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The following articles will be considered for publication: original research papers, reviews, rapid communications, case studies and letters to the Editor.

All articles will be critically reviewed by the editors and invited referees within 2 months.

Full details may be found in the section Instructions to Authors at the end of this issue.

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**Programme and Abstracts of the 10th EPNS Congress,
25–28 September, 2013, Brussels, Belgium**



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ERS 2	MRI of fetal and infant brain development – Alec Aeby, Marie Cassart	
ERS 3	Macrocephaly: clinical and molecular work-up – Marie Cecile Nassogne, Yves Sznajder	
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	Lunch symposium Viropharma	Copper Room
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PP2	Epilepsy 1 – Chair: Peter Baxter	p. S33
PP3	Neuromuscular and movement disorders – Chair: Michèle Willemsen	p. S36
PP4	Neurometabolic disorders chair – Chair: Rudy Van Coster	p. S39
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	NCL genetics and diagnostic algorithm – A. Schulz	
	Therapeutic perspectives and palliative care – A. Kohlschütter	

13:30–14:30	Special Lecture on Dravet syndrome: Diagnostic problems and current treatment options Organisation: Brabant Pharma	Copper Room
14:30–16:00	Plenary session 2: Neuromuscular disorders Chairs: Gunnar Buyse and Thomas Sejersen	Gold Room
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IL 7	Outcome measures in childhood neuromuscular disorders: New concepts and standards – <i>Eugenio Mercuri</i>	
IL 8	Gene-derived therapeutic approaches for childhood neuromuscular diseases – <i>Nathalie Goemans</i>	
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IL 10	Cognitive dysfunction in idiopathic epilepsy – <i>Eliane Roulet-Perez</i>	
IL 11	Outcome in West syndrome – <i>Zvonka Renner</i>	
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O24 - 1725	Autonomic dysfunction in children with Guillain-Barré syndrome Aziz M, Watson L, Plant N, Vassallo G (UK)	p. S8
O25 - 2018	Risks of relapse and severe outcome in children with a clinically isolated acute transverse myelitis at onset: a French-British collaborative study Deiva K, Absoud M, Niotalkis G, Hemingway C, Lim M, Tardieu M (France)	p. S8
O26 - 1915	Immunological studies in rapid-onset obesity with hypothalamic dysfunction, hypoventilation, and autonomic dysregulation (ROHHAD) syndrome Biancheri R, Napoli F, Calcagno A, Ceccherini I, Hacohen Y, Jacobson L, Lang B, Vincent A, Maghnie M (Italy)	p. S8
O27 - 2082	Anti-myelin oligodendrocyte glycoprotein antibody positivity in children with demyelinating episodes Hughes SE, James S, Flynn P, Smyth G, McKinstry S, Rennie I, Hanrahan D, Peake D, Tirupathi S (UK)	p. S9
O28 - 1989	Children in England with narcolepsy during the H1N1 (swine 'flu) pandemic: clinical features in those receiving AS03 adjuvanted pandemic A/H1N1 (2009) influenza vaccine and in unvaccinated cases Winstone AM, Stellitano L, Verity CM, Shneerson JM, Andrews N, Stowe J, Miller E (UK)	p. S9
O29 - 1951	Childhood encephalitis: epidemiological, clinical and radiological characteristics and their impact on the outcome Liptai Z, Ujhelyi E, Mihaly I, Barsi P (Hungary)	p. S9
O30 - 1893	Guillain-Barré syndrome in UK children: H1N1 vaccinations, preceding infections and clinical features Verity C (UK)	p. S10
16:30–18:00	Parallel session 6: Cerebral palsy Chairs: Florian Heinen and Bernard Dan	
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O32 - 1912	Brain volume reduction in young adults with perinatal hypoxic-ischaemic encephalopathy Bregant T, Rados M, Vasung L, Zadnik V, Derganc M, Evans AC, Neubauer D, Kostovic I (Slovenia)	p. S10
O33 - 2123	Visual spatial perceptual profiles in children with developmental coordination disorder or in very premature children with cerebral palsy Gonzalez Monge S (France)	p. S11

O34 - 1931	Innovative application of the motion graph deviation indexes for the quantification of the pre-post BTX – a upper limb movement changes Darras N, Vanezis T, Tziomaki M, Pasparakis D, Papavasiliou A (Greece)	p. S11
O35 - 1861	Cerebral visual impairment and cerebral palsy: two sides of the same coin? Fazz E, Galli J, Micheletti S, Rossi A, Franzoni A (Italy)	p. S11
O36 - 2035	Clinical correlation of arcuate fasciculus lateralization in developmental dysphasia Komárek V, Vydrová R, Kyněl M, Šanda J, Vránová M, Štěrbová K, Kršek P (Czech Republic)	p. S12
O37 - 1898	Use of serious gaming to increase motivation of cerebral palsy children during rehabilitation Bonnechère B, Jansen B, Omelina L, Da Silva L, Mougeat J, Heymans V, Vandeuren A, Rooze M, Van Sint Jan S (Belgium)	p. S12
O38 - 1645	Brain lesions relate to gait pathology in children with unilateral and bilateral cerebral palsy Van Gestel L, Ortibus E, Meyns P, De Cock P, Sunaert S, Feys H, Duysens J, Jaspers E, Desloovere K (Belgium)	p. S12
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Thursday, 26 September 2013

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ERS 5	Neonatal EEG/AEEG – Daniele Hasaerts, Geraldine Boylan
ERS 6	Spasticity diagnosis and management – Bernard Dan, Jean-Paul Misson
08:30–10:00 Plenary session 3: Epileptic encephalopathies Gold Room	
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IL 13	Animal models and pathophysiology of epileptic encephalopathy – Aristea Galanopoulou
IL 14	Treatable neonatal epilepsies – Barbara Plecko
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10:30–12:15 Parallel session 7: Combined EPNS/EACD session: Up-to-date management cerebral palsy	
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IL 16	Botulinum toxin therapy – Antigone Papavassiliou
IL 17	Deep brain stimulation – Jean-Pierre Lin
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O40 - 2159	Hypomyelinating leukodystrophy due to recessive mutations of GJC2 (connexin 47): clinical and radiological characteristics in 18 patients Renaldo F, Tonduti D, Dorboz I, Masliah J, Giraud G, Elmaleh M, Orivoli S, Beraud-Majorel C, Drunat S, Chalard F, Barthez MA, Desguerre I, Quijano-Roy S, Rodriguez D, Boespflug-Tanguy O (France) p. S13
O41 - 1941	Mutation spectrum and clinical characteristics in hypomyelination with atrophy of the basal ganglia and cerebellum (H-ABC) Hamilton EM, Vanderver A, Siriwardena K, Pinelli L, Schiffmann R, Blaser S, Naidu S, van Berkel CG, Polder E, Abbink TE, Wolf NI, van der Knaap MS (The Netherlands) p. S13
O42 - 1909	FOXG1 gene: phenotype-genotype relation in Spanish patients Pineda Marfa M, O'Callaghan Gordo M, Gerotina Mora E, Quandt Herrera E, Rabaza Gairí M, Brandi Tarrau N, Cortès Saladelafont E, Roche Martínez A, Armstrong Morón J (Spain) p. S14
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O44 - 1703	Deficiency of the E3 ubiquitin ligase TRIM2 causes early-onset axonal neuropathy Ylikallio E, Pöyhönen R, Hilander T, Paetau A, Lönnqvist T, Tyynismaa H (Finland) p. S14
O45 - 1612	RATE: randomised clinical trial of rapamycin in children with tuberous sclerosis complex and intractable epilepsy Overwater IE, Rietman A, Bindels-de Heus GCB, Moll HA, Elgersma Y, Wit MCY (The Netherlands) p. S14
O46 - 1548	Long term follow-up of clinical and neurographical abnormalities in eight Croatian patients with triple A syndrome Barisic N, Dumic M, Kusec V, Lehman I, Bunoza B, Grdjan P, Ivanja V (Croatia) p. S15
O47 - 1530	Outcome of surgical treatment of 64 TSC-associated subependymal giant cell astrocytomas Kotulska K, Roszkowski M, Mandera M, Daszkiewicz P, Grajkowska W, Jurkiewicz E, Borkowska J, Jozwiak S (Poland) p. S15
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O49 - 2118	A clinical advisory board for a rare disease (Prader-Willi syndrome) Blichfeldt S, Farholt S (Denmark) p. S16

O50 - 1933	Normative data of the 6-minute walk test in healthy boys aged 5–12 years and correlations with anthropometric variables and myometry Goemans N, Klingels K, Boons S, Verstraete L, Peeters C, van den Hauwe M, Feys H, Buyse G (Belgium)	p. S16
O51 - 2115	Clinical presentation and genetic causes of Charcot Marie Tooth disease in a paediatric cohort Niermeijer JMF, Rustenburg L, Van Ruissen F, Verhamme C, Baas F, Poll-The BT (The Netherlands)	p. S16
O52 - 2063	Spectrum of cerebellar and anterior horn cell degeneration caused by EXOSC3 mutations Burglen L, Nguyen S, Cances C, Cuisset JM, Julia S, Metreau J, Lion-François L, Legall A, Amsallem D, Gelot A, Billette de Villemeur T, Rodriguez D (France)	p. S17
O53 - 1995	Long-term outcome after vegetative state due to near-drowning and quality of life of the families Kluger G, Kirsch A, Hessenauer M, Lahl O, Steinbeis von Stülpnagel C (Germany)	p. S17
O54 - 1853	Manifestations of Cowden syndrome in childhood Schieving JH, Padberg GWAM, Willemsen MAAP (The Netherlands)	p. S17
O55 - 1566	Incidental white matter lesions in children presenting with headache Bayram E, Topcu Y, Karaoglu P, Yis U, Cakmakci HG, Hiz SK (Turkey)	p. S17
O56 - 1721	The role of probabilistic tractography in the surgical treatment of pediatric brainstem gliomas Máté A, Kis D, Vörös E, Barzó P (Hungary)	p. S18
12:30–13:30	Lunch and lunch symposia	
	Lunch symposium Biomarin	Copper Room
	Lunch symposium Novartis	Silver Room
	Lunch symposium EISAI Europe	Gold Room

