dilated cardiomyopathy (DCM) is frequent and can precede loss of ambulation by many years.

Methods: Our patient presented with difficulties in climbing stairs, fatigue and limited walking distance at age 10y. Serum-CK was markedly elevated to 10.600U/l. Genetic testing revealed compound heterozygote mutations in *FKRP* (c.947C>G and c.826C>A). Echocardiography showed DCM.

Over a 5 y. period muscle weakness progressed with a reduction of 200m in the 6 minutes walking test, increasing shortness of breath (SOB) on mild exercise (with normal pulmonary function tests and sleep studies), severe fatigue and weight loss. His North Star Ambulatory Assessment (NSAA)-score before HTx was 20. This was accompanied by deterioration of his ejection fraction (LVEF) as measure of cardiac function (echocardiography/MRI) from 45% at initial diagnosis to 25% and progression of severe leftventricular dilatation from 45mm to 69mm before HTx despite maximal heart failure treatment (4-fold anticongestive medical treatment and regular Levosimendan infusions).

Results: Decision for HTx was made following multidisciplinary and ethical discussion. Our patient (15 y.) underwent HTx with an uncomplicated postoperative course and was discharged home 4 weeks following HTx. At 6 months post-HTx walking distance increased to 1km with no breathing difficulties and fatigue during daily activities. BMI raised from 14 to 16kg/m^2. He started an apprenticeship in digital science. Motor activities improved documented with an actual NSAA-Score of 28 (+8). Cardiac function is normal.

Conclusion: HTx can be a treatment option in patients with LGMD R9. SOB, reduction of walking distance and fatigue can be caused by heart failure due to DCM. This needs to be differentiated from muscular and respiratory problems. Normalised heart function after HTx can improve or stabilise motor function. In patients with mild to moderate neuromuscular involvement and end-stage DCM long-term prognosis is closely linked to the possibility of heart transplant.

ABSTRACTS

Topic: Neurogenetics

EPNS25_cr235 - Pathogenic variants in CERT1 as a cause of intellectual disability in two unrelated cases

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Case report

Introduction:

The ceramide transporter (CERT) plays a key role in converting ceramide into sphingomyelin, a lipid essential for cell membrane and myelin integrity. Pathogenic variants in the CERT1 gene (COL4A3BP) were first identified in 2015 as the cause of Intellectual Developmental Disorder, Autosomal Dominant 34 (MIM 616351). We report two unrelated cases recently diagnosed with pathogenic CERT1 variants.

Case report:
- Case 1: A 14-month-old female presented with severe global developmental delay, axial hypotonia, and facial dysmorphisms (broad forehead, epicanthus, inverted V-shaped upper lip, short philtrum, and macroglossia). WES revealed a de novo pathogenic variant in CERT1 (c.779C>T p.(Ser260Leu)).
- Case 2: A male child born to consanguineous parents exhibited developmental delay, axial hypotonia, and progressive microcephaly with facial dysmorphisms (arched eyebrows, midfacial hypoplasia). MRI identified cerebellar vermis, corpus callosum, and hippocampal malformations. WES detected a CERT1 variant (c.136_144dup p.(Thr46_Ala48dup)) inherited maternally.

Conclusions:

Intellectual Developmental Disorder, Autosomal Dominant 34 associated with CERT1 mutations, also known as Neurodevelopmental disorder with hypotonia, speech delay, and dysmorphic facies is extremely rare. Common features include intellectual disability and expressive language impairment, distinctive dysmorphic features and ataxia. Although most of the described cases are *de novo*, we have detected one case of maternal inheritance in our series.

ABSTRACTS

Topic: Cerebrovascular Disorders

EPNS25_cr236 - From Crisis to Catastrophic Success: Rituximab in Pediatric CNS Vasculitis

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Case report

Primary central nervous system vasculitis (PCNSV) is a rare disorder of unknown etiology that exclusively affects the brain and spinal cord. Treatment typically involves glucocorticoids, either alone or in combination with cyclophosphamide, and generally yields favorable outcomes. However, given the significant adverse effects of cyclophosphamide in pediatric patients, rituximab has emerged as a safer alternative. Therefore, exploring alternative treatment options for PCNSV remains essential. In this case report, we present a pediatric patient with angiography-positive PCNSV who exhibited a dramatic and favorable response to a treatment protocol consisting of corticosteroids and rituximab, marking the first such documented case in this age group.

A 16-year-old male with a history of learning difficulties was admitted following a focal seizure. Brain MRI revealed extensive inflammatory lesions involving both gray and white matter, as well as the brainstem, with contrast enhancement. During follow-up, he developed slurry speech and gait instability over the course of several months.
Neurological examination demonstrated significant impairment, particularly in tandem gait. Comprehensive laboratory investigations, including blood and cerebrospinal fluid analyses, were conducted to evaluate potential malignant, infectious, and inflammatory causes; however, no significant abnormalities were identified. A brain biopsy was performed but yielded non-diagnostic results. Subsequently, digital subtraction angiography demonstrated contour irregularities at the level of the bilateral middle cerebral artery and lenticulostriate arteries. After excluding all possible infectious and inflammatory etiologies, a diagnosis of PCNSV was confirmed.
The patient initially received a 3-day course of high-dose methylprednisolone, followed by a tapering regimen of oral prednisone. Subsequently, four doses of rituximab (375 mg/m² weekly) were administered. Follow-up imaging after rituximab treatment demonstrated near-complete resolution of contrast-enhancing active lesions. Clinically, the patient exhibited significant improvement.

In this report, we present the first documented case of a pediatric PCNSV patient with angiographic findings who exhibited a dramatic response to rituximab. PCNSV should be considered a potential cause of subacute and relapsing inflammatory encephalopathy in children. However, before establishing this diagnosis, other conditions such as multiple sclerosis, sarcoidosis, recurrent acute disseminated encephalomyelitis, and primary central nervous system lymphoma must be excluded. Further studies are warranted to better define the role of rituximab as an alternative to cyclophosphamide in pediatric PCNSV or as a potential first-line treatment option.

ABSTRACTS

Topic: Neurometabolic Disorders

EPNS25_cr237 - Opercular Syndrome as a Rare Manifestation of Anti-NMDA Receptor Encephalitis: A Case Report

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Case report

Opercular syndrome is a rare form of pseudobulbar palsy that is characterized by insufficient voluntary function of bilateral facial, lingual, pharyngeal and masticatory muscles. However, the autonomic and reflexive involuntary functions are intact. The most common causes of this syndrome are stroke, multiple sclerosis, head injury, tumor, infectious agents especially herpes simplex encephalitis.In children congenital abnormalities in opercular area, also be a reason.

13 year old girl admitted to the Emergency Department with headache, altered conciousness, dysphagia and slowed down speech. On magnetic resonance imaging (MRI) bilateral hyperintense abnormalities, especially left hemisphere, insular cortex, perirolandic and parasaggital area had been shown. Because of suspected herpes simplex encephalitis intravenous acyclovir treatment had been applied. Not completely clinical improvement had been succeded.

On our examination, her psychomotor activity was increased, dysarthric and slowed down speech was present. Cranial nerve examination was normal but no voluntary movements of tongue, mouth and pharynx although involuntary movements were existent. Awakeness electroencephalogram showed diffuse delta and tetha activity. The result of polimerase chain reaction assay for type 1 herpes simplex virus in the cerebrospinal fluid (CSF) was negative. The Anti-N-Methyl-D-Aspartate receptor antibody test was positive in the autoimmune panel investigation in CSF. MRI revealed abnormal hig signals in the bilateral frontotemporal regions with a predominance of left temporal area. Additionally, increased leptomeningeal contrast enhancement and diffusion restriction compatible with cytotoxic edema were observed. Pulse methylprednisolone treatment was started with the diagnosis of Anti-N-Methyl-DAspartate receptor autoimmune encephalitis, post-suspected herpetic encephalitis was confirmed. As there was no clinical improvement, intravenous immunglobulin treatment was added. Since complete recovery could not be achieved, rituximab infusion was started. After 4 weeks of rituximab therapy she has shown improvement in speech, swallowing and voluntary movements of mouth and tongue. In addition, cognitive impairment and emotional lability was remarkably improved.

This case highlights the necessity for clinicians to maintain a high index of suspicion for autoimmune encephalitis in patients presenting with encephalitic symptoms, especially when initial treatments fail. Early recognition and timely initiation of appropriate immunotherapy, including second-line agents like rituximab, are essential for improving patient outcomes. Further research is warranted to optimize treatment protocols and to better understand the pathophysiology of anti-NMDAR encephalitis, particularly in atypical presentations such as opercular syndrome.

ABSTRACTS

Topic: Neurogenetics

EPNS25_cr238 - Mega-corpus-callosum syndrome with cerebellar hypoplasia and cortical malformations (MCC-CH-CM) related to MAST1 gene: an accurate electroclinical case description

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Case report

Purpose: To describe the clinical presentation, diagnosis, and long-term follow-up of a patient with MCC-CH-CM syndrome associated with a MAST1 gene variant. As a very rare condition with only 16 reported cases, seizures are frequently noted, but few reports have described the epileptic features of this syndrome. This study focuses on the electro-clinical characteristics, emphasizing their relevance for diagnosis and treatment.

Method: We present the case of a 16-year-old patient diagnosed with MCC-CH-CM, who has been followed at our center since his 22 months. The patient's clinical progression, electroencephalogram (EEG) patterns, MRI findings, and genetic analysis are reviewed.

Results: The patient presented at 3 months axial hypotonia, followed by global development delay as documented by Griffith Developmental Scale evaluations. He presents with spastic tetraparesis, ocular dispraxia, severe cognitive disability and is nonverbal. In pre-puberal age he developed behavioural problems and a sleep disorder. At 3 months, the patient exhibited focal seizures and underwent treatment with Valproic Acid, with partial response. He was subsequently started on Levetiracetam and Clobazam. Seizures during childhood varied in semiology, including tonic-clonic ones, and increased in frequency, often being triggered by fever or strong emotions. The patient's EEG revealed interictal abnormalities, including theta alfa-like activity with medium-high voltage on the anterior and vertex regions associated with spike-and-wave patterns, that activate during sleep. MRI showed mega-corpus callosum with cerebellar hypoplasia, abnormalities of the posterior cranial fossa, brainstem hypoplasia and septum pellucidum cyst. Genetic analysis (WES) identified a de novo MAST1 variant (c.1549G>A, p.Gly517Ser).

The patient's phenotype is consistent with the previously described characteristics of MAST1 mutations, which include hypotonia, developmental delay, and varying degrees of motor and cognitive impairment. Seizures are also common in these patients; however, due to the limited number of reported cases, it has not yet been possible to define a typical semiology.

Conclusions: This case underscores the complexity of MAST1-related disorders, a protein recently recognised as fundamental in neurodevelopment. It emphasizes the need for further research on their electroclinical profile, therapeutic prospects, and the diagnostic role of MRI. Investigating clinical variability and potential electroclinical markers remains crucial.

ABSTRACTS

Topic: Infectious and Inflammatory Diseases/ Neuroimmunology

EPNS25_cr239 - A Severe Case of Juvenile-Onset Systemic Lupus Erythematosus with Multisystem Involvement Including Encephalopathy

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Case report

Objectives: Systemic lupus erythematosus (SLE) is a chronic autoimmune disease with multisystemic involvement. Neuropsychiatric involvement in SLE is a significant cause of morbidity and mortality. Herein, we report a male patient diagnosed with neuropsychiatric lupus (NPSLE) with multisystem involvement.

Case Report: A 12 year old male patient was referred to our hospital for persistent fever for 10 days, drowsiness, fluctuating levels of consciousness, weight loss over two months. His past medical history was remarkable for cervical lymphadenopathy noted four months earlier. On systemic examination; photosensitivity, malar and widespread maculopapular rash, hepatomegaly, pleural effusion and acrocyanosis were noticed. Neurological examination revealed fluctuating consciousness with episodes of unresponsiveness, agitation and delirium with no additional neurological deficits. The differential diagnoses included autoinflammatory diseases, lymphoma, and sepsis. Laboratory tests showed pancytopenia, positive direct Coombs, hyperferritinemia, hypofibrinogenemia, hypertriglyceridemia, hypocomplementemia, macroscopic hematuria, nephrotic range proteinuria, elevated pancreatic enzymes, and positive ANA antibodies. Cerebrospinal fluid analyses were normal. Craniospinal MRI revealed mild cerebral atrophy, EEG was consistent with encephalopathy. Skin punch biopsy confirmed lupus dermatitis, and renal biopsy was consistent with class IIIA lupus nephritis. Re-evaluation of prior excisional lymph node biopsy showed necrotizing histiocytic reaction while bone marrow aspiration biopsy indicated hemophagocytosis. Based on these findings, the patient was diagnosed with SLE-associated macrophage activation syndrome. Treatment included pulse steroids, anakinra, cyclophosphamide, plasma exchange, and IVIG. Maintenance therapy involved hydroxychloroquine and corticosteroids. During follow-up, encephalopathy and systemic symptoms regressed significantly over two months, although mild cognitive and behavioral disturbances persisted three months after discharge.