Friday, 27 September 2013

07:30–08:15 Early Rise sessions 7–9	
ERS 7	Functional brain imaging – Xavier De Tiège, Margot Taylor
ERS 8	Advances in genetic diagnosis – Anna-Elina Lehesjoki, Jeroen Breckpot
ERS 9	Sleep disorders – Patrick Van Bogaert, Sonja Scaillet
08:30–10:00 Plenary session 4: Auto-immune disorders Gold Room	
<i>Chairs: Marc Tardieu and Colin Kennedy</i>	
IL 18	Auto-immune encephalitis – Joseph Dalmau
IL 19	Auto-immune CNS disorders in primary immune deficiencies – Banu Anlar
IL 20	The spectrum of anti-myelin oligodendrocyte glycoprotein antibody associated demyelinating diseases in children – Kevin Rostasy
10:00–10:30 Coffee Break and poster viewing	
10:30–12:15 Parallel session 10: Movement disorders 2	
<i>Chairs: Mary King and Sameer Zuberi</i>	
IL 21	Mary King
IL 22	Sameer Zuberi
O57 - 1880	Progressive ataxia, hyperkinetic movement disorder with myoclonic jerks and falls in a toddler: think of cerebral folate deficiency!
	Toelle SP, Wille D, Schmitt B, Scheer I, Thöny B, Plecko B (Switzerland) p. S18
O58 - 2017	Gabapentin can improve dystonia severity, transfers, sitting, sleep, mood and pain in children
	Liow N, Marianczak J, Kirk E, Tomlin S, Lumsden D, Gimeno H, Kaminska M, Perides S, Lin JP (UK) p. S18
O59 - 1906	Alternating hemiplegia and ATP1A3 gene: evolution of 12 cases into adulthood. Genotype–Phenotype correlations
	Ramirez-Camacho A, Panagiotakaki E, Poncelin D, Nicole S, Lesca G, Arzimanoglou A (France) p. S19
O60 - 1707	Ataxia and areflexia precede progressive myoclonus ataxia in young children with GOSR2 mutation
	van Egmond ME, Verschuuren-Bemelmans CC, Nibbeling EA, Elting JW, Sival DA, Brouwer OF, de Vries JJ, Kremer HP, Sinke RJ, Tijssen MA, de Koning TJ (The Netherlands) p. S19
O61 - 1802	Tyrosine hydroxylase deficiency. The Greek experience
	Pons R, Syrengelas D, Gkika A, Dinopoulos A, Orfanou I, Serrano M, Artuch R, Youroukos S (Greece) p. S19
10:30–12:15 Parallel session 11: Neurometabolic disorders	
<i>Chairs: Rudy Van Coster and Marjo van der Knaap</i>	
O62 - 1673	The natural history of late infantile CLN2 disease: striking homogeneity of clinical progression in two independently obtained large clinical cohorts
	Schulz A, Nickel M, Downs M, Mezey J, Landy H, Sondhi D, Jacoby D, Wittes J, Crystal R, Kohlschütter A (Germany) p. S20
O63 - 1788	Diagnosing the tip of an iceberg in a potentially treatable neurometabolic disorder: cerebral creatine deficiency syndromes
	Haliloglu G, Oguz KK, Onol S, Tokatli A, Coskun T, Topcu M (Turkey) p. S20
O64 - 1920	Zellweger spectrum manifestations in adulthood
	Berendse K, Engelen M, Wanders RJA, Waterham HR (The Netherlands) p. S20
O65 - 1997	Hematopoietic stem cell transplantation in juvenile metachromatic leukodystrophy
	Groeschel S, Bley A, Kühl JS, Kehrer C, Müller I, Kohlschütter A, Weschke B, Krägeloh-Mann I (Germany) p. S21
O66 - 1608	Hypomyelination and congenital cataract: three additional patients carrying novel mutations
	Biancheri R, Traverso M, Rossi A, Gazzero E, Assereto S, Baldassari S, Fruscione F, Abdalla EM, Fassad MR, Ruffinazzi G, Savasta S, Zara F, Minetti C (Italy) p. S21
O67 - 2165	Phenotypical variation in vanishing white matter disease
	van der Lei HDW, Gerver JAM, van Berkel CGM, van der Knaap MS (The Netherlands) p. S21
O68 - 2091	Neurological phenotypes in Niemann-Pick type C disease: unraveling an overlooked neurometabolic disorder
	Lourenço CM, Van der Linden V, Bonfim D, Ribeiro E, Marques Jr W (Brazil) p. S21
O69 - 1973	MRI in the diagnosis of peroxisomal disorders when laboratory tests fail
	van der Knaap MS, Ferdinandusse S, Vanderver A (The Netherlands) p. S22
O70 - 1720	Brain volumetry and clinical scoring in patients with CLN2 disease: a diagnostic tool to monitor disease progression
	Löbel U, Nickel M, Nestrasil I, Sedlacik J, Kohlschütter A, Schulz A (Germany) p. S22

O71 - 2078	Brain gene therapy for metachromatic leukodystrophy Sevin C, Roujeau T, Piguët F, Sondhi D, Colle MA, Raoul S, Deschamps JY, Bouquet C (France)	p. S22
10:30–12:15	Parallel session 12: Fetal and neonatal neurology Chairs: Marc D'Hooghe and Linda De Vries	
O72 - 1702	Concordance between head circumference growth and neurological impairment among four clinical presentations of microcephaly Coronado R, Giraldo J, Macaya A, Roig M (Spain)	p. S23
O73 - 1935	SBA and control muscle ultrasound density from pre- to postnatal life Verbeek RJ, Sollie KM, Mulder PB, van der Hoeven JH, Hoving EW, Sentner CP, Sival DA (The Netherlands)	p. S23
O74 - 2025	Benefits of universal newborn screening for permanent childhood hearing impairment to reading comprehension in adolescence: early confirmation of deafness matters Kennedy CR, Pimperton H, Chorooglou M, Kreppner J, Mahon H, Powers SG, Peacock J, Stevenson JE, Terleksi M, Worsfold SM, Yuen HM (UK)	p. S23
O75 - 1987	Specific impairment of functional connectivity between language regions in former early preterms Wilke M, Hauser T-K, Krägeloh-Mann I, Lidzba K (Germany)	p. S23
O76 - 1901	Neurodevelopmental outcomes of newborns requiring a brain MRI: a retrospective study Papandreou A, Poulton C, Kermod R, Ramesh CA (UK)	p. S24
O77 - 1605	Thrombophilic genes polymorphisms in children with perinatal brain injury Baranov DA, Lvova OA, Kuznetsov NN, Kovtun OP, Plaxina AN, Kolmogortseva VD (Russia)	p. S24
O78 - 1870	Neuro-imaging and neurodevelopmental outcome in preterm infants with a periventricular haemorrhagic infarction located in the temporal and frontal lobe Soltirovska Salamon A, Groenendaal F, Van Haastert IC, Rademaker CM, Benders MJ, Koopman-Esseboom C, de Vries L (The Netherlands)	p. S24
O79 - 1599	Prognostic value of conventional EEG in asphyxiated term newborns treated with hypothermia: experience in 20 cases Aeby A, Khabbache K, Van Overmeire B, Vermeylen D, Van Bogaert P (Belgium)	p. S25
O80 - 1570	Cognitive outcome in childhood following unilateral perinatal brain injury van der Aa NE, van Buuren LM, Dekker HC, Vermeulen RJ, van Nieuwenhuizen O, van Schooneveld MMJ, de Vries LS (The Netherlands)	p. S25
12:30–13:30	Lunch and lunch symposia	
	Lunch symposium Cyberonics	Copper Room
	Lunch symposium Actelion	Silver Room
13:30–14:30	Selected poster presentations 5–8	
PP5	Varia (sleep, oncology, trauma) – Chair: Richard Newton	p. S41
PP6	Neurogenetic and mitochondrial disorders – Chair: Haiki Rantala	p. S44
PP7	Epilepsy 2 – Chair: John Stephenson	p. S47
PP8	Learning disorders/Immunology – Chair: Günter Bernert	p. S50
13:30–14:30	Round table on sulthiame in childhood epilepsy Chair: T. Lerman-Sagie	Silver Room
14:30–16:00	Plenary session 5: Treatment of neurometabolic disorders Chairs: Barbara Plecko and Linda De Meirleir	Gold Room
	<i>Session dedicated to Gilles Lyon</i>	
IL 23	Treatment of the monoamine neurotransmitter disorders – Manju Kurian	
IL 24	Treatment of mitochondrial diseases – Ingrid Tein	
IL 25	Treatment of neurodegeneration with brain iron accumulation (NBIA) – Susan Hayflick	
16:00–16:30	Coffee break and poster viewing	
16:30–18:15	Parallel session 13: Combined EPNS/ICNA session Chairs: Pratibha Singhi and Sergio Rosemberg	
IL 26	HIV and paediatric neurology – Jo Wilmshurst	
IL 27	Malaria and paediatric neurology – Charles Newton	
IL 28	Paediatric neurology in Africa – Michael Boele van Hensbroek	