Conclusions: In patients with NPSLE, such as the current case, where encephalopathy occurs without parenchymal or vascular involvement, systemic inflammation and cytokine storms, as well as antibodies crossing the central nervous system, are thought to contribute to the pathogenesis. The presence of NPSLE indicates disease severity and is closely associated with increased morbidity and mortality.

ABSTRACTS

Topic: Neurogenetics

EPNS25_cr240 - Atypical febrile seizures as initial manifestation of a complex brain malformation associated with a FIG4 variant

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Case report

Introduction:
Neuronal migration disorders constitute a broad group of central nervous system malformations associated with intellectual disability, developmental delay, and epilepsy. We present a case of complex cortical development malformation whose first clinical manifestation was an atypical febrile seizure.

Case report:
A 3-year-old girl presented atypical febrile seizures characterized by focal onset and prolonged duration. MRI revealed a complex cortical malformation in the left hemisphere, including temporo-occipital polymicrogyria. EEG showed irritative activity with spikes in the left anterior temporal region. Genetic analysis through a targeted sequencing panel for cortical dysplasias identified a heterozygous variant of uncertain significance in FIG4 (c.1376G>A, p.R459Q), previously associated with bilateral temporo-occipital polymicrogyria. The patient, now 12 years old, remains seizure-free on eslicarbazepine monotherapy.

Conclusions:
Atypical febrile seizures warrant further investigation with neuroimaging and EEG to rule out underlying causes. Identification of a complex brain malformation on MRI and a FIG4 variant, previously associated in the literature with bilateral temporo-occipital polymicrogyria, provided diagnostic clarity and highlighted the role of genetics in understanding complex cortical malformations.

ABSTRACTS

Topic: Neurometabolic Disorders

EPNS25_cr241 - Many faces of PMM2-CDG: Posttraumatic Stroke-Like Episodes

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Case report

Introduction
Congenital disorders of glycosylation (CDG) are multisystemic metabolic disorders with significant phenotypic variability. The most common subtype PMM2-CDG, presents with isolated neurological symptoms or combined neurological and systemic features. The classical phenotype includes developmental delay, hypotonia, ataxia, dysmorphic features, inverted nipples, and abnormal fat distribution. Stroke-like episodes (SLEs) occur in 20–55% of cases. Neuroimaging typically reveals temporal, parietal, and occipital lobe involvement with subcortical white matter abnormalities, independent of vascular territories. Coagulation and perfusion abnormalities do not fully explain these events. Recently, hypoglycosylation-driven channelopathy has been proposed as a pathomechanism.

Case 1
An 8.5-year-old girl with a homozygous PMM2 variant presented with vomiting and altered speech (aphasia to slurred speech) after a fall from a 50 cm-high couch. Cranial CT was unremarkable, and stroke-protocol MRI showed no diffusion restriction. EEG demonstrated persistent left-hemispheric slowing, with asymmetric hypoperfusion on perfusion MRI. Symptoms resolved within 24 hours, and follow-up perfusion MRI showed resolution.

Case 2
A 6.5-year-old boy with Dandy-Walker malformation and a compound heterozygous PMM2 variant presented with drowsiness after a fall. Cranial CT was normal, and he was discharged after observation. The next day, persistent drowsiness and headache prompted MRI, revealing diffusion hyperintensity in the right parieto-occipital region without ADC restriction. He later developed seizures, with EEG showing right-hemispheric delta slowing. Follow-up imaging demonstrated progressive diffusion restriction in the right parietotemporal region, extending to the thalamus and hippocampus, interpreted as postictal changes. Perfusion MRI revealed hyperperfusion in these areas. Hemiplegia and facial paralysis improved within 72 hours. Subsequent imaging showed near-symmetrical perfusion-diffusion patterns, except for minor residual hyperperfusion and diffusion restriction in the right hippocampus.

Conclusions
SLEs are a significant neurological complication in PMM2-CDG, often affecting non-vascular territories. Even minor trauma may trigger these episodes, requiring vigilance. Our findings highlight the importance of early post-traumatic neurological assessment, as symptoms may evolve unpredictably. Neuroimaging, particularly perfusion MRI and diffusion-weighted imaging, is essential for detecting and monitoring these events. Serial imaging is recommended when initial studies are inconclusive. These cases emphasize the need for tailored imaging protocols in CDG patients with post-traumatic neurological symptoms and a better understanding of underlying mechanisms for preventive and acute treatment strategies.

ABSTRACTS

Topic: Miscellaneous

EPNS25_cr242 - Pediatric Melkersson–Rosenthal: a case report

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Case report

Objective
The purpose of this case report is to increase awareness of such a rare and probably underestimated syndrome, to improve diagnosis rates
Pediatric Melkersson–Rosenthal is a rare condition Characterized clinically by a triad of synchronous or metachronous symptoms: recurrent peripheral facial palsy, oro-facial oedema , and a fissured tongue; However, only 8–25% of the cases show the complete triad
The etiology of this disease is still unclear. However, genetic factors, immune functions alteration, infections, and allergic reactions have been suggested
Methods
We report a pediatric case with complete clinical triad of Melkersson–Rosenthal syndrome
Information were reviewed including sex, age at presentation, ethnicity, presence of facial paralysis with affected side and number of relapses, presence of orofacial oedema or lingua plicata, positive family history, comorbidities, and treatment
Results
A 09 -year-old male patient with non-family history referred to our hospital with an acute left peripheral facial palsy classed (House–Brackmann grade V).
Her mother reported that he has experienced this problem two times at the age of 05 and 07 years of age, and it fluctuates in severity and side
On physical examination he had dropping of the left corner of the mouth, along with
Bell's sign positivity (inability to close the left eye); There was subtle swelling lips
Her tongue was normal in color, muscle bulk and sensorimotor function but had deep radially arranged fissures
The remainder of the neurological examination were normal
the patient was treated with steroids bolus followed by a tapering dose for 25 days
Facial palsy gradually resolved after the third week of treatment (House–Brackmann grade II)

Conclusions
MRS in children is rare, and only few pediatric cases have been diagnosed so far.
The association between facial oedema , facial paralysis in a child with a fissured tongue should alert the physician

ABSTRACTS

Topic: Neuromuscular Disorders

EPNS25_cr243 - Newly diagnosed myasthenia gravis in a patient with myelin oligodendrocyte glycoprotein associated transverse myelitis

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Case report

OBJECTIVES: We aimed to emphasise that shorter follow-up intervals and symptom screening in patients with neuroimmune diseases such as myelin oligodendrocyte glycoprotein associated disease (MOGAD) are important to ensure early diagnosis of additional autoimmune disease.

METHODS: A patient with a previous history of myelin oligodendrocyte glycoprotein (MOG) antibody-associated transverse myelitis was diagnosed with myasthenia gravis after new onset of ophthalmoplegia and weakness.

CASE: A 14-year-old girl who was diagnosed with MOG antibody-related transverse myelitis 8 years ago after weakness in the lower extremities, gait disturbance, urinary incontinence and a history of paraplegia presented to the paediatric neurology outpatient clinic with complaints of drooping of both eyelids, shifting of the eyes, dysphagia, lisping of the tongue and weakness. Physical examination revealed bilateral ptosis and ophthalmoplegia. Electromyography was planned: A significant decreased response was observed in the repetitive nerve stimulation test, supporting a post-synaptic conduction defect at the neuromuscular junction. Anti-acetylcholine receptor antibody test result was negative. No thymic abnormality was found on thoracic magnetic resonance imaging (MRI). The patient was started on 180 mg/day pyridostigmine orally with the diagnosis of myasthenia gravis and intravenous immunoglobulin (IVIG) treatment at 2 gr/kg per month was given for 3 months and a positive clinical response was obtained.

CONCLUSIONS: Autoimmune diseases can present concomitantly and patients with neuroimmune diseases such as MOGAD are more likely to develop other autoimmune diseases than the general population. Ocular and systemic symptoms in a patient with MOG ab positive transverse myelitis require careful evaluation considering the possibility that it may be the first sign of myasthenia gravis. Therefore, follow-up and symptom screening of patients with neurological autoimmune diseases at shorter intervals is important to ensure early diagnosis of additional autoimmune disease.

ABSTRACTS

Topic: Neuromuscular Disorders

EPNS25_cr244 - Successful Management of SMA Type 1 with Gene Therapy and Rescue Nusinersen Following a Severe Adverse Event

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Case report

Background: Spinal muscular atrophy (SMA) is a genetic disorder caused by biallelic mutations in the *SMN1* gene, which encodes the survival motor neuron (SMN) protein, essential for motor neuron function and survival. Insufficient levels of SMN protein lead to progressive degeneration of motor neurons in the brainstem and spinal cord, resulting in progressive muscle weakness. The severity of SMA is primarily determined by the number of copies of the *SMN2* gene, which produces only 10% of functional SMN protein. Currently, three therapeutic options address the underlying SMN protein deficiency in SMA: (1) gene replacement therapy (*onasemnogene abeparvovec*), and (2) two treatments that enhance *SMN2* gene splicing to increase SMN protein levels—*nusinersen*, an intrathecally administered antisense oligonucleotide, and *risdiplam*, an orally administered small-molecule splicing modifier.

Objectives To report a case of successful management of SMA type 1 with gene therapy, followed by rescue treatment with nusinersen in the setting of a critical medical deterioration.

Methods This report describes the clinical course of a female infant diagnosed with SMA type 1 at 1.5 months of age, when she presented with progressive feeding difficulties, hypotonia, and muscle weakness. Genetic testing confirmed a homozygous deletion of exons 7 and 8 of the *SMN1* gene and the presence of two copies of *SMN2*. She required nasogastric tube feeding, and her CHOP INTEND score was 9/64.

She received gene therapy (*onasemnogene abeparvovec*) at 2 months of age. One month later, she developed sepsis and respiratory distress due to a urinary *Escherichia coli* infection, leading to clinical deterioration requiring intubation and mechanical ventilation. Given the severity of her clinical condition and while the therapeutic effect of gene therapy was not yet evident, nusinersen was initiated as a rescue measure to provide a more immediate enhancement of SMN protein production during this critical phase.

Her clinical course improved significantly, allowing for extubation one week after initiating nusinersen. She completed four doses of nusinersen, during which her respiratory status remained stable, and she showed notable clinical recovery. Four months later, her CHOP INTEND score improved to 27/64, and she regained the ability to feed orally.

Conclusions

This study suggest that in SMA patients who, despite gene therapy, experience severe acute functional deterioration, additional therapeutic modalities aiming to enhance SMN protein levels may be considered.

ABSTRACTS

Topic: Movement Disorders/ Cerebral Palsy

EPNS25_cr247 - An unusual cause of acute involuntary movement disorder in a previously well child

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Case report

Objective: A case report to review an unusual cause for acute involuntary movement disorder in a previously well child

Method: We review a case of an 8 year old previously well girl, who presented with acute onset of involuntary movements. She had no significant past history except a sore throat 10 days prior.

She has a previous history of mild motor delay (walked at 21 months) but no delay in speech and was intellectually normal. Involuntary movement affected her handwriting, feeding and some clumsiness with walking which resulted in falls. Speech was also noted to be more slow and quiet.

She was bright and interactive with frequent choreoathetoid movements worse when still and less obvious with purposeful movements. The movements were noted during sleep with increasing frequency. Gait was unsteady and ataxic and she had past pointing in both her upper limbs. No nystagmus or dysdiadochokinesia was noted. Her Fogg test was positive and there were no other focal neurological deficits noted.

MRI of her head showed mild prominence of her left cerebellar folia, with no changes on interval scanning. Despite extensive investigations we did not find any evidence to suggest an infective, toxic, autoimmune aetiology to explain her symptoms.

The cerebellar findings, exacerbation of choreoathetosis in sleep and mild gross motor delay prompted us to look at genetic profiles. She was found to have a pathogenic missense variant in ADCY5, (p.Ala726Thr). ADCY5 dyskinesia is a hyperkinetic movement disorder with infantile to late-adolescent onset of chorea, athetosis, dystonia, myoclonus, or a combination of these[1].The gene is highly expressed in striatum and myocardium and exerts effects via multiple intracellular signalling pathways[2].Neuroimaging findings vary with the majority being normal and some having mild T2 hyperintensities in the putamen and rarely cerebellar/ basal ganglia atrophy.

Conclusion: This case highlights the need to consider ADCY5 genetic mutation as a cause for a child presenting with acute choreoathetosis that worsens in sleep, cerebellar hypoplasia/ atrophy in the absence of evidence for infectious, toxic, autoimmune and paraneoplastic aetiology.

Reference

[1]Chen DH et al- ADCY5-related dyskinesia: Broader spectrum and genotype-phenotype correlations. Neurology. 2015;85:2026–35

[2]Halls ML, Cooper DMF. Adenylyl cyclase signalling complexes - Pharmacological challenges and opportunities. Pharmacol Ther. 2017;172:171–80

ABSTRACTS

Topic: Neurorehabiltation

EPNS25_cr250 - Motor developmental trajectory of a child with SYNGAP1 mutation under early intervention service: a case study

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Case report

Objective

SYNGAP1 mutation was reported to cause developmental and epileptic encephalopathy (DEE), which may result in global developmental delay, moderate-to-severe cognitive impairment, autism spectrum disorder, and generalized epilepsy with spontaneous and reflex seizures. In this case, we aimed to investigate the trajectory of motor development under early intervention service.

Methods

Gross motor evaluation and training was conducted by a main physical therapist. Developmental evaluation reports from occupational therapist, speech and language therapist, psychologist, medical records from physician's clinic notes, genetic testing reports were reviewed.

Results

This 5-year-old boy with no relevant perinatal medical history. He was referred to our center because he could not sit independently at the age of 9 months. His parents reported that he can roll over by himself at the age of 8 months. At that time, marked hypotonia with diffusely diminished deep tendon reflexes were noted, and the gross motor quotient was 70 assessed by Peabody Developmental Motor Scales, second edition. The intervention of physical therapy started immediately, and also a comprehensive developmental assessment was arranged. After training, he could sit independently at the age of 16 months, crawl at the age of 19 months, creep at the age of 2 years, and walk independently for 5 steps at the age of 2 years 5 months old. During this period of time, MRI and WES were done and showed no significantly abnormal, but the EEG showed some epileptiform discharged. Finally, SYNGAP1 mutation was diagnosed at the age of 42 months old. Now, he can walk stairs step by step, run on the treadmill for 5 minutes. He also went to kindergarten to join the activities with peers, played on the slides and climbing frame.

Conclusion

For case of SYNGAP1 mutation, the diagnosis and treatment of symptoms are very crucial, to improve the effects of DEE. Meanwhile, continuous early intervention should also be provided to improve the motor development and social integration for the case and their family.

ABSTRACTS

Topic: Movement Disorders/ Cerebral Palsy

EPNS25_cr251 - Diagnostic Challenges: Misdiagnosis of ATAXIA-TELANGIECTASIA (AT) as Cerebral Palsy in a Young Girl

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Case report

Background: Ataxia-telangiectasia (AT) is an autosomal recessive disorder characterized by cerebellar ataxia, telangiectases, immune defects, and a predisposition to malignancy. Chromosomal breakage is a feature.

Methods: Observational study**.**

Results: This case study will allow us to describe the clinical features of a girl who has been genetically diagnosed with a mutation in the ATM gene. 8 years old young girl, from the age of 6, gait disturbances are noted. She suffers from acute respiratory viral infection 13 times a year.

Key Differentiating Factors:

Clinical features: On examination, small telangiectasias are noted in the eyeball. Choreatetic movements of the fingers are noted. Gait with a wide base of support, with staggering, more to the right. There is also hyperkinesis of the tongue and facial muscles, and choking when eating liquid food.

MRI of the brain: Neuroimaging studies, in particular MRI, can reveal characteristic abnormalities in Ataxia-Telangiectasia, such as cerebellar atrophy, which differ from typical symptoms in cerebral palsy.

Genetic Testing: Genetic analysis can definitively confirm the presence of mutations in the ATM gene, which is crucial in order to determine the prognosis of the disease.

Discussion: In this clinical case, the patient had been diagnosed with cerebral palsy for many years and was referred for another round of rehabilitation therapy. However, following a thorough review of the medical history, physical examination, MRI, and genetic testing, the diagnosis was revised to ataxia-telangiectasia, leading to adjustments in the treatment plan.

Conclusion:

Thus, in case of ataxia with telangiectasia without lesion of the brain substance, which is characteristic of typical cerebral palsy in children, it is necessary to conduct a genetic examination.

ABSTRACTS

Topic: Neuromuscular Disorders

EPNS25_cr252 - Mutaion of BCAS3 nonsense variant cause HEMARS Syndrome in a girl

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Case report

BCAS3 microtubule-associated cell migration factor (BCAS3) is a large, highly conserved cytoskeletal protein previously proposed to be critical in angiogenesis and implicated in human embryogenesis and tumorigenesis. Here, we established BCAS3 nonsense variant (NM_017679.5(BCAS3):c.1630C>T (p.Arg544Ter)) as causative for a neurodevelopmental disorder. We report 4-year old-girl nonsense homozygous variant in BCAS3 gene. The patient had severe developmental delay, delayed walking, speech with few words, and autistic features. No seizure history. The patient also had microcephaly and short stature. In neruological examination hyperreflexia, lower limb spasticity, spastic gait. In MRI; posterior thin corpus callosum, cerebellar and cerebral atrophy, delayed myelination observed. In cases with severe developmental delay, hyperreflexia, hypotonia, and cerebral developmental anomalies, HEMARS syndrome should always be considered. In our knowledge; this is the first nonsense variant BCAS3 variant case in our country.

ABSTRACTS

Topic: Neurogenetics

EPNS25_cr255 - Migrating partial seizures in infancy caused by SLC25A22 mutation

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Case report

The SLC25A22 (OMIM: 609302, Solute Carrier Family 25, Member 22) gene encodes for a mitochondrial glutamate/H+ symporter and is involved in the mitochondrial transport of metabolites across the mitochondrial membrane. We hereby report a 2-months-old girl presenting with early-onset epileptic encephalopathy, hypotonia, and global developmental delay. Whole exome sequencing identified a homozygous mutation in SLC25A22 gene (c.350A>G; p.Gln117Arg), as the likely cause of the disease. The phenotype of our patient and EEG recordings related with developmental and epileptic encephalopathy, leading to severe hypotonia complex form of disease associated with extremely rare SLC25A22 variant and in our knowledge this is the first case of Türkiye.

ABSTRACTS

Topic: Neuromuscular Disorders

EPNS25_cr257 - Diagnostic challenges and clinical variability in nemaline myopathy: a report of two interesting cases with compound heterozygous variants

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Case report

Nemaline myopathy (NM) is a group of autosomal recessive inherited disease characterized by phenotypic and genotypic heterogeneity, named after findings from muscle biopsy findings. In NM, six different clinical presentations have been identified along with 13 genetic mutations. Our study aims to describe two different NM cases where we encountered difficulties in the diagnostic process.

Case 1: A 6-year-old patient, born late preterm and with a one-week NICU stay due to feeding difficulties, was evaluated for hypotonia and delayed gross motor milestones. Creatine kinase (CK) levels were normal, except one mild elevation (227 IU/dL). She walks unsupported but had difficulty running and climbing, with dysmorphic face, bell-shaped chest, and joint hyperlaxity. Needle EMG suggested myopathy, showing early recruitment with low-amplitude motor unit potentials. Array CGH, and CES (Clinical exome sequencing) were unremarkeable. Two years later, WES+CNV (Whole ES+Copy number variation) analysis detected c.3694C>G point mutation and a deletion in 2q23.3 in the other allele of the NEB gene, leading to diagnosis of recessive NM. RNA studies and parental tests are ongoing.

Case 2: A 5-year-old girl with joint contractures, hypotonia, and gross motor delay had history of prenatal reduced fetal movements and noted leg joint contracture after birth. She began using an orthosis at 2 months due to developmental hip dysplasia. She achieved head control at 12 months, sit unsupported at 3 years, but could not walk. The patient had kyphoscoliosis, cutis laxa, pectus excavatum, lower limb spasticity, and required orthoses. CK levels were normal. Muscle biopsy showed mild myopathic changes. WES identified NEB gene variants (c.3358A>G and c.183_184ins) as trans compound heterozygous, confirmed by family study.

These cases highlight the diagnostic challenges in NM patients with compound heterozygous variants. The prioritization of genetic testing and its in diagnostic processes have suggested that muscle biopsy could be utilized earlier in such cases.

ABSTRACTS

Topic: Movement Disorders/ Cerebral Palsy

EPNS25_cr258 - Postencephalitic Parkinsonism: therapeutic challenges in a rare secondary movement disorder

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Case report

Introduction
Neurologic complications of Enterovirus infections include aseptic meningitis, acute flaccid paralysis and rhombencephalitis. The latter typically present about a week after prodromal flu-like symptoms with progressive lethargy, ophthalmoplegia, autonomic dysfunction, neuropsychiatric symptoms and movement disorders such as myoclonus, ataxia or akinesia. Involvement of thalamus, basal ganglia and spinal cord is also possible. A potential preferential tropism for the substantia nigra has also been described, which may result in a postencephalitic Parkinsonism due to presynaptic dopamine denervation.

Case Report
A 7-year-old girl was brought to the emergency department due to persistent fever, progressive lethargy, dysarthria, and gradual development of an akinetic paraparesis associated with upward gaze palsy. The cerebrospinal fluid was positive for enterovirus. The Magnetic Resonance Imaging scan showed T2 hyperintensities of the brain stem with extended bilateral asymmetric lesions of the Substantia nigra. A DaTScan revealed dopaminergic nigrostriatal denervation. After initial therapy with high-dose corticosteroids (20 mg/kg/day methylprednisolone for 5 days) and intravenous immunoglobulin (2g/kg), symptomatic therapy was initiated with Levodopa/carbidopa with gradual improvement. At the 6 months follow-up, the girl presented a hypokinetic-dystonic syndrome partially responsive to treatment with Levodopa. She subsequently developed motor fluctuations and wearing-off phenomena that required progressive Levodopa dosage increase (up to 12 mg/kg/day) along with fractionation of the doses (5 times/day). Eventually, for the persistence of motor fluctuations and the appearance of painful OFF dystonia, add-on treatment with Selegiline was started along with a Levodopa-Carbidopa-Ascorbic Acid solution when needed, with partial benefit. In the following months the patient additionally developed a failure of the ON response, especially in the evening, for which Pramipexole adjunctive therapy was started, with partial efficacy.

Conclusions
This case highlights how postencephalitic parkinsonism represent a rare but often very disabling cause of acquired movement disorders. Therapeutic challenges include the frequent need for multi-drug therapy and uncertainty about indications and response to invasive treatments (Deep Brain Stimulation, infusion therapies).

ABSTRACTS

Topic: Movement Disorders/ Cerebral Palsy

EPNS25_cr260 - Complex movement disorders in inflammatory diseases – still idiopathic?

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Case report

Objectives:

Dystonias are among the most common movement disorders in childhood. Based on clinical characteristics like age of onset, disease course, body distribution and temporal pattern of the movement disorder, further diagnostics should be performed concerning disease aetiology. We want to discuss the case of a boy with a childhood onset, progressive movement disorder with varying clinical presentation, resulting in debilitating dystonia. After extensive diagnostics without conclusive findings, a levodopa trial was started and evaluated with video recordings that will be presented with the family's consent.

Results:

A boy, who was treated at our hospital because of chronic non-bacterial osteitis, coeliac disease with failure to thrive and congenital larynx papillomas, presented with a movement disorder at the age of eight years. Parents reported a reduced walk endurance and supposedly progredient weakness of the legs with broad-based gait. After five months, the exercise-dependent gait disturbance worsened with a walking distance of 400m. After nine months, he presented with increasing muscle weakness during the day that made him unable to walk independently in the evening. He used splints because of stumbling and a wheelchair for longer distances. Neurologic examination showed signs of ataxia, reduced reflexes and task-dependent dystonia worsening with exhaustion predominantly of the lower limbs. Comprehensive tests for neurodegenerative autoimmune diseases, including Langerhans cell histiocytosis with lumbar puncture, brain and spine imaging, electrophysiology, pulmonary function tests and whole genome sequencing, came back negative. Celiac diet was strictly controlled due to persisting failure to thrive with muscle-wasting. The multiple inflammatory autoimmune diseases and continuous deterioration lead us to try a steroid pulse therapy without any positive effect. Based on the clinical presentation and the debilitating course disorder we started a levodopa trial for presumably idiopathic dystonia. After 8 weeks the movement disorder ameliorated. Standing on one leg, walking on heels, tightrope walking and walking without splints was possible again, and a wheelchair was not needed anymore. To date, we have not found any link between the movement disorder and the inflammatory diseases, and the movement disorder's long-term outcome is pending.