16:30–18:15	Parallel session 14: Learning disabilities, ADHD and autism <i>Chairs: Patrick Berquin and Sergiusz Jozwiak</i>	
O81 - 1871	Motor cortical inhibition in ADHD: modulation of the transcranial magnetic stimulation-evoked N100 during a go/nogo task D'Agati E, Hoegl T, Dippel G, Curatolo P, Bender S, Kratz O, Moll GH, Heinrich H (Italy)	p. S25
O82 - 1582	Preliminary data on the use of cigarettes, alcohol and drugs in a follow-up study of adolescents with Tourette syndrome Groth C, Debes N, Skov L (Denmark)	p. S26
O83 - 2038	Do rolandic spikes on EEG at ADHD assessment influence on ADHD subtype and the use of methylphenidate for ADHD? Socanski D, Herigstad A (Norway)	p. S26
O84 - 1965	Improving motor learning in a rat model of ADHD Soderlund GBW, Bergquist F (Norway)	p. S26
O85 - 1992	Cortico-vocal coherence in autism spectrum disorders Suarez Garcia S, Clumeck C, Bourguignon M, Wens V, Op de Beeck M, Marty B, Soncarrieu M, Deconinck N, Delvenne V, Goldman S, Van Bogaert P, De Tiège X (Belgium)	p. S26
O86 - 1830	Cognitive functions in school-children with frontal or temporal epilepsy – long term study Mazurkiewicz-Beldzinska M, Kondracka J, Szmuda M, Matheisel A (Poland)	p. S27
O87 - 1771	Long-term simvastatin treatment for cognition and daily life in children with neurofibromatosis type 1: results from the NF1-SIMCODA trial van der Vaart T, Plasschaert E, Rietman AB, Renard M, Oostenbrink R, Vogels A, de Wit MC, Descheemaeker MJ, Vergouwe Y, Catsman-Berrevuets CE, Legius E, Elgersma Y, Moll HA (The Netherlands)	p. S27
O88 - 1682	Effects of methylphenidate on functional networks activation in children with attention deficit hyperactivity disorder Berquin P, Querne L, Service de Fall S, Delignieres A, Simonnot A, Le Moing A-G (France)	p. S27
O89 - 1600	Language development at 2 years is correlated to brain microstructure in the left superior temporal gyrus at term equivalent age: a diffusion tensor imaging study Aeby A, De Tiège X, David P, Balériaux D, Van Overmeire B, Metens T, Van Bogaert P (Belgium)	p. S28
16:30–18:15	Parallel session 15: Epilepsy <i>Chairs: Sameer Zuberi and Oebele Brouwer</i>	
O90 - 2157	Treatment of electrical status epilepticus in sleep (ESES): a systematic review and meta-analysis Van den Munckhof B, Van Dee V, Liukkonen E, Sagi L, Loddenkemper T, Sánchez Fernández I, Braun KPJ, Jansen FE (The Netherlands)	p. S28
O91 - 1581	Compensatory visual system adaptations after hemispherectomy in children Koenraads Y, van der Linden DCP, van Schooneveld MMJ, Imhof SM, Porro GL, Braun KPJ (The Netherlands)	p. S28
O92 - 2108	The classification of epilepsies using the ILAE revised terminology and concepts for organization of seizures and epilepsies and ICD-10 – challenges in clinical practice Iliescu C, Barca D, Budisteanu M, Burloiu C, Butoianu N, Minciu I, Motoescu C, Tarta-Arsene O, Craiu D (Romania)	p. S28
O93 - 2003	Different aspects in the evaluation of vagus nerve stimulation efficacy among children with therapy-refractory epilepsy Orosz I, Buck E, Sperner J, Thyen U (Germany)	p. S29
O94 - 1758	Cardiac and respiratory autonomic dysfunction in childhood epilepsy Jansen K, Varon C, Van Huffel S, Lagae L (Belgium)	p. S29
O95 - 1739	Severe myoclonic epilepsy in infancy: clinical and neuropsychological analysis according to age at diagnosis of SMEI El M'Kaddem B, Christiaens F, van Rijckevorsel F, Nassogne MC (Belgium)	p. S29
O96 - 1638	Electrical status epilepticus in sleep (ESES): etiology, clinical picture and course Aleksandrova I, Bojinova V, Dimova P (Bulgaria)	p. S30
O97 - 1635	Treatment of electrical status epilepticus in sleep (ESES): efficacy and unsolved questions Dimova P, Alexandrova I, Bojinova V (Bulgaria)	p. S30
O98 - 1979	Intravenous methylprednisolone for the treatment of infantile spasms Aburahma A, Al-Sharqawi S (Jordan)	p. S30
18:15–19:00	Meet the Expert sessions <i>Sessions where delegates can meet experts to ask advice on specific cases</i>	
	Movement disorders – Emilio Alvarez Fernandez	
	Epilepsy – Alexis Arzimanoglou	
	Hereditary polyneuropathies – Peter De Jonghe	

Saturday, 28 September 2013

08:30–09:00	General Assembly EPNS	Gold Room
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09:00–11:00	Special symposium: The future of paediatric neurology <i>Chairs: Florian Heinen and Peter Baxter</i>	Gold Room
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IL 29	Gene therapy strategies for genetic leucodystrophies – <i>Nathalie Cartier-Lacave</i>
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IL 30	Stem cell therapy in paediatric neurology – <i>Pierre Vanderhaegen</i>
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IL 31	Closed loop treatment systems in epilepsy – <i>Lieven Lagae</i>
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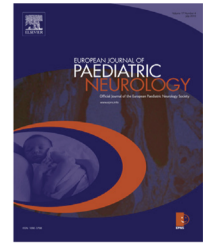
IL 32	Diagnostics in new white matter diseases – <i>Marjo van der Knaap</i>
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11:00–12:00	Highlights in Paediatric Neurology organized by the EPNS board
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Closing ceremony



Official Journal of the European Paediatric Neurology Society



Abstracts of of EPNS 2013 – 10th European Paediatric Neurology Society Congress, 25–28 September 2013, Brussels, Belgium

ORAL PRESENTATIONS

Wednesday 25 September 2013

Parallel session 1: Movement disorders 1

Chairs: Michèl Willemsen and Emilio Alvarez Fernandez

O1 - 1990

Clinical spectrum of dopamine transporter deficiency syndrome: from infantile parkinsonism-dystonia to juvenile parkinsonism

Ng J, Li Y, Zhen J, Kakar N, Ahmad J, Thiele H, Kubisch C, Rider N, Strauss K, Holmes-Morton D, D'Agnano D, Anikster Y, Carducci C, Hyland K, Rostein M, Leuzzi V, Borck G, Reith MEA, Kurian MA. *Neurosciences, Institute Child Health-UCL, UK* – j.ng@ucl.ac.uk

Objective: Dopamine transporter deficiency syndrome (DTDS) is a newly described neurotransmitter disorder that presents with progressive infantile onset parkinsonism-dystonia [1]. It is characterized by raised CSF homovanillic acid: 5-hydroxyindoleacetic acid (HVA: HIAA) ratio of >5.0 . It is caused by pathogenic mutations in SLC6A3 that encodes for the dopamine transporter (DAT). In order to better define this disorder, we describe new clinical phenotypes, novel genotypes and in vitro functional studies in a new cohort of DTDS patients. **Methods:** Patients presenting with parkinsonism and/or dystonia associated with a raised CSF HVA: HIAA were identified. SLC6A3 mutational analysis was performed, with in vitro functional studies of all identified missense mutations. **Results:** Eight patients were identified (5 males) from 5 unrelated families. Four presented with a progressive movement disorder from childhood but four presented with a juvenile parkinsonian phenotype and prominent tremor (currently aged 16–34 years). The diagnosis was delayed in all cases (range 0.5–33 years) post-onset of symptoms. Mutation screening of SLC6A3 revealed novel, previously unreported mutations in all patients (missense and splice site mutations). In vitro functional studies demonstrated that mutant DAT showed reduced dopamine uptake with reduced dopamine binding affinity, surface binding and substrate recognition. Immunoblotting studies implicate absent/impaired glycosylation of DAT and abnormal trafficking of DAT in DTDS. **Conclusion:** We report a cohort of patients with the classical features of DTDS [1] as well as identification of new DTDS patients with features of juvenile parkinsonism, thereby expanding the clinical disease phenotype. Functional analysis of mutant DAT implicates trafficking defects as a novel disease mechanism in DTDS. As a “cerebral palsy mimic”, we conclude that DTDS remains under-recognised and misdiagnosed,

leading to delayed diagnosis. The identification of adult DTDS patients suggests that neurotransmitter analysis and SLC6A3 testing should be considered in the neurological investigation of juvenile parkinsonism phenotypes. **Reference:** 1. Kurian MA. *Lancet Neurol.* 2011;19(1):54–62

O2 - 2122

Dystonia in previously well children – two years experience in a UK tertiary centre

Pathak D, Whitney A, Forrest K, Kirkham F. *University Hospitals Southampton, UK* – dbnrnphthk@gmail.com

Objectives: To report the results of investigation for acute dystonia and increase awareness of the possibility of anti-NMDA encephalitis. **Material and methods:** The index case was a 4 year old child of Chinese origin who had recently moved from Hong Kong and presented with acute onset gait abnormality with falls and dystonic and choreiform movements. Few days later he developed mood swings and behavioural problems. There was no recent history of intercurrent illness. We audited 18 other cases of acute dystonia in previously well children who presented during 2011–12. **Results:** The index case had normal inflammatory markers including ESR, ASOT, anti DNase B and ANA. T2-weighted MRI brain was normal. His blood was positive for anti- NMDA antibody while his identical twin brother, who had no movement disorder, was negative. He was treated with five days high dose Methyl Prednisolone followed by weaning course of Oral Prednisolone over four weeks. This resulted in resolution of his abnormal movements completely. His behaviour is improving. Of the 18 children with acute dystonia, 9 were girls. Median age was 13 (range 1–16) years; Five (27%) had abnormal MRI in the form of high signal focus in caudate nucleus, Labrune Syndrome, high signal in both parietal lobes of uncertain significance, mild cerebral atrophy and iron deposition in basal ganglia. One had dopa-responsive dystonia, one had previously diagnosed ADEM and another had non-kinesogenic paroxysmal dyskinesia. Of 5 who had anti-Streptococcal antibodies, 3 had high anti- DNase titre (>400). Three were tested for anti NMDA antibody; all were negative. Ten (55%) underwent genetic testing but no diagnoses have yet been made although 3 have family history. **Conclusion:** Acute dystonia in previously well children is common in Neurology practice. It is important to diagnose treatable causes including NMDA encephalitis and Dopa- responsive dystonia, as well as recognizing rare genetic forms.