Conclusion:

Childhood dystonias are a heterogenic group of diseases that require detailed and thorough differential diagnostics to investigate the aetiology. In case of no suggestive findings for an acquired or inherited cause of the movement disorder, the dystonia is considered idiopathic. For debilitating dystonias, a levodopa trial can be considered, even without pathologic results in laboratory, radiologic or genetic tests.

ABSTRACTS

Topic: Infectious and Inflammatory Diseases/ Neuroimmunology

EPNS25_cr261 - A peculiar case of post-infectious bulbar palsy

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Case report

We present a case of a young male of 16 years old at the time of admission.

After approximately two years of recurrent upper respiratory tract infections he finally was admitted to our hospital in the infectious diseases department with recent signs of dysphonia and dysphagia in severe and chronic sinusitis.
No pathological signs were observed on the first neurological physical examination, apart from the involvement of some cranial nerves, in particular the X and XII cranial nerves and a possible subtle involvement of the IX and XI ones.
The patient underwent the following diagnostic work out :
-instrumental investigations (neck and chest CT scan, Brain MRI, facial mass MRI): no lesion was found apart from a chronic sinusitis with signs of inflammatory involvement of the neighboring meninges.
-laboratory tests on both serum and cerebrospinal fluid (neurotropic viruses, Anti borrelia antibodies, botulism, CNS autoantibodies (including antibodies anti-MOG), antiacetyl choline antibodies, anti-MUSK .
-neurophysiological study (electromyography and conduction velocity).

All tests came back normal.
The only significant result was a weak positivity of anti-GD1a autoantibodies in serum.

The patient, who in the meantime underwent gastrostomy placement for enteral nutrition, was treated with cycles of intravenous IG, high-dose methylprednisolone with slight improvement in general conditions and neurological signs.
In the end we decided to propose a third-line immunomodulatory intervention with rithuximab.

After the first administration the patient began to show more important signs of improvement, but after the second one we witnessed a dramatic improvement with almost complete recovery of phonation and the possibility of resuming oral feeding.

This represented a diagnostic challenge, with the need to carry out many differential diagnoses in a clinically critical situation.
Bulbar palsy refers to a range of different signs and symptoms linked to impairment of function of the glossopharyngeal nerve (CN IX), the vagus nerve (CN X), the accessory nerve (CN XI), and the hypoglossal nerve (CN XII).
This may be caused by any of a number of genetic, vascular, degenerative, inflammatory, and other underlying conditions.
Many post-infectious autoimmune diseases are associated with anti-ganglioside auto-antibodies in their pathogenesis. In particular anti-GD1a ganglioside antibody is an important marker of Guillain–Barré syndrome

ABSTRACTS

Topic: Movement Disorders/ Cerebral Palsy

EPNS25_cr262 - Lee Silverman Voice Treatment (LSVT® LOUD) in children with dysarthria (LSVT® KIDS) – A multiple individual case study

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Case report

Background

With around 50,000 affected children in Germany, childhood dysarthria represents a relevant patient cohort in speech therapy that has been little researched. Affected children are particularly limited in their socialization process and ability to participate. The effectiveness of LSVT® LOUD for adults with dysarthria has been scientifically proven many times. The aim of this study was to explore whether a modified version of LSVT® LOUD -LSVT® KIDS- is as effective as LSVT® LOUD for adults.

Methods

This pilot multiple individual case study, designed as a pre/post study with follow-up examinations at four different time points, included four children with dysarthria due to cerebral palsy. The intervention phase consisted of 60-minute sessions of child-adapted LSVT® LOUD therapy four times per week, supplemented by guided home training over a period of four weeks. No speech therapy treatment was provided during the waiting period between the last therapy session and the follow-up examination.

Therapy effects were assessed at all test points using a German screening tool for dysarthria in children (BoDyS-KiD), measurements of average speech volume, and the scale for intelligibility in context.

Results

The results indicate a positive trend. 50% of the children showed a significant increase in average speaking volume up to the last therapy session and the follow-up examination. The BoDyS-KiD screening showed improvements in all children in the pre/post comparison.

Conclusion

The results of our multiple individual case study have demonstrated that LSVT® KIDS shows promising effects as a modified version of LSVT® LOUD therapy for children with dysarthria due to cerebral palsy. Based on these findings, a prospective randomized controlled trial is recommended to validate LSVT® LOUD for pediatric therapy.

ABSTRACTS

Topic: Neuro-Oncology

EPNS25_cr263 - A case series of Methotrexate-induced acute encephalopathy mimicking acute ischemic stroke

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Case report

Objective: MTX-induced acute encephalopathy due to methotrexate (MTX), which is frequently used in the treatment of childhood acute lymphoblastic leukemia (ALL), presents with a wide range of clinical findings, including altered mental status, stroke-like symptoms, seizures, and headache. MTX-induced stroke-like neurotoxicity is difficult to distinguish clinically and radiologically from acute ischemic stroke. Herein, we report 5 patients previously with ALL who presented with confusion, loss of muscle strength, paresthesia, and seizures after MTX treatment, which clinically and radiologically mimic stroke-like symptoms, and were diagnosed with MTX-induced encephalopathy.

Case Series: Five patients (aged 10 to 17 years) receiving chemotherapy for ALL were studied. All patients had focal or generalized muscle weakness and paresthesia; three had seizures, one had aphasia, one had central facial palsy, and one had dystonia. Brain magnetic resonance imaging showed T2/FLAIR hyperintensity and diffusion restriction in the centrum semiovale in all patients. Two patients were treated with Ca-folinate and two with leucoverin. Complete recovery was observed in three patients within 5-10 days and in one patient within 24 hours. One patient recovered with paraparesis.

Conclusion: MTX-induced encephalopathy, one of the stroke mimics, should be considered as a potential factor in patients with ALL presenting with stroke-like symptoms (hemiparalysis, facial palsy, confusion, and seizures), and it is important to recognize these cases and avoid unnecessary thrombolytic and/or anticoagulant treatment.

ABSTRACTS

Topic: Infectious and Inflammatory Diseases/ Neuroimmunology

EPNS25_cr265 - Anti-Zic4 Antibody Positive Pediatric Autoimmune Encephalitis: A Case Report

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Case report

Introduction: Autoimmune encephalitis (AE) is a rare inflammatory disease of the central nervous system characterized by antibodies targeting neuronal cell surface proteins, receptors, and ion channels. Although N-methyl-D-aspartate receptor, myelin oligodendrocyte glycoprotein, and glutamic acid decarboxylase antibodies are the most common in childhood, many other antibodies have been identified. In adults, the presence of anti-Zic4 antibodies has been associated with Zic4 antibody-positive AE and paraneoplastic cerebellar syndromes.

Case Presentation: A 14-year-old male presented with confusion, speech disorder, and seizures. He had headache, weakness, and increased sleepiness for the past week. On neurological examination, the patient was lethargic, deep tendon reflexes were absent in the extremities, and the Babinski sign was positive bilaterally. Laboratory tests showed normal CSF glucose, protein, and IgG index. Serum and CSF anti-MOG antibody, aquaporin-4 antibody, oligoclonal band, and autoimmune encephalitis panel were negative, except for serum anti-Zic4 antibody, which was positive. All infectious, metabolic, and rheumatological investigations were negative. Electroencephalography showed diffuse low voltage. Brain MRI showed T2/FLAIR signal enhancement and diffusion restriction in the temporal and frontal cortex and basal ganglia. Based on the clinical, laboratory, and radiological findings, the patient was diagnosed with anti-Zic4 antibody-positive autoimmune encephalitis. Intravenous methylprednisolone and intravenous immunoglobulin were administered.

Conclusion: The diagnosis of AE in children is difficult due to the overlap with other diseases and the complexity of behavioral changes. To the best of our knowledge, this is the first pediatric case of isolated anti-Zic4 antibody-positive autoimmune encephalitis reported here.

ABSTRACTS

Topic: Neuromuscular Disorders

EPNS25_cr267 - A Charcot Marie Tooth case with a rare mutation diagnosed by Whole Exom Sequencing

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Aim: Charcot-Marie-Tooth disease type 1J (CMT1J) is an autosomal dominant sensorimotor peripheral neuropathy characterized by distal muscle weakness and atrophy, as well as distal sensory impairment, predominantly affecting the lower limbs and resulting in gait abnormalities. Additional features may include foot deformities, upper limb or hand involvement, and decreased or absent deep tendon reflexes.

Case: An 11-year-old female patient with a complaint of gait disturbance for 2 years presented with a complaint of stumbling and falling when walking for 1 year. On physical examination, the patient had a wide base gait with a prominent arch and pes cavus deformity in both feet. She was able to walk on her toes, but not on her heels. There were no deep tendon reflexes in the lower extremities. Distal atrophy was present. An electromyography (EMG) performed in another hospital before the patient presented to us showed severe motor polyneuropathy in the upper and lower limbs and asymmetric sensory polyneuropathy with partial axonal but predominantly demyelinating involvement. There was no pathology on craniospinal magnetic resonance imaging (MRI). No mutation in CMT Multiplex Ligation-dependent Probe Amplification (PMP22 gene) was detected in genetic testing performed prior to enrollment. There was no pathology on the neuromuscular panel which included 41 genes.

The patient was admitted to hospital with a pre-diagnosis of chronic inflammatory demyelinating polyradiculoneuropathy (CIDP) due to severe motor polyneuropathy. The patient was given 2 g/kg intravenous immunoglobulin (IVIG) for 5 days. There was no change at the follow-up examination one month later. IVIG treatment was repeated with readmission to hospital. After the patient failed to respond to IVIG treatment, the diagnosis was re-evaluated. Repeat EMG showed a chronic axonal polyneuropathy pattern with large, long-lasting motor unit potential (MUP) transitions and advanced dilution patterns in the muscles studied. CIDP/nodopathy evaluation was negative (contactin-1, cntn1/caspr-1, neurofascin 155 -186). Whole exome sequencing (WES) analysis was sent. In the final WES analysis of the patient : A heterozygous c.4271C>T / p.Thr1424Met pathogenic mutation was detected in the analysed regions of the TPR3 gene. This result is expected to cause autosomal dominant Charcot-Marie-Tooth demyelinating disease type 1J.

Conclusions: Although we could not initially make a diagnosis with a gene panel including 41 genes, we insisted on the genetic diagnosis of our patient and detected a rare genetic defect not included in the gene panel by WES.

ABSTRACTS

Topic: Neurogenetics

EPNS25_cr268 - GLS gain of function - widening the spectrum of neuroectodermal diseases

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Case report

Background: Glutaminase (GLS)-gene encodes the enzyme GLS, that catalyses the deamination of glutamine (gln) into glutamate (glt). Loss- and gain-of-functions (LoF/GoF) are described. Assuming a GoF-GLS variant glutamat excess is associated with oxidative stress, a common cause of cataract and neuronal damage. GLS is highly expressed in brain and kidney. GLS GoF was found in a total of two patients, with extremely high glutamate levels in brain in the MR-spectroscopy (MRS) and elevated glt/gln ratio in urine. They showed a variable phenotype with infantile cataract, mild or profound developmental delay, uncontrolled motoric agitation, erythematic subcutaneous nodules, profound axial hypotonia and epilepsy.

Methods: We present a currently 30-month-old girl with severe neurodevelopmental delay, muscular hypotonia, hyperexcitability and chilblain-like lesions, which was noticed at the age of approx. 4 months. Over time she showed an onset of secondary microcephaly, movement disorder with myoclonia and dystonia, leading to sleep disturbance. She had two febrile convulsion. Several EEGs and eye examination were normal. Whole genome sequencing (WGS) detected a likely pathogenic de novo GoF variant in the GLS gene (c.1412A>G; p.GLN471Arg). Cranial MRI at the age of 12 months showed delayed myelination. The biochemical investigations revealed slightly increased glt/gln ratio in urine once, while it was normal in plasma and cerebrospinal fluid. The MRS (3 Tesla Philips, PRESS short TE: 35 ms) at the age of 28 months showed elevated glutamate and low glutamine in cortex, basal ganglia and white matter.