O3 - 2102

GLUT1 deficiency syndrome from infancy into adulthood: a follow-up study

Leen WG, Taher M, Mewasingh LD, Willemsen M. *Department of Neurology, Radboud University Medical Centre, Donders Institute for Brain, Cognition and Behaviour, Nijmegen, The Netherlands – w.leen@neuro.umcn.nl*

Background: GLUT1 deficiency syndrome (GLUT1DS) is a treatable neurometabolic disorder in which glucose transport into the brain is disturbed. Since the disorder is known for only two decades, little is known about the prognosis of GLUT1DS. **Objective:** Our purpose was to investigate the evolution of symptoms in patients with the classical, complex phenotype of GLUT1DS from infancy into adulthood. **Methods:** We have performed a systematic literature review as well as a cohort study, including adult GLUT1DS patients with a complex phenotype (aged 18 years and older). **Results:** The literature search yielded a total of 86 adult GLUT1DS patients of which 26 patients (30%) with a complex phenotype. Seven GLUT1DS patients with a complex phenotype were prospectively followed in our clinic from childhood into adulthood. In general, epilepsy was a prominent feature during infancy and childhood. During adolescence, however, epilepsy diminished or even disappeared, but new paroxysmal movement disorders such as paroxysmal exercise-induced dyskinesia appeared. These paroxysmal movement disorders responded well to the modified Atkins diet (video). **Conclusion:** In general, in patients with a complex phenotype of GLUT1DS variation of symptoms over time is seen, with epilepsy as the most disabling symptom during childhood and movement disorders during adolescence or early adulthood. The modified Atkins diet is a good alternative for the ketogenic diet for the treatment of GLUT1DS related paroxysmal movement disorders in adolescents and adults.

O4 - 2020

Electroneuromyography parameters in hereditary and congenital ataxia

Milic Rasic V, Brankovic V, Mladenovic J, Kosac A, Todorovic S. *Clinic for Neurology and Psychiatry for Children and Youth, Medical Faculty, University of Belgrade, Belgrade, Serbia – vedrana.milic.npk@gmail.com*

Introduction: Early onset hereditary (HA) and congenital ataxia (CA) are heterogeneous group of disorders. Associated non-cerebellar signs (pyramidal, extrapyramidal, cognitive, ocular, neuropathy) could be a clue in differentiating subtypes of HA and CA. **Objectives:** To examine the value of electroneuromyography (ENMG) studies in the diagnostic protocol of early onset ataxia subtypes. **Material and methods:** ENMG was performed in 40 patients (F:22; M:18) who were diagnosed (Friedreich ataxia 16; other subtypes of HA: 14 and CA: 10) at the Clinic for neurology and psychiatry for children and youth from 2002 to 2012. ENMG was performed on the Premier (Medelec) apparatus according to protocols DeLisa (2005). We analyzed amplitude of SNAP, SCV, motor TL, amplitude of CMAP and MCV in all patients, and needle EMG test in patients with abnormal motor conduction study. The mean duration of the disease at the ENMG test was 5.8 ± 6.8 (0.5 – 27yr). SARA scale was used for determining score of cerebellar dysfunction. Molecular genetic tests: PCR for dynamic mutation and the direct sequencing in SACS and ANO10 genes were performed. **Results:** Neuropathy was detected in 25 (62.5%) patients. All patients with Friedreich ataxia (FA) had neuropathy, which was statistically significant with the other tested group ($p < 0.001$). 50% patients (7/14) of non-Friedreich HA and 20% of CA patients had a neuropathy, without statistically significant difference between them. Demyelinating neuropathy did not exist in any group. The most frequent subtype was sensory axonal

neuropathy (almost all FA pt). Motor axonal neuropathy was present in 4 patients- 3 of them with ANO10 mutation. Sensory and motor axonal neuropathy was detected in 4 patients (two with define genotype- SACS and ATXN2 gene mutations). **Conclusion:** ENMG could be useful test in planning genetic study for hereditary and congenital ataxias, particularly in autosomal recessive forms.

Parallel session 2: Epileptic encephalopathies

Chairs: Raili Riikonen and Alec Aeby

O5 - 1819

Impaired slow wave sleep downscaling in infantile spasms with hypsarrhythmia

Fattinger S, Schmitt B, Bölsterli B, Critelli H, Jenni O, Huber R. *University Children's Hospital Zurich, Switzerland – sara.fattinger@lispi.uzh.ch*

The epileptic encephalopathy West Syndrome is characterized in the EEG by multifocal spike waves and high amplitude slow frequency activity (hypsarrhythmia), which is most pronounced during non-REM (NREM) sleep, and is often accompanied by developmental regression. The underlying pathophysiology of the encephalopathy is unknown and infantile spasms can be effectively treated with corticosteroids. In the epileptic encephalopathy ESES it was recently shown that the pathological changes in the sleep EEG impair sleep dependent renormalization of network synchronisation. In healthy individuals, neuronal synchronisation increases during the day, which is reflected in steep slow waves during initial NREM sleep, and decreases back to baseline level in the course of sleep. This renormalization of neuronal synchronicity is thought to be important for efficient learning the next day. We hypothesised that hypsarrhythmia may impair the renormalization of neuronal synchronicity in West Syndrome patients. We analysed retrospectively the overnight sleep EEG of 15 untreated patients (6 ± 2.4 months) with infantile spasms and hypsarrhythmia and two follow-up nap recordings (under and after treatment with corticosteroids). Data were compared to healthy age and gender matched controls. In patients the overnight decrease of the slope of slow waves was reduced ($p < .05$) resulting in significantly steeper slope of slow waves towards the end of the night ($p < .001$). During the nap, under treatment the slope of slow waves was significantly reduced in patients compared to controls ($p < .05$). However, after the treatment period the slope was similar between patients and controls. In conclusion, our results show evidence for an impaired overnight reduction of neuronal synchronisation in West Syndrome patients. Such impaired sleep dependent renormalization of network synchronization may contribute to the developmental regression seen in these patients. Moreover, treatment with corticosteroids leads to a pronounced reduction of neuronal synchronicity, which might contribute to a normalization of network synchronization after treatment.

O6 - 2105

KCNT1 mutations in a national cohort of children with migrating partial seizures of infancy

McTague A, Meyer E, Appleton RE, Lascelles K, Desurkar A, Kneen R, Kurian MA. *Neurosciences Unit UCL, London, UK – a.mctague@ucl.ac.uk*

Objectives: Migrating partial seizures of infancy (MPSI) is a severe, early onset epileptic encephalopathy characterised by frequent and intractable focal seizures and developmental delay. KCNT1 encodes a sodium activated potassium channel and is a recently

described cause of MPSI.1 We evaluated our UK cohort of MPSI patients for mutations in KCNT1. **Material and methods:** Patients were recruited via a national surveillance study and detailed phenotyping was performed to delineate clinical, EEG, radiological and pathological features. A combined strategy of whole exome sequencing (Illumina paired-end library preparation and sequencing on a Hi-Seq platform) and direct Sanger sequencing was employed for molecular genetic investigation. For Sanger sequencing, the genomic KCNT1 DNA sequence was taken from Ensembl and primer pairs for all exons and flanking intronic regions were designed using primer3 software. Exons were amplified by PCR, sequenced by the BigDye terminator method and analysed with Chromas/Sequencher software. **Results:** Fourteen patients met the electroclinical criteria for a diagnosis of MPSI. Two different missense mutations were identified in 30% of patients tested. One mutation (c.2800G>A, p.A934T) was found in several patients and has been previously reported.¹ Another mutation (c.811G>T, p.V271F) is a novel, previously unreported variant. These mutations are not seen in 1000 Genomes or other databases of genetic variation. Amino acid residues affected by these variants were highly conserved throughout species. **Conclusions:** KCNT1 is a significant disease-causing gene in MPSI. However as we have demonstrated, this condition is genetically heterogeneous and further genetic aetiologies are yet to be discovered. Given the genetic heterogeneity of EIEE, the phenotypic spectrum of KCNT1 is likely to extend beyond this specific electroclinical syndrome. **Reference:** 1. Barcia G, Fleming MR, Delignières A, Gazula VR, Brown MR, Nabbout R, et al. De novo gain-of-function KCNT1 channel mutations cause malignant migrating partial seizures of infancy. *Nat Genet* 2012; 44: 1255–9.

O7 - 2139

Epilepsy and PCDH19 mutation: electrophysiological features

Chemaly N, Kaminska A, Chiron C, An I, Pinard JM, Gauthier A, Arbués AS, Dulac O, Nabbout R. *Neuropediatrics department, Centre de référence des épilepsies rares, Necker Enfants Malades Hospital, Paris, France* – nicola.chemaly@nck.aphp.fr

PCDH19 mutations were first described in female patients affected with epilepsy with mental retardation. Clinical phenotype associated with PCDH19 mutations is considered to be a Dravet like syndrome. The aim of this study was to better characterize the electrophysiological characteristics of patients with positive PCDH19 mutation. 13 patients aged from 4 to 24 years at the time of the study with PCDH19 mutations were included. Longitudinal EEG videos were retrospectively reviewed (ictal and interictal). Interictal video EEGs recorded during cluster of seizure showed a slowed background activity for age in all patients, with focal slow waves and spike waves, predominantly frontal or temporal in 11 patients. On the EEG recordings of 2 patients at 4 and 9 months, we registered periodic generalized discharges of slow waves and fast rhythmic activity without any clinical seizure. Interictal EEG recorded during seizure free periods showed normal or slightly slowed background activity in 7 patients, and the persistence in 6 patients of abnormalities which consisted of slowed activity in central regions (2/6), focal spikes (2/6), or generalized spike wave discharges (2/6). Ictal video EEG recorded showed in 3 patients frontal temporal initiation of seizure. One patient presented with atypical absences associated with myoclonus with generalized abnormalities on the EEG that were persistent during follow up. In patients with PCDH19 mutations, based on the clinical presentation, differential diagnosis includes i) Dravet syndrome because of fever sensitivity and frequent seizures events and ii) focal epilepsy due to the type of seizures. The combination of focal abnormalities with global alteration of the background activity on the EEG helps in the early identification of these patients, altogether with the clinical presentation, allowing an earlier molecular diagnosis.

O8 - 2053

Epileptic spasms beyond infancy. Is LOES more than a description?

Schoonjans A, Kenis S, Verhaert K, Van de Vel A, Ceulemans B. *Antwerp University Hospital, Belgium* – an-sofie.schoonjans@telenet.be

Objective: Epileptic spasms (ES) are defined as clinical spasms associated with epileptic activity on the electroencephalogram (EEG). Although epileptic spasms are usually associated with West syndrome, they can also be seen in association with other epilepsy syndromes. Late-onset epileptic spasms (LOES) are epileptic spasms starting after the first year of life. The aim of this study was to determine whether this condition represents a variant of the classic West syndrome, a precursor of the Lennox-Gastaut syndrome or a specific age related epileptic encephalopathy. **Method:** We retrospectively reviewed the files of children who presented, between 1990 and 2012, with epileptic spasms after the age of 12 months. **Results:** We report 10 patients (7 male/3 female) with LOES followed at our pediatric neurology department. The mean age at onset of the epileptic spasms was 18.8 months (SD 5.0m). Four patients showed a normal development until the appearance of the ES. The etiology of those 4 patients was defined as cryptogenic. Interictal EEG showed hypsarrhythmia in 3/10 patients, modified hypsarrhythmia in 3/10 and focal epileptic activity in 2/10 patients. The ES were successfully treated in 7 patients after a mean duration of 9.9 months (SD 6.7m). Nevertheless only 3 out of those 7 patients persisted to be seizure free. The 3 patients for whom the ES could not be treated were cryptogenic and showed an evolution towards the Lennox-Gastaut syndrome. Overall the outcome was poor with severe neurocognitive impairment in all except one patient. **Conclusion:** LOES are epileptic spasms starting beyond infancy. We hypothesize that in children with a cryptogenic etiology LOES is an epileptic encephalopathy which positions itself between the West syndrome and the Lennox-Gastaut syndrome. In children with a symptomatic etiology LOES is the expression of a secondary epileptic encephalopathy starting after the age of one year.

O9 - 2019

Similar early characteristics but variable neurological outcome of patients with a de novo mutation of KCNQ2

Milh M, Boutry-Kryza N, Suter-Sardo J, Mignot C, Auvin S, Villeneuve N, Roubertie A, Héron B, Kaminska A, Altuzara C, Blanchard G, Ville D, Barthez H, Héron D, Afenjar A, Dorison N, Billette de Villemeur T, Vercueil L, Perrier J, Lesca G, Villard L. *Marseille, France* – mathieu.milh@ap-hm.fr

Background: Early onset epileptic encephalopathies (EOEEs) are dramatic heterogeneous conditions in which aetiology, seizures and/or interictal EEG have a negative impact on neurological development. Several genes have been associated with EOEE and a molecular diagnosis workup is challenging since similar phenotypes are associated with mutations in different genes and since mutations in one given gene can be associated with very different phenotypes. Recently, de novo mutations in KCNQ2, have been found mutated in about 10% of EOEE patients. Our objective was to confirm that KCNQ2 was an important gene to include in the diagnosis workup of EOEEs and to fully describe the clinical and EEG features of mutated patients. **Methods:** We have screened KCNQ2 in a cohort of 71 patients with an EOEE. To be included in the cohort, patient's epilepsy should begin before three months of age and be associated with abnormal interictal EEG and neurological impairment. Brain MRI should not show any structural abnormality. **Results:** Out of those 71 patients, 16 had a de novo mutation in KCNQ2 (23%). Interestingly, in the majority of the cases, the initial epileptic features of these patients were comparable to those previously described in the case of be-

nign familial neonatal convulsions (BFNS) also caused by KCNQ2 mutations. However, the interictal background EEG was altered and displayed multifocal spikes or a suppression-burst pattern. The ongoing epilepsy and development were highly variable but overall severe: 15/16 had obvious cognitive impairment, half of the patients became seizure-free, 5/16 could walk before the age of 3 and only 2/16 patient acquired the ability to speak. **Conclusion:** This study confirms that KCNQ2 is frequently mutated in neonatal onset epileptic encephalopathy. We show here that despite a relatively stereotyped beginning of the condition, the evolution is highly variable in terms of epilepsy and of cognitive evolution.

O10 - 1986

Effective use of low dose of rufinamide after an initial worsening effect in Lennox-Gastaut patients

Corny J, Papon A, Bellavoine V, Storme T, Merdarius D, Ilea A, Bourdon O, Auvin S. *Pediatric Neurology & Pharmacy Departments, Robert Debré University Hospital, Paris, France – auvin@invivo.edu*

Rufinamide is a new antiepileptic drug that has been approved for Lennox-Gastaut syndrome (LGS). Rufinamide is usually initiated at 10mg/kg/day, followed by a titration of 10mg/kg/day every two days, until a maintenance dose of 45mg/kg/day. We conducted a retrospective study in the epilepsy unit of Robert-Debré Children University Hospital, Paris, France. We identified 22 patients treated with rufinamide for at least three months (January 2010–December 2012): n=10 LGS, n=6 infantile spasms and n=4 epileptic encephalopathy including tonic seizures. The patient with a decrease of 50% at least of the seizure frequency was defined as responder. Responder rate was 78.9% (19 patients). Our data showed that we did a slow titration (mean titration duration = 13.5 weeks). Initiation doses used were lower than the recommended dose (mean dose: 3.6 mg/kg/day). Regarding the responders, the mean maintenance dose was 10.5 mg/kg/day (3–27 mg/kg/day): 7.9 mg/kg/day for LGS patients and 13.5 mg/kg/day for other epileptic syndromes. All responders had other concomitant AEDs, and 100% of responders had concomitant VPA treatment (mean dose = 26.4 mg/kg/day). During the titration, 10/15 patients were aggravated at the mean dose of 13.2 mg/kg/day (5–25 mg/kg/day): 11.9 mg/kg/day for LGS patients and 16.5 mg/kg/day for other epileptic syndromes patients. No worsening of the seizure frequency was observed among the non-responders group. All patients that experienced a worsening regain the positive effect on seizure frequency with the down titration. Rufinamide was effective in most of the patients. We observed an efficacy with a low dose of rufinamide. Surprisingly, 10/15 experienced an increase of seizure frequency during the up-titration period after they have had a decrease of the seizure frequency. The efficacy of rufinamide was then observed with the use of a lower dose. Rufinamide was well tolerated.

O11 - 1866

Successful use of Fenfluramine as add-on treatment in Dravet syndrome: a two year prospective follow up

Ceulemans B, Neels P, Boel M, Jorens P, Lagae L. *Epilepsy Center for children and Youth, Pulderbos, Belgium – berten.ceulemans@uza.be*

Objective: Long term effect of fenfluramine as an add-on antiepileptic drug treatment in Dravet syndrome. **Methods:** In 2012 we published the results of 12 patients with Dravet syndrome treated with fenfluramine as add-on anti-epileptic drug. 7 were seizure free for at least 1 year. We now reviewed the results of the prospective follow up period (2011 and 2012) In this period, detailed seizure diaries were kept and cardiac evaluations were performed at least once a year. **Results:** Four out of 7 patients

remained completely seizure free for the next 2 years. In the other 3 patients only rare seizures were observed. One patient had 3 tonic-clonic seizures after tapering benzodiazepines in 2011 and 3 in a stress situation in 2012. One patient had one day of 4 tonic-clonic seizures in 2011 and 3 in 2012. He is now 6 months seizure free after increase of sodium valproate. The third patient had only 2 fever induced tonic-clonic seizures in 2011 and 1 in 2012. One patient had more than 75% seizure frequency reduction in 2010. The seizure frequency further diminished and she had only 4 tonic-clonic seizures in 2011 and 2 in 2012. From the two non-responding patients one still remains non-responder and the other one became seizure free for the last 6 months of 2012. Two new patients were started on fenfluramine. Both had more than 75% reduction with disappearance of status epilepticus and only sporadic tonic-clonic seizures. Seizure free periods were seen for 3 months in one child and 6 months in the other. We did not observe new cases of valvulopathy in this cohort. **Conclusion:** Also in this prospective follow up, the results of add-on fenfluramine as anti-epileptic drug in Dravet syndrome are very promising. No new cardiac side effects were seen.

O12 - 1838

CDKL5 mutations and antiepileptic drugs tolerability

Magalhães C, Carrilho I, Ribeiro A, Chorão R, Santos M. *Centro Hospitalar do Porto, Portugal – c-magalhaes@netcabo.pt*

Objectives: The phenotype of CDKL5 (cyclin-dependent kinase-like 5) gene mutations includes early-onset refractory epilepsy, severe psychomotor delay, autism and mild dysmorphic features. Our aim is to report our patients' clinical features and its response to antiepileptic drugs. **Material and methods:** From our database, we selected three patients with CDKL5 gene mutations, all from Northern Portugal. **Results:** We report three nonrelated girls aged eight, six and two years old. They all have severe developmental delay, autistic features and hypotonia. Epilepsy started within the first six months of life, with several types of seizures including spasms. Two are still refractory to treatment, while the other one was difficult to control for a period of time, but then had few seizures. Initial electroencephalographic records were normal, evolving to multifocal epileptiform activity with burst suppression. In all the girls several antiepileptic drugs with different mechanisms of action were used. They all presented severe side effects related to the drugs, such as marked sedation, hypotonia, and aggravation of epileptic seizures, even with lower doses and independently of the drugs. **Conclusions:** CDKL5 gene is known to be involved in brain development, but most of its functions are still unclear, as is the relationship with MECP2 (methyl-CpG-binding protein 2) gene. This disorder, previously known as atypical Rett syndrome, has its own characteristics, including epilepsy starting during the first year of life, severe motor and mental impairment and autism, with normal initial electroencephalograms evolving to severe epileptic encephalopathy patterns. The extreme sensibility to antiepileptic drugs, common to these patients, although not yet reported, may be an important feature of the disorder allowing earlier diagnosis.