Results: WGS detected a likely pathogenic de novo GoF variant in the GLS gene and excluded a LoF. The clinical presentation together with the increased glut/gln ratio in MRS comparable to the two described patients confirmed the pathogenicity of the new variant. In addition to Perampernel a therapy with Memantine was recently started with the aim to block toxic glutamate effects and alleviate the symptoms of hyperexcitability and movement disorder, which improved at the present time.
Conclusion: The glutamate excess, detected in a 3-Tesla-MRS, is comparable with the two other patients with GoF GLS variant and therefore confirms the diagnosis. Our patient's phenotype, although cataract was absent, supports the assumption that glutamate excess causes a new type of neuroectodermal disease. Specific therapy has not been described before. Follow-up on therapy, sequential video recordings of the movement disorder and standardized developmental testing will be available at the time of the presentation.

ABSTRACTS

Topic: Neuromuscular Disorders

EPNS25_cr270 - Congenital myasthenic syndrome as a rare cause of episodic apnoea - case report

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Case report

Apnea in newborns and infants is defined as episodes of cessation of breathing lasting at least 20 seconds or a shorter duration but accompanied by bradycardia or oxygen desaturation. In differential diagnostics, we must consider the broad aetiology of central, obstructive, or mixed apnea.

Our case report presents a rare cause of infant apnoea in a patient with congenital myasthenic syndrome (CMS), a heterogeneous group of genetically determined diseases characterised by impaired neuromuscular transmission. In the absence of typical fatigable weakness, establishing a diagnosis of CMS could be challenging when the clinical picture of myasthenic signs is not so evident.

The case report presents a male infant born after 39 weeks gestation with episodes of desaturation and agitation on the first day of life during breastfeeding that required intubation. Developing bronchopneumonia or central apnoea was considered the aetiology of the condition. After improvement, he was discharged to home care. At the age of one month, he was admitted for recurrent episodes of desaturation, agitation and symmetric jerking of the chin and upper limbs. Despite repeated EEG examinations without epileptic discharges, epileptic seizures were initially considered in the differential diagnosis. The antiseizure treatment (phenobarbital, levetiracetam valproate, carbamazepine) was ineffective. During the following eight months, the patient underwent seven similar episodes requiring intubation in most cases. This period of the patient's life was also complicated by the development of necrotising enterocolitis with ileostomy and acute gastroenteritis due to adenovirus. During the mentioned stress complications, the frequency of apnoea episodes increased. At the age of four months, we considered CMS as a possible aetiology and started pyridostigmine treatment. The performed genetic analysis of the NGS myasthenic syndrome gene panel identified two variants of uncertain significance in the *SLC5A7* gene associated with presynaptic congenital myasthenic syndrome. The response to the pyridostigmine treatment was favourable, with reductions in episodic apnoea. During the child's further development, signs of psychomotor developmental delay were present, but there were no significant signs of fluctuating muscle weakness.

From a paediatric neurologist's perspective, the CMS should be considered in cases of differential diagnosis for newborn or infant apnoea, even in the absence of muscle weakness.

ABSTRACTS

Topic: Fetal and Neonatal Neurology

EPNS25_cr272 - Familial hyperekplexia in six members of the same family

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Case report

Objectives: To present a case of hyperekplexia diagnosed in a neonate, which led to the identification of the same condition in five maternal relatives, highlighting the importance of genetic evaluation.

Methods: A neonate with a family history of congenital stiffness, involving five maternal relatives, was admitted to the NICU due to muscle hypertonia, transient stiffness with immobility, feeding difficulties and apneic episodes. A comprehensive diagnostic workup was performed in the context of differential diagnosis, including electroencephalography, cranial ultrasound, magnetic resonance imaging of the brain, examination of cerebrospinal fluid neurotransmitters, basic metabolic screening and whole exome sequencing (WES).

Results: WES identified a mutation in the glycine receptor alpha 1 (GLRA1) gene, confirming the diagnosis of neonatal hyperekplexia. The neonate was treated with clonazepam, leading to clinical improvement.

Conclusions: Early recognition and diagnosis of neonatal hyperekplexia is crucial to prevent serious complications such as apneic episodes and sudden death. Accurate differentiation from conditions like epilepsy ensures appropriate management, improving the infant's quality of life. Furthermore, genetic diagnosis enables targeted genetic counseling for families and early intervention for affected individuals.

ABSTRACTS

Topic: Neuromuscular Disorders

EPNS25_cr273 - A rare case in childhood: the mutation of FUS gene in amyotrophic lateral sclerosis

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Case report

Objectives: Amyotrophic lateral sclerosis(ALS) is a fatal neurodegenerative disease associated with upper and lower motor neuron degeneration, characterized by progressive muscle weakness, atrophy and paralysis. FUS mutation associated ALS, also known as ALS6, is extremely rare in childhood. We aim to present our 13-year-old patient, who is the youngest patient with ALS associated with FUS mutation, and to review the cases in the literature.

Methods: A 13-year-old male patient was admitted to our outpatient clinic with complaints of difficulty in walking and balance disturbance for three months. It was learned that the patient's mother died at the age of 21 with dysphagia and muscle wasting in less than a year. On neurologic examination of child, muscle strength was decreased in all extremities, more prominently in the lower extremities, and fasciculation of tongue was present. Deep tendon reflexes were obtained, there were no pathologic reflexes. He had difficulty walking without support.

Results: Electromyography revealed findings consistent with anterior horn motor neuron disease. Brain magnetic resonance imaging supported the diagnosis of ALS. No abnormality was found in cerebrospinal fluid examination, metabolic disease and malignancy screening. Clinical exome analysis (CEA) was performed for genetic diseases associated with anterior horn motor neuron involvement. CEA revealed a heterozygous pathogenic missense variant in the FUS gene (c.1574C>T p.Pro525Leu). The average onset age of ALS6, which is much earlier than the average onset age of other ALS types. Cases with onset in the 2nd decade have been reported in the literature. Juvenile FUS mutations have an aggressive disease progression and the time from onset to death or tracheostomy is usually less than two years. Our patient became wheelchair dependent within three months. Less than a year after the diagnosis, the patient is currently bedridden and has swallowing and feeding difficulties.

Conclusions: Although it is possible to detect FUS gene defects among genetic causes of ALS in the adult age group, all cases of ALS in childhood are rare. Our study may raise awareness in terms of detecting the symptoms and understanding the phenotypes of FUS-related ALS cases. Rapid disease progression and prominent bulbar symptoms in ALS patients should suggest the possibility of FUS-related ALS.

ABSTRACTS

Topic: Infectious and Inflammatory Diseases/ Neuroimmunology

EPNS25_cr275 - Early and late onset macular edema in fingolimod use: A report of two cases

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Case report

Objective: Fingolimod-associated macular edema (FAME) is a rare complication, primarily understood through case reports. Although a case report noted a patient with visual impairment 24 hours after a 0.5 mg dose, FAME mainly occurs within the first few months of treatment. However, this complication can also rarely present later. In 16-year-old female and 20-year-old male patients with early and late-onset FAME, respectively, who presented without visual complaints, we underscored the significance of conducting baseline and regular macular thickness measurements at 3-4 month intervals.

Method: Clinical, imaging characteristics of the cases were obtained from the hospital database.

Results: A 16-year-old female patient, who experienced her initial clinical manifestation at 11 years and was monitored without intervention, received a diagnosis of relapsing-remitting multiple sclerosis (RRMS) after a second episode 5 years later. Fingolimod therapy was initiated due to substantial lesion burden. During the third month of treatment, routine ophthalmological examination and optical coherence tomography (OCT) revealed macular edema with a 16/20 vision. Fingolimod administration was discontinued. Two months after cessation, follow-up ophthalmological examination and OCT results were normal (20/20 vision). The second patient, a 20-year-old male with RRMS, experienced his initial clinical attack at 9 years. Nine years later, he had a second clinical attack, prompting intramuscular interferon beta-1a therapy. About one year after starting interferon, the patient had a third clinical attack, leading to its discontinuation. Fingolimod was initiated due to significant lesion burden. Baseline vision was 20/20. The patient experienced two years of remission on this regimen. However, at the end of the second year, ophthalmological evaluation and OCT identified unilateral macular edema, without visual complaints (20/20 vision). Consequently, fingolimod treatment was terminated. Two months after cessation, the macular edema completely resolved without subsequent vision problems.

Conclusion: Consistent with the phase III MS study (Kappos, L. Et al.) and its extensions, macular edema occurred 3 months after fingolimod was started in our first patient. Our second case exhibited late-onset macular edema (after 12 months), a phenomenon documented in the literature for a subset of patients. FAME cases can be unilateral or bilateral and can present with blurred vision, decreased vision, or no symptoms. Macular edema developed in 2 of 15 patients started on fingolimod for RR-MS in our clinic, suggesting this complication may be more frequent than thought. Patients should be followed up with periodic ophthalmological examination and OCT for this complication.

ABSTRACTS

Topic: Infectious and Inflammatory Diseases/ Neuroimmunology

EPNS25_cr276 - Polymicrogyria and MOG Antibodies: What Role Do They Play in Paediatric New-Onset Seizures?

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Case report

This case presents a previously healthy 12-year-old boy who developed new-onset focal seizures. Initial 1.5T MRI revealed left-sided fronto-temporal polymicrogyria (PMG). Twenty days later, he experienced a second episode, and a repeat 3T MRI showed bilateral thalamic hyperintensities and subtle FLAIR hyperintensities in the posterior insular cortex, suggesting inflammation. Cerebrospinal fluid analysis indicated pleocytosis, and serum/CSF testing confirmed high-titer anti-MOG antibodies (Abs). The patient had no other neurological symptoms or encephalopathy and was treated with high-dose corticosteroids. At a two-month follow-up, the patient showed no further neurological signs, with improved MRI findings. While PMG accounted for the seizures, the presence of bilateral thalamic lesions and anti-MOG-Abs positivity complicated the diagnosis. The patient experienced seizures without cerebral irritation, diverging from classical FLAMES descriptions. Immunotherapy led to clinical improvement, but the role of MOG-Abs remains uncertain. The co-occurrence of polymicrogyria (PMG) and MOG-Abs positivity in a pediatric patient with new-onset seizures raises questions about the relationship between structural brain malformations and autoimmune inflammation and whether seizure-only phenotypes can be an expression of MOG-Abs-associated disease (MOG-AD).

ABSTRACTS

Topic: Neurometabolic Disorders

EPNS25_cr277 - Spinal cord involvement associated with mitochondrial disease NDUFS6

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Case report

Introduction

The NDUFS6 gene encodes the NADH ubiquinone oxidoreductase subunit 6 of complex I of the mitochondrial respiratory chain. Three phenotypes associated with this mitochondrial disease have been described: severe neonatal lactic acidosis, Leigh/Leigh-like syndrome, and neuropathy and optic atrophy. Fourteen patients have been reported in the literature without spinal cord involvement. We present a patient diagnosed with mitochondrial disease (NDUFS6) who presents with Leigh phenotype and spinal cord involvement.

Clinical Case

A 3-year-old male patient was evaluated in Pediatric Neurology for motor regression and lower limb weakness of 2 to 3 months' duration. Simple motor delay was observed. The physical examination revealed dysarthria, lower limb weakness, hyporeflexia, and ataxic gait. Cranio-spinal MRI demonstrated symmetrical hyperintensity in the basal ganglia, thalamus, cerebral peduncles, brainstem, and cervical and dorsolumbar spinal cord, as well as perimedullary vascular tortuosity. Metabolic studies detected elevated lactate in blood and cerebrospinal fluid (CSF), a lactate/pyruvate ratio greater than 10, and elevated alanine and hydroxybutyrate within normal limits in CSF. Infectious and autoimmune screenings were negative. With the clinical suspicion of mitochondrial disease, treatment with biotin, riboflavin, thiamine, coenzyme Q10, and carnitine was initiated, resulting in clinical stability. Next-generation sequencing (NGS) confirmed mitochondrial disease by identifying the 309+5G>A variant in homozygosity in the NDUFS6 gene, with both parents being heterozygous for the 309+5G>A NDUFS6 variant.

Conclusions

Mitochondrial diseases are rare entities that have targeted treatment, so the presence of motor regression and symmetrical involvement of the basal ganglia and spinal cord requires early metabolic screening to establish early therapy.