O13 - 1691

High dose (4 mg/kg/day) versus usual dose (2 mg/kg/day oral prednisolone in the treatment of infantile spasms: a randomized open trial

Prabaharan C, Aneja S, Sharma S, Seth A. *Lady Hardinge Medical College, New Delhi, India – drprabac@gmail.com*

Objectives: Infantile spasms comprise a difficult-to-treat epileptic encephalopathy of young children. Effective treatment options include ACTH and vigabatrin, which are expensive in develop-

ing countries. Recent studies have shown good efficacy of high dose prednisolone. There are no studies comparing high versus usual dose prednisolone. Hence this study was planned to compare the efficacy and tolerability of high dose (4 mg/kg/day) versus usual dose (2mg/kg/day) oral prednisolone in the treatment of infantile spasms. **Material and methods:** Children aged 3 months to 2 years with infantile spasms and EEG evidence of hypsarrhythmia or its variants were randomized to receive either high dose (4mg/kg/day) or usual (2 mg/kg/day) dose prednisolone. Children with active tuberculosis and severe acute malnutrition were excluded. The primary outcome was cessation of spasm for at least 48 hours on day 14. The proportion of adverse effects in both the groups was also compared (Clinicaltrials.gov identifier NCT01575639). **Results:** Out of 63 children enrolled, 31 were in the high dose group, and 32 in the usual dose group. Spasm cessation at day 14 was significantly higher in the high dose group as compared to the usual dose group [16/31 (51.6%) versus 8/32 (25%), $p=0.03$]. The proportion of adverse effects such as weight gain, hypertension, irritability, and infections were comparable in both the groups. None of the patients required discontinuation of treatment for adverse effects. **Conclusion:** High dose prednisolone was found to be more efficacious in the treatment of infantile spasms as compared to usual dose prednisolone with a comparable safety profile.

Parallel session 3: Mitochondrial disorders

Chairs: Linda De Meirleir and Ingrid Tein

O14 - 1917

Hypomyelination with brain stem and spinal cord involvement and severe leg spasticity (HBSL): mutations in DARS are responsible

Wolf NI, van der Knaap MS, de Coe IFM, Vanderver A, Leventer RJ, Damiani S, Simons C, Juneja M, Verma IC, Prabhakar P, Blaser S, Raiman J, Abbink TEM, Taft R. *Department of Child Neurology, VU University Medical Center, Amsterdam, The Netherlands – n.wolf@vumc.nl*

Objective: To improve diagnosis in children with hypomyelination. **Patients and methods:** Four patients were identified with a novel hypomyelinating disorder using MRI pattern recognition. Whole exome sequencing (WES) was performed in two children and one parent. One additional patient with a comparable different MRI pattern underwent WES in an independent project. **Results:** MRI showed a homogeneous mildly increased T2 signal of the supratentorial white matter consistent with hypomyelination and in addition hyperintense T2 signal of the anterior brain stem, the superior and inferior cerebellar peduncles and the dorsal columns of the spinal cord over its entire extent. WES revealed homozygous and heterozygous missense mutations in DARS, coding for the cytoplasmic aspartyl tRNA synthetase. Five more patients with a similar MRI pattern were identified subsequently, all with mutations in DARS. One mutation, c.766A>C, was found in three unrelated families from India and Pakistan. Clinical symptoms started in the first year of life and included nystagmus and leg spasticity. Cognition was mildly impaired in the younger children. Two developed epilepsy. We called this disorder HBSL (hypomyelination with brain stem and spinal cord involvement and severe leg spasticity) to underline the MRI similarities with LBSL (leukoencephalopathy with brain stem and spinal cord involvement and elevated lactate) which is caused by mutations in DARS2, the mitochondrial counterpart of DARS. **Conclusions:** MRI pattern recognition is possible also in hypomyelinating disorders and allows identification of novel disorders. WES is able to pinpoint the genetic defect also in small groups of single patients. Mutations in DARS cause a hy-

pomyelinating white matter disorder, HBSL, with characteristic MRI changes.

O15 - 2036

Early onset mitochondrial encephalomyopathy with pulmonary hypertension due to [Fe-S] cluster deficiency

Abela L, Rohrbach M, Häberle J, Mayr H, Ahting U, Nuoffer JM, Scheer I, Bauer A, Hug M, Klauwer D, Plecko B. *Department of Child Neurology, Childrens Hospital, University of Zürich, Switzerland – lucia.abela@kispi.uzh.ch*

Introduction: Recently iron cluster [Fe-S]-synthesis defects have been recognized as one possible cause of combined respiratory chain defects. The [Fe-S]-cluster is needed for synthesis of lipoic acid, which serves as a cofactor in all respiratory chain complexes. **Patient:** we here describe a 33 GW preterm female infant of non- consanguineous parents with BW, BL and HC within 50th-75th PC. Neonatal feeding problems and recurrent bradycardia and apnea necessitated 4 weeks of hospitalization. She developed visual contact and social smile by 8 weeks of age. At age 10 weeks failure to thrive and severe apnea lead to readmission. Cardiac ultrasound revealed severe pulmonary hypertension. Cranial MRI showed diffuse leukodystrophic supra- and infratentorial changes with diffusion restriction on T2 weighted images. Plasma and CSF lactate were markedly increased and glycine levels in plasma and CSF were moderately increased. Biochemical analysis of a fresh muscle biopsy showed a combined defect in complex I, II and III; PDHC activity was not measured due to limited sample size. Reduction of lipoic acid could be assessed by Western Blot analysis in a peripheral blood smear. Immediate treatment with thiamine, riboflavine, coenzyme Q10, sodium benzoate and L-carnitine could not alter the rapidly progressive course with respiratory insufficiency, severe muscular hypotonia, recurrent seizures and death at age 3.5 months. Molecular analysis of the NFU1 gene revealed one novel splice site mutation in exon 6. Analysis of cDNA for identification of the second allele is pending. **Conclusions:** Defects of [Fe-S]-cluster synthesis can be suspected by elevated lactate and glycine in plasma. NFU1 deficiency seems to produce a distinct and recognizable phenotype with associated primary pulmonary hypertension and a short window of opportunity for therapeutic interventions. Preliminary data on poor mitochondrial uptake of orally administered lipoic acid warrant further studies.

O16 - 1908

A homozygous mutation in IB57 involved in intramitochondrial iron-sulfur cluster synthesis causes severe encephalopathy and myopathy in two neonates

Vanlander A, Wilbrecht C, Ajit Bolar N, Smet J, De Paepe B, De Lattre E, Van Laer L, Loeys B, Lill R, Van Coster R. *Department of Pediatrics, Division of Pediatric Neurology and Metabolism, Ghent University Hospital, Gent, Belgium – arnaud.vanlander@ugent.be*

Background: Combined OXPHOS deficiencies involving complexes I and II have recently been detected in patients with deficient iron-sulfur cluster (ISC) biogenesis. So far, patients were reported with pathogenic mutations in NFU1 and BOLA3 presenting with severe encephalomyopathy at young age. **Objective:** Two siblings with combined deficiency of complex I and II were investigated for possible defect in ISC. **Patients and methods:** The siblings presented soon after birth with severe encephalomyopathy and died in the neonatal period. Biochemical investigations showed increased lactate in serum and increased glycine in CSF. Considering the consanguineous descent a search for genes in homozygous regions related to ISC metabolism was performed. **Results:** Isolating IBAS7 as a strong candidate gene, sequencing detected a homozygous mutation (c.941A>C) in the two siblings

and a heterozygous carrier status in both parents. Western blotting showed a severe decrease of CRM for the IBA57 protein. The protein amount in the complexes I and II was significantly decreased. Transfection experiments in HeLa cells demonstrated that the mutation was pathogenic and that excessive degradation of the IBA57 protein was responsible for the defective ISC biosynthesis. **Conclusion:** This is the first report of a pathogenic mutation in IBA57 in human.

O17 - 1786

Exome sequencing reveals heterozygous mutations in the ADCK3 gene in siblings with cerebellar atrophy but extreme phenotypic variability

Blumkin L, Leshinsky-Silver E, Zerem A, Yosovich K, J alas C, Lev D, Lerman-Sagie T. *Metabolic Neurogenetic Service, Pediatric Neurology Unit, Wolfson Medical Center, Holon, Sackler School of Medicine, Tel-Aviv University, Tel-Aviv, Israel – uba.blumkin@gmail.com*

Objectives: Primary CoQ10 deficiency is a rare, autosomal recessive, clinically heterogeneous disorder caused by defects in proteins involved in the coenzyme Q synthesis pathway and presents with five major phenotypes. Mutations in the ADCK3 gene have been associated with the ataxic form of CoQ10 deficiency. We describe a highly variable clinical presentation of cerebellar ataxia in two sisters with ADCK3 gene mutation. **Material and methods:** The younger sister demonstrates early onset rapidly progressive cerebellar ataxia accompanied by motor and non-motor cerebellar features, as well as cognitive decline and psychiatric problems. Mitochondrial respiratory chain enzyme analysis in muscle showed a decrease in complex I+III. Progressive cerebellar atrophy was demonstrated on serial brain MR imaging. Coenzyme Q10 supplementation, started at the age of 5 years led to a significant improvement in motor and cognitive abilities with partial amelioration of the cerebellar signs. Discontinuation of this treatment resulted in worsening of the ataxia, cognitive decline and severe depression, associated with a significant progression of the cerebellar atrophy. The older sister, who is 32 years old, has non progressive dysarthria and clumsiness from the age of 10 years and MRI reveals cerebellar atrophy. **Results:** Exome sequencing identified compound heterozygosity for a known (Th582del) and a novel (P602R) mutation in the ADCK3 gene. **Conclusion:** Patients with primary CoQ10 deficiency due to ADCK3 mutations can demonstrate a wide spectrum of clinical presentations even in the same family. It is difficult to diagnose CoQ deficiency based solely on the clinical presentation. Exome sequencing can provide the molecular diagnosis but since it is expensive and not readily available, we recommend a trial of CoQ treatment in patients with ataxia and cerebellar atrophy even before confirmation of the molecular diagnosis.

O18 - 1777

Thiamine transporter-2 deficiency: a reversible cause of encephalopathy in children.

Pérez-Dueñas B, Ortigoza JD, Serrano M, Fons C, Muchart J, Rebollo M, Molero M, Casado M, Artuch R. *Department of Child Neurology, Sant Joan de Déu Hospital, University of Barcelona, and CIBER-ER, ISCIII, Spain – bperez@hsjdbcn.org*

Background: SLC19A3 mutations cause thiamine transporter-2 deficiency, a recently recognized cause of reversible encephalopathy. Thiamine is an essential cofactor of 3 mitochondrial enzymes involved in pyruvate oxidation and brain energy production. **Aims:** To establish clinical-biochemical-radiological criteria for early diagnosis and treatment of SLC19A3 defects. **Patients and methods:** Two siblings presented with recurrent episodes of encephalopathy between 5 and 17 years, associating dysto-

nia, cranial nerve palsy, seizures, and T2-signal abnormalities within the cerebral cortex, basal ganglia and thalami. Thiamine administration reversed these abnormalities in a few days and the children remained asymptomatic after a three-year follow-up. A 30-day-old infant presented with lactic acidosis, lethargy, opisthotonus and brain lesions affecting the periorlandic cortex, putamina and medial thalami. 48 hours after thiamine administration irritability, feeding difficulties and opisthotonus disappeared and the patient recovered consciousness. Biochemical analysis was normal in both siblings but detected lactic acidosis and high excretion of alpha-ketoglutarate in urine in the infant with Leigh encephalopathy; these findings normalized after thiamine administration. SLC19A3 mutation analysis revealed the following mutations in combined heterozygosis (c.74dupT, c.980-14A>G) and in homozygosis (c.68G>T). **Results:** Based on our experience and on the literature review, the following diagnosis criteria were established: a) Episodes of acute encephalopathy presenting with seizures, dystonia, ataxia or brain stem dysfunction; b) Symmetric involvement of the striatum, medial thalami, brain cortex and infra-tentorial structures (tectal part of the midbrain, pons, cerebellar white matter or dentate nuclei); c) Lactic acidosis and alpha-ketoglutarate excretion during infancy; d) Rapid clinical and radiological improvement after thiamine supplementation. **Conclusions:** Thiamine-transporter 2 deficiency causes acute encephalopathy and mitochondrial dysfunction in children. Early recognition after clinical-radiological-biochemical criteria allows reversing the phenotype with thiamine administration and also differentiating this entity from other causes of acute encephalopathy in children (i.e. hypoxia, mitochondrial encephalopathy, nutritional Wernicke, rhomboencephalitis).

O19 - 1664

Succinyl-CoA ligase deficiency: report on the first patient resulting from a combined defect in SUCLG1 and SUCLG2 genes

Zafeiriou DI, Batzios S, Vargiami E, Willemsen M, Morava E, van den Heuvel L, Smet J, Van Coster R, Seneca S, Wanders R, Waterham H, Wevers R. *1st Department of Pediatrics, Aristotle University of Thessaloniki, Greece – jeff@med.auth.gr*

Succinyl-CoA ligase (SUCL) deficiency represents an encephalomyopathic form of mitochondrial DNA depletion syndromes. This mitochondrial matrix protein consists of an a subunit, encoded by SUCLG1 gene, and a b subunit encoded by either SUCLA2 or SUCLG2 genes. So far, mutations in SUCLA2 and SUCLG1 have been reported in literature. We describe the fatal clinical course of an 8 month-old girl with a combined defect in SUCLG1 and SUCLG2. Since the first months of her life the patient demonstrated retardation of gross motor development and generalized hypotonia. Elevated methylmalonic and 3-hydroxyisovaleric acid in urine, in combination with an increase in 3-hydroxyisovalerylcarnitine in plasma acylcarnitine analysis was found. Neuroimaging at this point revealed enlarged subarachnoid spaces and symmetric T2-hyperintense lesions of the basal ganglia. The patient developed progressively severe myopathy with pronounced muscle weakness and dystonia. Brain MRI at 26 months of age demonstrated deterioration with bilateral increased attenuation of putamen and caudate nuclei, severe brain atrophy and ventriculomegaly. Lactate increase was present throughout the patients' clinical course. Brainstem auditory evoked potentials revealed sensorineural hearing impairment. The constellation of the above findings prompted a diagnostic workup for SUCL deficiency. Muscle respiratory-chain enzyme activity analysis showed complex I deficiency while the quantitation of mtDNA content demonstrated moderate depletion. Direct sequencing analysis of SUCLA2 and SUCLG1 revealed a heterozygous mutation in SUCLG1 gene. Further sequencing of the SUCLG2 gene led to the identification of a second mutation. Enzymatic activity analysis in fibroblasts showed decreased SUCL

activity leading to the hypothesis that the described mutations result in disruption of the assembly of the different subunits of the enzyme. Our data extend the knowledge on the genetic defects causing SUCCL deficiency. We suggest that SUCCL2 sequencing should take place in the case where only one disease causing mutation in either SUCCL1 or SUCCL2 is found.

O20 - 1660

Leigh syndrome: a multicenter study of natural history

Sofou K, de Co IF, de Angst IB, Isohanni P, Pihko H, Östergaard E, Naess K, De Meirleir L, Tzoulis C, Uusimaa J, Mankinen K, Bindoff LA, Tulinius M, Darin N. Mitochondrial Clinical and Research Network (MCRN), Sweden – kalliope.sofou@vgregion.se

Background: Leigh syndrome (LS) is an early-onset, progressive neurodegenerative disorder, associated with defects involving mitochondrial oxidative phosphorylation. It is the most common distinct mitochondrial disease phenotype in children. **Objectives:** To study the phenotypic and genotypic spectrum of patients with LS, characterise the clinical course and identify predictors of survival in a large cohort of patients. **Material and methods:** A retrospective study of patients with LS followed at eight European centres specialising in mitochondrial diseases: Gothenburg, Rotterdam, Helsinki, Copenhagen, Stockholm, Brussels, Bergen and Oulu. An electronic database was developed for data collection. All centres obtained ethical approval for the conduction of this study. **Results:** A total of 130 patients with LS were included, 77 with identified pathogenic mutations. Median age at onset of symptoms was 7 months. Seventy-four patients experienced acute exacerbations and/or relapses requiring hospitalisation, of whom 40% necessitated intensive care. Fifty-one patients (39%) died at a median age of 2.4 years. The presence of pathological signs at birth and history of seizures were associated with significantly higher occurrence of acute exacerbations/relapses. Clinical onset ≤ 6 months of age, history of failure to thrive, admission to intensive care unit and brainstem dysfunction on neuroimaging, were significantly related to poor survival. Among patients with identified pathogenic mutations, those with m.8893T>G, SURF1 and SLC19A3 mutations were found to have poorer survival and more widespread lesions on neuroimaging, compared with patients having other pathogenic mutations. **Conclusions:** To our knowledge, this is the first study performed in a large cohort of patients to describe the natural history of LS and to identify genotype-phenotype correlations and predictors of survival.

O21 - 1552

Biotin-responsive basal ganglia disease revisited: clinical, radiologic, and genetic findings

Tabarki Melaiki B, Al Hashem A, Al Shafi S, Al Shahwan S, Zuccoli G. Department of Pediatrics, PSMMC, Riyadh, Saudi Arabia – btabarki@hotmail.com

Background: Biotin responsive basal ganglia disease is a treatable neurometabolic condition resulting from mutations in the SLC19A3 gene. **Objective:** To investigate the clinical, genetic, and neuroradiologic data of BBGD and clarify the disease spectrum. **Methods:** We investigated all patients attending our Division of Pediatric Neurology with a genetically proven diagnosis of BBGD between 2009 and 2012. All patients underwent a detailed medical history and clinical examination, extensive laboratory investigations including genetic tests, and brain MRI. Finally, we conducted a systematic review of the literature. **Results:** We enrolled 15 patients meeting the diagnostic criteria for BBGD, and analyzed the data on 16 patients from 5 previous reports. The BBGD occurred predominantly in preschool/school-aged patients in the Saudi population, but it was also observed in other

ethnic groups. The typical clinical picture consisted of recurrent subacute encephalopathy leading to coma, seizures, and extrapyramidal manifestations. The brain MRI typically showed symmetric and bilateral lesions in the caudate nucleus and putamen, infra- and supratentorial brain cortex, and in the brainstem. Vasogenic edema characterized the acute crises as demonstrated by DWI/ADC. Atrophy and gliosis in the affected regions were observed in patients with chronic disease. Early treatment with a combination of biotin and thiamine resulted in clinical and neuroradiologic improvement. Death and neurologic sequelae including dystonia, mental retardation, and epilepsy were observed in those who were not treated or were treated late. **Conclusions:** BBGD is an underdiagnosed pan-ethnic treatable condition. Clinicians caring for patients with unexplained encephalopathy and neuroimaging showing vasogenic edema in the bilateral putamen and caudate nuclei, infra- and supratentorial cortex, and brainstem should consider this disorder early in the hospital course because a therapeutic trial with biotin and thiamine can be lifesaving. Our study also provide new insights into the disease: 1/the neuroimaging features, 2/the pathogenesis, and 3/the treatment as thiamine is main treatment.

O22 - 1585

New insights into the spectrum of phenotypes and genotypes in Leukoencephalopathy with brain stem and spinal cord involvement and lactate elevation (LBSL)

Hamilton EM, van Berge L, Steenweg ME, Linnankivi T, Uziel G, Krägeloh-Mann I, Brautaset NJ, Andrews I, de Co IF, van Berkel CG, Polder E, Scheper GC. VUMC Amsterdam, The Netherlands – e.hamilton@vumc.nl

Objectives: Leukoencephalopathy with Brain Stem and Spinal Cord Involvement and Lactate Elevation (LBSL) is a rare autosomal recessive disorder with a distinctive MRI and spectroscopy pattern, clinically characterized by slowly progressive ataxia, spasticity and dorsal column dysfunction. Patients have mutations in the DARS2 gene. Recent observations indicate that the clinical variety of the disease is much wider than initially thought. The aim of this study was to make an inventory of the clinical characteristics and genotypes in LBSL patients and to explore a possible genotype-phenotype correlation. **Material and methods:** A cross-sectional observational study was performed in 78 patients with two DARS2 mutations. Clinical information was collected via questionnaires and an inventory was made of the DARS2 mutations in our patients as well as those previously published. **Results:** Medical information was obtained on 66 patients. The clinical severity varied from neonatal onset, rapidly fatal disease to an adult onset disorder with a slow and mild course. The most common phenotype was characterized by childhood onset and gradual neurological deterioration. In total, 60 different DARS2 mutations have been identified (13 novel). Except for four published cases, all patients were compound heterozygous. The groups of patients sharing the same two mutations were very small, precluding a formal genotype-phenotype correlation. However, some combinations of mutations were consistently associated with a benign phenotype. **Conclusions:** This study describes the natural course and genotype in the largest cohort of LBSL patients to date. There is a wide variability in clinical severity, and patients have numerous different mutations. In most cases, the disease has a relatively slow and mild course, but in some cases the disease has an early- infantile onset and leads to death within 2 years. The available evidence suggests that the genotype influences the phenotype, but larger numbers of patients are necessary to confirm this.