ABSTRACTS

Topic: Neurogenetics

EPNS25_cr278 - Diagnosis through multi-omics: a complex neurodevelopmental case solved by integration of genomics and proteomics

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Case report

Objectives
Multi-omics techniques, developed through advances in high-throughput and computational technologies, allow the simultaneous analysis of multiple biological layers. These approaches provide a comprehensive molecular view, enabling disease diagnosis, revealing new therapeutic targets, and supporting personalized medicine. We present a case demonstrating that the application of multi-omics techniques can be crucial to interpret complex data and solve undiagnosed cases.

Methods
The patient is a 15 years-old female with short stature, mild facial dysmorphisms, ataxia, EEG abnormalities, borderline IQ, progressive cerebellar atrophy associated with cerebellar white matter abnormalities, and iron deposition in the basal nuclei. Notably, at the age of 13, the patient was also diagnosed with metastatic Ewing sarcoma. Whole genome analysis (WGS) was performed through a research project on unsolved diseases. Subsequently, immunoblot, cell functional studies, proteomic profiling and transcriptomics were carried out in order to investigate the impact of genetic variants of unknown significance (VUS).

Results
WGS on the trio revealed two VUS in compound heterozygosity: PPP1R21 c.1728G>T, a missense variant inherited by the father, and PPP1R21 c.292_294delTCT, an in-frame deletion inherited by the mother. PPP1R21 encodes for a regulatory subunit that modulates the activity of protein phosphatase 1, influencing various cellular processes, particularly the endosome maturation pathway. When we first assessed the patient, less than 20 cases with PPP1R21-related developmental disorder (NEDHFBA) had been reported, all carrying homozygous truncating/splicing variants and displaying more severe phenotypes. Immunoblot studies were carried out to confirm an impact on the corresponding protein. Proteomics allowed the identification of key pathophysiological pathways and confirmed the results of previous studies on fibroblasts derived from a patient with bi-allelic PPP1R21 variants, thus overall confirming the pathogenicity of our variants. Transcriptomic studies revealed an altered expression of genes that are known to be involved in other neurodevelopmental disorders.

Conclusions
These are the first functional data showing that missense and in-frame variants can cause a milder phenotype in the spectrum of NEDHFBA. Our data exemplify the application of combined omics techniques to confirm VUS pathogenicity and to minimize diagnostic odysseys in orphan diseases. This approach may also pave the way for future therapeutic approaches.

ABSTRACTS

Topic: Miscellaneous

EPNS25_cr279 - Unilateral absence of Cerebellar hemisphere - An incidental finding

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Case report

Unilateral cerebellar hypoplasia or agenesis is a rare congenital pathological condition characterised by symptoms ranging from mild asymptomatic to severe symptomatic cases.

We report the case of a 14 years old boy with absence of right cerebellar hemisphere incidentally discovered by MR imaging. He was admitted to our ward with symptoms of intermittent vomiting for 2 years. MRI brain scan showed almost complete absence of right hemisphere of cerebellum. Vermis and the left cerebellar hemisphere were normal.

He had mild autism and was attending a mainstream school. According to mother, antenatal and immediate postnatal period was uneventful. He developed left handedness when he was about a year old. He began to walk at the age of 1 year but was unstable and prone to falls, especially during the first 3 years. However, it wasn't severe enough to warrant brain imaging. He had mild intentional tremor on the right arm and the heel-to-shin test on the right side was not as slick as on the other side. There was no nystagmus and his speech was clear.

Vomiting subsided after few days spontaneously. It was eventually found to be related to school anxiety as vomiting episodes coincided with term times and completely subsided during school holidays.

The aetiology of Cerebellar agenesis or hypoplasia are variable ranging from genetic, vascular to in-utero exposure to toxins or infections. Complete unilateral absence is considered to be secondary to severe vascular insult like infarct or haemorrhage, which we suspect in this case. The outcome is variable ranging from a near normal asymptomatic life to unilateral cerebellar signs and developmental impairment. Involvement of Vermis is often, but not always, associated with a poorer outcome.

ABSTRACTS

Topic: Neurometabolic Disorders

EPNS25_cr280 - xPOLG-Related Disorders: Mildly Elevated Liver Transaminases, Language Delay, and EEG Abnormalities – A Case Report

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Case report

The *POLG* gene encodes mitochondrial DNA polymerase, which is responsible for the replication of the mitochondrial genome. Mutations in *POLG* can cause early childhood mitochondrial DNA (mtDNA) depletion syndromes or later-onset syndromes arising from mtDNA deletions. In most cases, *POLG* mutations lead to clinical manifestations only in compound heterozygotes and are considered predominantly recessive diseases. The clinical diagnosis of mitochondrial disease caused by *POLG* mutations is challenging due to its insidious onset and overlapping spectrum of symptoms affecting multiple organ systems. However, five main phenotypes have been identified: Alpers-Huttenlocher syndrome (AHS), Childhood Myocerebrohepatopathy Spectrum (MCHS), Myoclonic Epilepsy Myopathy Sensory Ataxia (MEMSA), Ataxia Neuropathy Spectrum (ANS), and Progressive External Ophthalmoplegia (PEO). *POLG* mutations can result in drug-resistant epilepsy, ataxia, neuropathy, and myopathy, and should be considered in such cases.

Here, we present a 4-year-old girl who was initially evaluated for mildly elevated liver transaminases and language delay. Subsequently, EEG abnormalities were noted, and muscle weakness was observed. The observed symptoms raised concern for a potential metabolic disorder, leading to whole-exome sequencing (WES), which revealed that she inherited *POLG* mutations from both parents: c.926G>A from her mother and c.2209G>C from her father.

The symptoms and severity of mitochondrial diseases caused by POLG mutations vary significantly depending on the clinical phenotype. However, these disorders predominantly affect tissues with high energy demands, such as the nervous system, muscles, and liver. Although diagnosing these conditions remains challenging due to their broad spectrum of symptoms, the widespread use of genetic testing has greatly facilitated the diagnostic process.

ABSTRACTS

Topic: Infectious and Inflammatory Diseases/ Neuroimmunology

EPNS25_cr281 - A Case of Isolated Oculomotor Nerve Palsy with Positive Serum Ganglioside GD3 IgG Antibody

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Case report

An eight-year-old girl presented to medical attention with acute onset diplopia. She was born on term to nonconsanguineous parents, and her neurodevelopment was age appropriate. Physical examination revealed ptosis, anisocoria, absence of pupillary reflexes, exotropia on the right-hand side. She didn't have muscle weakness and deep tendon reflexes were normoactive. She was diagnosed with isolated oculomotor nerve palsy.

Lumber puncture revealed no signs of infection or any abnormality. Anti-Mog, Anti- Aquaporin-4 were negative.

Brain MRI showed enlarged perioptic CSF space on the right and the right optic papilla is flattened. A slight increase in signal on T2 was observed in the optic nerve close to the optic papilla. MR angiography was normal.

She was found positive for Anti-GD3 IgG. She received IVIG 2 gr/kg/total. On follow- ups she was fully recovered. She didn't have any sign of CMV infection.

The main known causes of isolated oculomotor nerve palsy include congenital, head trauma, cerebrovascular ischemic disease, neoplasms, aneurysms, postsurgical iatrogenic, demyelinating, migraine and infectious.

Isolated oculomotor nerve palsy due to Anti-GD3 antibodies is uncommon, so this rare case causing ptosis is presented due to its infrequent nature, such that awareness of the differential diagnosis of cranial nerve palsy and management.

ABSTRACTS

Topic: Fetal and Neonatal Neurology

EPNS25_cr282 - Early signs of SMA type 0 during a pregnancy: should SMN1 be systematically studied in prenatal neurology cases?

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Case report

A 28-year-old primigravida was referred to the fetal medicine unit at 20+3 weeks of gestation due to suspected fetal cardiopathy. Fetal ultrasound revealed a head circumference below the 5th percentile, normal nuchal fold, and an abnormal ventricular ratio suggestive of significant asymmetry. Fetal echocardiography indicated a moderate risk of aortic coarctation, a small ventricular septal defect (VSD), and persistent left superior vena cava. Fetal MRI showed a short corpus callosum and delayed cortical gyral development. An amniocentesis with QF-PCR and chromosomal microarray was normal. At 32 weeks, subtle edema was noted in the left foot. Whole-exome sequencing (WES) was inconclusive. Termination of pregnancy was performed at 36 weeks due to the presence of microcephaly, short corpus callosum, muscular VSD, suspected aortic coarctation, persistent left superior vena cava, and left foot edema.

In a subsequent pregnancy, fetal hydrops was detected, leading to termination at 12 weeks. Genetic studies, including QF-PCR and chromosomal microarray, were normal. Post-mortem WES was inconclusive.

During the third pregnancy, an increased nuchal translucency (2.4 mm) and absent ductus venosus a-wave were observed at 11 weeks. Chorionic villus sampling revealed normal QF-PCR and chromosomal microarray results. At 16 weeks, fetal echocardiography showed asymmetry of the cardiac chambers and potential VSD. By 20 weeks, left foot edema was noted again, along with a head circumference below the 5th percentile and a short corpus callosum. Echocardiography confirmed a small muscular VSD without significant cardiac asymmetry or aortic coarctation. The pregnancy was terminated at 20 weeks. Post-mortem WES was also inconclusive.

Re-analysis of all three affected fetuses revealed a homozygous deletion of the SMN1 gene and a single copy of SMN2, consistent with Spinal Muscular Atrophy (SMA) type 0, a severe prenatal form. Due to the complexity of SMN genes in high-throughput sequencing, results were validated using MLPA, confirming the complete absence of SMN1 and a single copy of SMN2. Genetic counselling was offered to the family with unaffected offspring.

This case highlights the importance of genetic evaluation for SMA in recurrent fetal abnormalities.

ABSTRACTS

Topic: Neurodevelopmental Disorders / Developmental Neuroscience

EPNS25_cr283 - A case of Bainbridge-Ropers syndrome

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Case report

Bainbridge–Ropers syndrome (BRPS) is characterized by failure to thrive, severe global development delay, feeding difficulties, hypotonia, growth retardation, intellectual disabilities, autism, sleep disturbance, and dysmorphic features. However, not every clinical manifestation is present and symptoms vary among patients.
We aimed to present a case with ASXL3 gene variant an extremely rare cause of developmental delay.
The 12-year-old boy was born full-term without complications during the first pregnancy and delivery. Motor development during the first year proceeded normally; however, at 1.5 years of age, significant cognitive developmental delay became evident. The child did not speak, exhibited hyperactivity, and behavioral disorder, and had difficulty making appropriate social communication.
Neuropsychological tests were performed at the age of 4 years. The child was diagnosed with an autism spectrum disorder.
Brain MRIs performed at ages 3 and 7 showed no pathological findings.
Whole-exome sequencing revealed a heterozygous variant c.6524T>C p.(Ile2175Thr), resulting in an amino acid change from Ile to Thr at position 2175 (uncertain significance). The parents were also tested, and the familial known ASXL3 variant was identified in the proband in the heterozygous state. Given the symptomatic state of the proband, a genetic diagnosis of autosomal dominant BRPS was made.
At 7 years old, the child began experiencing generalized tonic-clonic seizures. An EEG revealing interictal epileptic activity during sleep in the form of regular sharp-slow wave complexes in the right temporal region.
Throughout treatment, the patient was prescribed various combinations of anti-seizure medications, including Valproic acid (VPA), Lamotrigine (LMT), Levetiracetam (LEV), Carbamazepine (CBZ), Ethosuximide (ETH), Topiramate (TPM), and Clonazepam (CNZ), ketogenic diet. Despite these treatments, complete seizure remission was not achieved.
He has daily seizures in the form of atonic seizures as well as tonic seizures during sleep with occasional secondary generalization. EEG is consistent with Lenox-gastaut syndrome.
The patient is undergoing multidisciplinary rehabilitative therapy with poor effect. his psychomotor development is severely delayed. At present, he lives at home with no special support (due to behavioral difficulties).
This case represents a more distinctive phenotype of BRPS than previously described.
Although the clinical manifestations of BRPS were non-specific, finding an intellectual disability, behavioral disturbances, and autism spectrum disorder may raise the clinicians' suspicion about the diagnosis.

ABSTRACTS

Topic: Neurometabolic Disorders

EPNS25_cr284 - Acute metabolic encephalopathy with refractory status epilepticus in Succinic Semialdehyde Dehydrogenase Deficiency

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Case report

Objective: Characterization of acute metabolic encephalopathy and refractory status epilepticus (SE) associated with febrile illness in Succinic Semialdehyde Dehydrogenase Deficiency (SSADHD).

Methods: We report the case of a patient with SSADHD who presented with worsening behavioral concerns and new onset of seizures following febrile illness, describing clinical, EEG and neuroimaging features.

Results: A nine year old child with a history of global developmental delay, ataxic gait and moderate intellectual disability, with a genetically-confirmed diagnosis of SSADHD, presented with focal seizures and episodic psychomotor agitation following an upper respiratory tract infection with fever. Initial EEG showed interictal epileptiform discharges over the right posterior leads, while MRI showed no significant abnormalities. Seizures and behavioral changes persisted through treatment with oxcarbazepine, levetiracetam and EV prednisolone. A week after initial presentation the patient developed focal clonic seizures evolving into SE, with a continuous epileptiform discharge over the right temporo-occipital EEG leads. EV boluses of midazolam and phenytoin did not stop seizures; CI propofol, ketamine and midazolam were therefore used to achieve a burst-suppression pattern. Tentative suspension of sedation after two days resulted in a reoccurrence of seizures and appearance of hyperkinetic movement disorder. Repeat MRI showed FLAIR hyperintense regions in the left caudate nucleus and mesial temporal lobe. Phenobarbital, methylprednisolone, and lacosamide were subsequently added to the treatment with slight clinical benefits. Finally, the patient was started on vigabatrin and ketogenic diet, resulting in a significant reduction in seizure frequency, nearly two weeks after the onset of SE. At the time of discharge, a month after SE, there was a return to baseline of behavior, motor and verbal skills, with sporadic, brief seizures.

Conclusions: While it has been rarely reported in the literature, SSADHD can present with acute metabolic encephalopathy, associated with new onset of epileptic seizures or increased seizure burden, psychiatric or behavioral issues, basal ganglia lesions and movement disorders. As of today, there is a lack of evidence regarding possible markers of decompensation – which could include reduction in GABA CSF, blood and MRI spectroscopy levels – and therapeutic strategies, particularly in critical settings, resulting in delays in its recognition and effective treatment.

ABSTRACTS

Topic: Movement Disorders/ Cerebral Palsy

EPNS25_cr285 - Childhood-onset levodopa-responsive parkinsonism/dystonia – WARS2 deficiency movement disorder spectrum

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Case report

Introduction: A childhood-onset hyperkinectic movement disorder presenting with new-onset generalized myoclonic tremor, ataxia, and dystonia encompasses a broad differential diagnosis and workup including infectious, metabolic and genetic causes as well as paraneoplastic manifestations such as opsoclonus myoclonus ataxia syndrome.

Case Presentation: We present a 17-month-old Portuguese boy, born at 33 weeks and 5 days via cesarean section due to late fetal growth restriction, of healthy non-consanguineous parents. Despite his prematurity, he had a regular neonatal period. At the age of 17 months he was hospitalized to investigate a tremor syndrome that started 3 months before asymmetrically in the lower limbs progressing with generalization and adding postural instability. The parents reported he could seat by the age 6 months, but experienced motor development stagnation. The child also exhibited axial hypotonia, global mild-to-moderate bradykinesia, action-induced distal dystonia, with no spasticity and normal eye movement. Cognition and interaction were preserved. Diagnostic workup was negative for infection and paraneoplastic causes, and criteria for opsoclonus-myoclonus syndrome were not met. Brain-MRI showed mild ventriculomegaly and nonspecific widening of the frontotemporal subarachnoid space. Electroencephalogram was normal. Metabolic investigation revealed only a marked decrease in homovanillic acid (HVA) and 5-methyltetrahydrofolate (5-MTHF) in the CSF and urgent genetic testing was obtained with WES trio. The exome identified two variants in compound heterozygosity in WARS2 gene, establishing the diagnosis of WARS2 deficiency associated with parkinsonism-dystonia 3. A trial of levodopa (0.5-2mg/kg/day, max 5mg/kg/day) resulted in significant improvement by the fourth week at 1.2mg/kg/day.

Discussion: This case further contributes to a better understanding of the diverse phenotypic spectrum of WARS2 deficiency, that includes two major phenotypic manifestations: epilepsy and movement disorders. This case emphasizes the importance of prompt genetic testing in early-onset movement disorders, given that it can significantly impact the choice of symptomatic and/or disease modifying treatment and grant access of patients to clinical trials. In our case, the efficacy of levodopa in managing symptoms was evident. Further studies are essential to establish comprehensive diagnostic criteria and treatment protocols for this rare condition.

ABSTRACTS

Topic: Movement Disorders/ Cerebral Palsy

EPNS25_cr286 - Early onset genetic dystonia caused by a THAP1 variant presenting in a 6 year old girl.

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Case report

A 6-year-old female developed posturing of her left hand and foot, limping and dragging her left foot when walking. This became more pronounced over time and within six years it had progressed to involve her leg and right arm as well as painful neck posturing to the left. She had difficulties writing due to hand tremor. She began to find it difficult to stand for more than 2 minutes due to posturing of her feet.

Prior to onset of symptoms at age 6 years, the child had been well with normal development and no significant health problems. In her family history, her parents were both well, there was no history of consanguinity. She had one brother who had haemophilia A.

On examination she walked on the lateral edge of her left foot and striatal toe was evident bilaterally. She had dystonic posturing of her left hand and both feet and was relatively weak distally on her left hand and forearm and leg with present reflexes. She had good strength proximally. She had jerky movements of her left arm. On follow up eight months later she also had developed torticollis of her neck, to the left and increased tone in sternocleidomastoid muscle. She found it easier to walk than run. Dystonic posturing became progressively worse the longer she walked.

Investigations showed metabolic tests were normal. Nerve conduction studies were normal. MRI showed a band like T2 hyperintense signal involving the genu of the corpus callosum. There was symmetric susceptibility signal change involving the globi pallidi and substantia nigra and associated mild pallidal volume loss. Subtle T2 and FLAIR hyperintense signal was noted involving the dentate hila bilaterally. Appearances were suggestive of neurodegeneration with brain iron accumulation (NBIA) disorders. Ophthalmological examination was normal with no deposits of iron in the cornea or lens. Whole genome sequencing revealed a heterozygous variant [c.94C>T p.(Leu32Phe)] with REVEL score suggesting functional impact in THAP1 gene associated with DYT-THAP1 related dystonia (also known as DYT6 dystonia).

This is a rare genetic cause of early onset dystonia and this child presented at an atypically young age. MRI may be normal or non-specific at first, and can mimic NBIA. She was started on Gabapentin which helped with dystonic tremor but did not improve torticollis or walking ability. Botulinum toxin injection helped with painful neck spasms. She has been referred for deep brain stimulation.

ABSTRACTS

Topic: Neurogenetics

EPNS25_cr287 - DNM1L-associated autosomal-dominant encephalopathy due to defective mitochondrial and peroxisomal fission 1 in Ukrainian child with drug-resistant epilepsy with manifestation in adolescence

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Case report

Objectives. Autosomal-dominant (AD) lethal encephalopathy due to defective mitochondrial and peroxisomal fission 1 (OMIM 614388) – rare mitochondrial disease with variable age of onset, severity and phenotype comprised of neurodevelopmental regression, seizures, white matter anomalies etc. The cause is pathogenic variant of the DNM1L gene, that regulates intracellular mitochondrial and peroxisomal fission.

Methods. 15 years old boy with the diagnosis of drug-resistant focal epilepsy has been conducted genetic counselling in intensive care department. First signs occurred in 15 years – rapid fatigue during physical activity, muscle pain, tremor, seizures. Reproductive history of mother – 1 healthy daughter, 1 miscarriage. Instrumental methods: abdominal ultrasound – hepatomegaly; brain MRI - basal nuclei gliosis, lacunar infarcts of the frontotemporal lobes, thalamus ischemia; electroencephalography - focal poly-peak ictal epileptic activity in the left fronto-central area; spiral computer tomography – atelectasis of the lungs. Differential diagnosis has been carried out between measles and autoimmune encephalitis, thrombophilia and mitochondrial diseases. Genetic tests such as serum lactate/ammonia, urine oligosaccharides, blood amino acids and acylcarnitines, urine neurotransmitters and whole-exome sequencing (WES) have been conducted..

Results. Phenotype: congenital anomalies and dysmorphic facial features are absent. Metabolic testing – without pathology. Using WES heterozygous pathogenic de novo variant c.1246 C>T (p.Arg416Cys) of the gene DNM1L has been identified, that is consistent with with the encephalopathy due to defective mitochondrial and peroxisomal fission 1, AD. Therapy with sibazone, thiopantal, midazolam, pregabalin, hydazepam, intravenous immunoglobulins, topiramate, levotiracetam, clobazam and ketogenic diet had no effect.

Conclusions. Adolescent-onset drug-resistant epilepsy requires genetic counseling and multidisciplinary approach for differential diagnosis with mitochondrial diseases. Genetic research is important for choosing treatment tactics and prognosis.

ABSTRACTS

Topic: Neuromuscular Disorders

EPNS25_cr288 - Spinal muscular atrophy as a challenging diagnosis with coexisting sensory neuropathy

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Case report

A 6-year-old male, born to consanguineous parents, presented with global developmental delay, proximal muscle weakness, and abnormal gait. Initial genetic investigations, including array CGH, whole-exome sequencing (WES) and Fragile X testing, were inconclusive. Neurophysiology showed decreased sensory nerve amplitude potential and reduced sensory nerve action potentials in upper limbs and decreased F-waves and an absent skin sympathetic response in combination to polyphasic motor unit potentials with increased amplitude. An WES reanalysis revealed a homozygous NTRK1 pathogenic variant (p.Phe713Ser), confirming HSAN IV. Given the clinical suspicion of SMA driven by EMG findings, targeted SMN1/2 analysis in WES identified a homozygous deletion of SMN1, confirming an additional diagnosis of SMA. SMN2 copies were four compatible with the diagnosis of SMA type 3. During diagnostic procedure, the patient exhibited progressive motor deterioration, increased distal skin lesions, and prominent polymyoclonus over time. Ultrasound revealed a compatible pattern with a motor neuron disease and EMG was not repeated. He began treatment with nusinersen.

Diagnosing genetic neuromuscular disorders can be challenging, particularly in consanguineous families where multiple pathogenic variants may coexist. This case highlights the complexity of a dual genetic diagnosis involving HSAN IV and SMA in a pediatric patient from a consanguineous. Multidisciplinary collaboration between pediatric neurologists, pediatric neurophysiologists and molecular geneticists is essential for early detection of complex neurogenetic presentations and dual diagnoses.

ABSTRACTS

Topic: Neurogenetics

EPNS25_cr289 - GEMIN5 variants causes a neurodevelopmental disorder in Two Siblings

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Case report

***GEMIN5* variants causes a neurodevelopmental disorder in Two Siblings**

A 5-year-old boy first presented to medical attention whit developmental delay, hypotonia around 2 years of age. He was born on term to nonconsanguineous parents. His prenatal-natal-perinatal period was uneventful. He wasn't able to stand up or walk. When he was 2 years old, he had a sister, and she also had similar problems. She was born on term and her prenatal-natal-perinatal was uneventful. She can stand up, but she can't walk. We started to follow up these two siblings when they were 5 and 3 respectively. Physical examination revealed hypotonia, and hyperactive deep tendon reflexes.

No abnormalities were detected in routine biochemical examinations and metabolic studies such as ammonia, plasma and urine amino acid analysis, long chained fatty acid analysis, urine organic acid analysis, and tandem mass spectrometry. Ocular examination was normal. EMG were normal as well. Magnetic resonance imaging (MRI) of the brain showed diffuse cerebellar atrophy in younger sibling.

Chromosomal microarray analysis, Whole Exome Sequencing and Spinocerebellar Ataxia gene panel analysis were performed for both sibling, all came back inconclusive. Trio-WGS was performed and both siblings had *GEMIN5* heterozygous p. N13Qfs*118 (c.36dup) and heterozygous c.1080+5G>A variants. Then family segregation was performed; mother (p. N13Qfs*118 (c.36dup)) and father (c.1080+5G>A) both had one variant.

Biallelic variants in *GEMIN5* that give rise to a rare neurological syndrome which features developmental delay, cerebellar atrophy, and predominant motor dysfunction along with hypotonia. GEMIN5 is an indispensable component of the SMN assembly complex

In this report, we have shown that biallelic variants in *GEMIN5* cause developmental delay, motor dysfunction, and cerebellar atrophy. Also, we would like to emphasise on the importance of genetic tests' diagnostic yield.

ABSTRACTS

Topic: Neurometabolic Disorders

EPNS25_cr291 - Rare metabolic disorder (2-hydroxyglutaric aciduria) as a cause of leukodystrophy

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Case report

Introduction

2-Hydroxyglutaric Aciduria (2-HGA) is a rare metabolic disorder characterized by the accumulation of **2-hydroxyglutaric acid** in the body, leading to progressive neurological symptoms. The condition has three main forms: **L-2-HGA**, which typically presents in childhood with developmental delay, seizures, and movement disorders, **D-2-HGA**, which has a more variable presentation, ranging from mild to severe neurological impairment and combined **D,L-2-HGA**. Diagnosis is confirmed through urine organic acid analysis and genetic testing. There is no cure, but treatment focuses on symptom management and supportive care

Case Discription

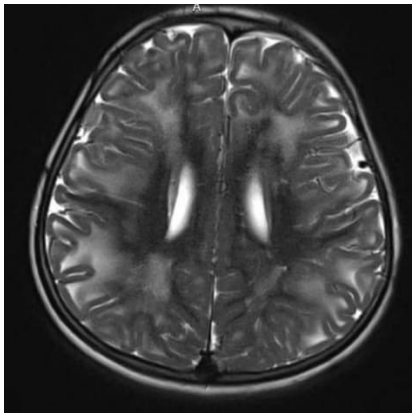
A 10-year-old girl from Kurdish refugee background presented with recurrent generalized tonic clonic seizures triggered by febrile illness. Her parents and grandparents were first degree cousins with a strong family history of epilepsy and early neonatal deaths. She had a normal delivery, mild speech delay and learning difficulty. She started to have seizures at the age of 2 years, almost five episodes each year lasting for 10-30 minutes. She had a normal neurological examination. Her urine for organic acid showed elevated 2-hydroxyglutaric acid consistent with diagnosis of 2-hydroxyglutaric aciduria, a rare metabolic disorder.

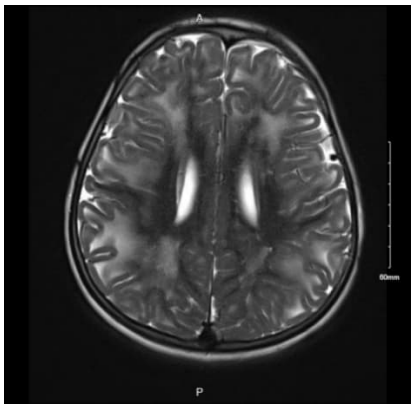
Discussion

2-hydroxyglutaric aciduria type 1, L-2-hydroxyglutaric aciduria and combined D,L-2-hydroxyglutaric aciduria have autosomal recessive pattern while D-2-hydroxyglutaric aciduria type 2 is considered autosomal dominant. The different types of 2-hydroxyglutaric result from mutations in several genes. 2-hydroxyglutaric type 1 is caused by mutation in the D2HGDH gene. Type 2 is caused by mutation in the IDH2 gene. L-2-hydroxyglutaric aciduria results from mutations in L2HGDH gene. MRI and CT findings are typically subcortical and paraventricular hyperintensities. Varying degrees of subcortical leukoencephalopathy and cerebellar atrophy have been observed. An increased incidence of brain tumors has also been reported.

MRI brain showed extensive subcortical white matter abnormality. EEG revealed multi regional epileptiform features that occurred independently, in particular over posterior temporal region bilaterally.

ABSTRACTS





Conclusion

2-hydroxyglutaric aciduria is a rare metabolic disorder with variable clinical presentations and genetic heterogeneity. Early diagnosis and management are crucial to mitigating neurological complications and improving patient outcomes.

Acknowledgement

We acknowledge the contributions of supervisor Dr. Kafil Shadani, our colleagues and supporting institutions in facilitating this care report.

ABSTRACTS

Topic: Neurogenetics

EPNS25_cr294 - Neurodegeneration with brain iron accumulation (NBIA) type 4 is associated with the mitochondrial membrane protein

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Case report

Objectives. A large number of diseases of accumulation in the brain require clarification - genetic research.

Methods. Neurological assessment of the patient's status, magnetic resonance imaging (MRI), virological and genetic research – NGS.

Results. At the age of 8, the boy's gait began to be disturbed, high arches of the feet appeared. Creatine phosphokinase levels and electromyography performed at the place of residence were normal (the speed of propagation of excitation along the membranes and the amplitude of M-responses from the muscles when testing the nerves - without pathology). During transcranial magnetic stimulation, conduction disturbances along the pyramidal pathways were found. The patient was examined and referred to our hospital for clarification of the diagnosis. Spasticity and pyramidal pathological signs prevailed in the neurological status. The cranial nerves were not altered. Heredity was not burdened. The boy's cognitive functions were not changed (studied at school). According to the MRI of the brain, changes from the pale spheres and black substances were detected, and the accumulation of metals in the basal ganglia was suspected. Together with geneticists, blood serum was sent for genetic research and revealed Neurodegeneration with brain iron accumulation (NBIA) type 4 is associated with the mitochondrial membrane protein OMIM: 614298, ORPHA 289560. A diagnosis is established in the early stages of the disease, but it requires further research to develop treatment methods in the world.

Conclusions. The patient is diagnosed with a neurodegenerative disease, which will progress over time. Further research is needed to develop treatments. The following shows taking baclofen and working with a physical therapist. A multidisciplinary approach helps in the diagnosis of complex neurodegenerative diseases.

ABSTRACTS

Topic: Neurogenetics

EPNS25_cr298 - Conditions mimicking alternating hemiplegia of childhood: diagnostic and therapeutic challenges in series of cases.

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Case report

Objectives: Alternating hemiplegia of childhood (AHC) is a rare neurological disorder marked by episodes of temporary paralysis on alternating sides of the body. Diagnosing AHC is challenging due to its complex symptoms, often resembling other disorders.

Methods: We present a series of 3 paediatric cases (2 girls and one boy) referred for neurogenetic diagnostics due to recurrent episodes of hemiplegia. All patients were assessed using the Rissardo et al. algorithm for AHC and met at least 4 of the 6 main Aicardi criteria. After ruling out causative variants in AHC-related genes (laboratory criterion of Rissardo et al.), they were reclassified as having conditions mimicking AHC and underwent individualized diagnostic procedures to determine the cause of their recurrent episodes of hemiplegia.

Results: An 8-month-old girl with alternating flaccid paresis for several hours, mainly affecting the upper limbs, appearing mainly after sleep, mild developmental delay and joint laxity was diagnosed with recurrent elbow dislocations after excluding genetic and metabolic causes. The second patient was a 16-year-old boy after chemotherapy treatment of congenital craniofacial hemangioma in infancy, with recurrent episodes of mainly right-sided hemiplegia, occasionally plegia of three limbs, mostly after physical exertion. Initially above episodes were interpreted as hand-eye coordination disorders and epileptic seizures. After excluding the genetic causes of recurrent hemiplegia, extended angiographic diagnostics revealed a carotid malformation on the right side, leading to insufficient brain blood supply during exertion. Flunarizine treatment resulted in significant improvement. The third patient, a 3-year-old girl with global developmental delay, dystonic gait disorders, bone lesions, macrocephaly, and epilepsy, was initially diagnosed with Sotos syndrome due to a likely pathogenic *NSD1* c.4039del *de novo* variant. She experienced alternating hemiplegia episodes lasting several hours, mainly triggered by rehabilitation and infections, which subsided with rest and sleep. Despite comprehensive diagnostics, the cause of hemiplegia remained undetermined. Flunarizine treatment completely controlled the episodes.

Conclusions: Following the latest AHC diagnostic algorithm proposed by Riccardo et al. allows for quick and effective selection of a group of patients with conditions mimicking AHC. This group may include patients with atypical vascular or orthopaedic diseases, as well as other genetic diseases in where interactions between genes associated with AHC should be suspected (e.g. *NSD1* gene can modify expression of genes associated with AHC through altereted methylation). Flunarizine treatment should be considered if the hemiplegia's pathomechanism indicates it.

ABSTRACTS

Topic: Fetal and Neonatal Neurology

EPNS25_cr301 - Transient neonatal myasthenia gravis

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Case report

Transient neonatal myasthenia gravis is a clinical entity that occurs in 10-20% of newborns of mothers with myasthenia gravis in the first 3–72 hours of life due to the transplacental transfer of antibodies to acetylcholine receptors. It is a self-limiting disease, lasting several days to months. Newborns do not produce antibodies, therefore the evaluation of antibodies is limited. The occurrence of the disease is not related to the severity of the disease, therapy, or mother's antibody titer, unlike arthrogryposis and polyhydramnios. However, certain treatment (in a mother) and good disease control can reduce the risk. Reoccurrence is possible among siblings. We present a case of transient neonatal myasthenia gravis in a floppy infant.

A male eutrophic term newborn was admitted on the first day of life to the Neonatal Intensive Care Unit due to hypotonia, facial diplegia, weak cry, poor sucking and swallowing reflexes, This was the mother's first pregnancy, during which she was monitored for Hashimoto's thyroiditis (euthyroid) and was treated with immunoglobulins (first trimester) and corticosteroids and pyridostigmine bromide (in the second half of pregnancy) due to myasthenia gravis. No other antenatal pathology was found (amniotic fluid was normal). The newborn was respiratory stable; he evacuated the stool properly. Haematological and biochemical parameters were appropriate for age. Brain ultrasound showed slightly voluminous choroid plexuses distally, as well as frontal and occipital periventricular echogenicity. A heart ultrasound showed an open foramen ovale. For the first two days of life, feeding was maintained parenterally, then enterally (nasogastric tube). On the sixth and seventh days of life, neostigmine was administered before meals. With orofacial stimulation and physical therapy, improvement in motor skills and feeding is noted up to the second week of life. The initially taken acetylcholine antibodies arrived positive, whereas the control (age two months) were negative. During further follow-up, a normal neurological status is recorded.

In conclusion, transient neonatal myasthenia gravis is a common complication of a relatively uncommon disease. Management of floppy infants is a challenge, particularly in neonatal emergencies, given the age and the wide spectrum of severe differential diagnoses. Recognizing the disease is important for an early rational approach, targeted therapy, interdisciplinary intervention, and optimal recovery.

ABSTRACTS

Topic: Neuro-Oncology

EPNS25_cr304 - Exploring Trametinib for Treating Plexiform Orbital Neurofibroma in an Infant

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Case report

Introduction: Plexiform Neurofibroma (PN) commonly occur as part of the genetic disorder known as neurofibromatosis type 1 (NF1). These benign tumors of the nerve sheath are generally identified in childhood and can experience rapid growth during this period. In 10% of cases, PNF affects the orbital-periorbital region, leading to various visual impairments (glaucoma, visual loss from amblyopia, optic nerve compression, and keratopathy). The clinical landscape has significantly changed due to recent regulatory approvals of the MEK inhibitors for children with NF1 and symptomatic, inoperable PN. Additionally, promising results from other clinical trials suggest that these developments have the potential to create a fundamental shift in the management of PNs.

Case report: We report a case of a child, born prematurely at 31 weeks of gestation, who was observed to have protrusion of the right eyeball. Brain and orbital MRI scans indicated the presence of an optic tumor with characteristics suggestive of a plexiform neurofibroma (PNF). The child was diagnosed with elevated intraocular pressure. Further physical examination confirmed the presence of multiple café-au-lait spots. We decided to start treatment with MEK inhibitor - Trametinib solution, when infant was 6 months old, which was supplied by Novartis on a Compassionate basis through their Managed Access Program. Apart from the drug supply itself, Novartis had no influence on any aspects of this report. Approval for treating such a young child has been obtained from the ethics committee. We plan to monitor brain and orbital MRIs, blood pressure and heart ultrasound, tumor volume, vision, glaucoma, and adverse effects, including atopic dermatitis, skin erythema and paronychia. During the first two months of treatment, the infant is in good general condition, with minor skin changes in the form of atopy, and the eye pressure is lower.

Conclusion: The ability to treat very young children is important since these tumors' growth rapidly at very early age and early intervention can not only help manage the tumor growth but also potentially prevent severe cosmetic and functional impairments that can deeply impact a child's quality of life. This underscores the importance of advancements in treatment options like MEK inhibitors, which offer new hope for managing such complex cases.

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