Parallel session 5: Immunology and infectious diseases

Chairs: Banu Anlar and Nina Barisic

O23 - 1732

Childhood relapsing immune-mediated polyneuropathy and hemolysis is associated with CD59 deficiency

Nevo Y, Ben Zeev B, Tabib A, Straussberg R, Anikster Y, Shorer Z, Fattal-Valeski A, Ta Shma A, Aharoni S, Rabie M, Zenvirt S, Goldshmidt H, Fellig Y, Shaag A, Mevorach D, Elpeleg O. Hadassah, Hebrew University Medical Center, Jerusalem, Israel – nevo@hadassah.org.il

Objective: The objective of the present study was to elucidate the molecular basis of a new clinical entity of childhood familial immune mediated relapsing polyneuropathy associated with chronic Coombs-negative hemolysis. Since infancy these children had recurrent episodes of weakness and hemolysis with partial improvement following immune modulating therapy. One child died at the age of 3.5 years while the others demonstrated severe lower limb paralysis. **Methods:** A founder mutation was searched for using homozygosity mapping followed by exome sequencing in 5 infants of North-African Jewish origin from 4 unrelated families. The expression of CD59, CD55, and CD14 was examined in blood cells by flow cytometry followed by Western blot of the CD59 protein. **Results:** homozygous missense mutation, p.Cys89Tyr in CD59, was identified in all patients. The mutation segregated with the disease in the families and had a carrier rate of 1:66 among Jewish subjects of North-African origin. The mutated protein was present in the patients' cells in reduced amounts and was undetectable on the membrane surface. **Discussion and conclusion:** CD59 deficiency is a common finding in RBCs and WBCs in patients with chronic hemolysis suffering from paroxysmal nocturnal hemoglobinuria in which the acquired mutation in the PIGA gene leads to membrane loss of glycosylphosphatidylinositol-anchored membrane proteins, including CD59. Based on the results of the present study, we suggest that the Cys89Tyr mutation in CD59 is associated with a failure of proper localization of the CD59 protein in the cell surface and decreased complement inhibition. This mutation is manifested clinically in infancy by relapsing peripheral demyelinating disease and chronic hemolysis.

O24 - 1725

Autonomic dysfunction in children with Guillain-Barré syndrome

Aziz M, Watson L, Plant N, Vassallo G. Department of paediatric neurology, Royal Manchester children's hospital, Oxford road, Manchester, UK – drmaziz@hotmail.com

Background: Guillain-Barré syndrome (GBS) is an autoimmune disorder causing motor, sensory and autonomic dysfunction. Autonomic disturbance involvements are of sweating, heart rate and rhythm, blood pressure, ileus and sphincter control. The primary aim of this study is to describe the incidence, severity and management of autonomic dysfunction and their relationship with clinical, CSF and neurophysiological features in a cohort of patients with GBS. **Methods:** A 10-year retrospective review of cases identified using the international classification of disease (ICD) code for GBS in a tertiary paediatric centre. **Results:** Twenty-seven patients were included in this study. Patients were aged 5.7 years (IQR 3.5–8.4 years) and 18 (18/27; 67%) were male. Autonomic dysfunction was seen in fourteen patients (52%). The length of hospital stay was 32.5 (15.5 – 53.5) days. Hypertension was the most observed autonomic dysfunction, seen in twelve patients (44%), tachycardia in four patients (14%) and bradycardia in one child (3%). The ECG were normal. There was no incidence

of altered temperature, sweating and ileus. The duration of hypertension was 11 (7.3 – 26) days and correlated with the length of hospital stay ($Rho=0.65$; $p=0.021$). Hypertension occurred 9 to 15 days from symptom onset and within 24 to 48 hours of maximum motor disability. Nine hypertensive patients required treatment; six were controlled with a single agent. Patients with more extensive motor disturbance (i.e four limb involvement) required more anti-hypertensive medications (Upper limb $Rho=-0.709$; $p=0.033$, lower limb $Rho=-0.72$; $p=0.029$). Hypertension resolved in all patients prior to discharge and was not related to grade of muscle weakness, CSF protein levels, IVIg therapy, severity of nerve conduction or subtype of GBS (AIDP, AMAN, AMSAN, and Miller fisher variant). **Conclusion:** Dysautonomia, mainly hypertension occurs early in the disease course when patients are at their clinical nadir and resolves before limb paralysis starts to improve.

O25 - 2018

Risks of relapse and severe outcome in children with a clinically isolated acute transverse myelitis at onset: a French-British collaborative study

Deiva K, Absoud M, Niotalkis G, Hemingway C, Lim M, Tardieu M. Department of Pediatric Neurology, National Referral Centre for Neuro-Inflammatory Diseases in Children, Hôpitaux Universitaires Paris-Sud, Le Kremlin Bicêtre, France – kumaran.deiva@bct.aphp.fr

Objective: To determine risk factors of relapse and severe outcome in children with isolated acute transverse myelitis (IATM) at onset. **Methods:** In this retrospective study, clinical and MRI datas of 95 children less than 16 years old with IATM followed in France and United Kingdom were gathered from 2004 to 2011. Clinical outcome at the last follow-up was assessed using the ASIA impairment scale and by Kutzke Disability score (DSS) and a severe outcome was defined when ASIA impairment scale was $<D$ and/or DSS score ≥ 4 . **Results:** Median age was 9 years (0.7–16) with a mean follow-up of 1.8 ± 1.7 years. Sixteen (17%) were diagnosed with a relapsing disease (multiple sclerosis in 14 and neuromyelitis optica in 2). Children with relapse tend to be significantly younger than children with a monophasic evolution (8 years (4–15) vs 10 years (0.7–16), $p=0.03$) and they frequently had a nadir of symptoms $\geq 24H$ (4 vs 49, $p=0.005$). Presence of brain MRI lesions at onset was more frequent in children who had a relapse (8/10 vs 20/62, $p=0.01$). Twenty-eight (30%) children had a severe outcome and was frequently observed in children who had a time to nadir of symptoms $\leq 24H$ and with sphincter dysfunctions ($p=0.02$ and $p=0.01$) while pleiocytosis $\geq 10/mm^3$ was frequently present in children with non severe outcome (7 vs 32, $p=0.01$). On MRI studies, gadolinium enhancement was significantly present in children with severe outcome (20/24 vs 16/48, $p=0.0001$). **Conclusion:** In this largest study of IATM in children, we have identified that age, time to nadir $\geq 24H$ and presence of lesions on brain MRI were associated with relapse while time to nadir of symptoms $\leq 24H$, sphincter dysfunction, absence of pleiocytosis and presence of gadolinium enhancement on brain MRI seems to be risk factors for severe outcome.

O26 - 1915

Immunological studies in rapid-onset obesity with hypothalamic dysfunction, hypoventilation, and autonomic dysregulation (ROHHAD) syndrome

Biancheri R, Napoli F, Calcagno A, Ceccherini I, Hacohen Y, Jacobson L, Lang B, Vincent A, Maghnie M. Child Neurology and Psychiatry Unit, Department of Neuroscience, Istituto Giannina Gaslini, Genova, Italy – roberta@biancheri.com

Objectives: To evaluate a possible role of autoimmunity in rapid-onset obesity with hypothalamic dysfunction, hypoventilation

and autonomic dysregulation (ROHHAD) syndrome. This disorder affects previously normal children at 2 to 4 years of age. In spite of a high suspicion for genetic etiology, disease-associated genetic variations have not been identified as yet. On the other hand, a paraneoplastic/autoimmune etiology has been suggested mainly because of the association with neural crest tumors. **Material and methods:** Six patients with ROHHAD underwent clinical, neurophysiological and neuroradiologic studies; serum antibodies to neuronal antigens (NMDAR, LGI1, CASPR2, dopamine receptor, AMPAR, Ganglionic AChR (autonomic), VGKC and VGCC), often found in association with tumours, were assessed. **Results:** All patients (2M, 4F) had normal birth size and no symptoms until 2–4 years, when they developed rapid weight gain (mean BMI Z-score +3.5SDS), hyperprolactinemia, water/salt balance disruption and behavioral problems or EEG alterations (4 patients). Central apnoeas were diagnosed at age 2–6.5 in 4 patients and non-invasive ventilation was started. Central adrenal insufficiency was found in 2 patients. 4 patients had growth hormone deficiency, 2 had central precocious puberty and 5 had central hypothyroidism. Brain MRI was normal or not significant in all patients. A retroperitoneal mass was found in 3 patients. None of their sera were positive for any of the neuronal antibodies tested. **Conclusions:** The possible autoimmune etiology of ROHHAD is based on the frequent association with neural crest tumors, the extensive infiltrates of lymphocytes and histiocytes in the hypothalamus of some patients, and a partial response to intravenous immunoglobulin, rituximab and cyclophosphamide. We investigated the sera for most of the known autoantibodies associated with different forms of immune-mediated encephalitis, but all results were negative. Additional studies to look for novel autoantibodies are needed.

O27 - 2082

Anti-myelin oligodendrocyte glycoprotein antibody positivity in children with demyelinating episodes

Hughes SE, James S, Flynn P, Smyth G, McKinstry S, Rennie I, Hanrahan D, Peake D, Tirupathi S. *Department of Neurology, Royal Belfast Hospital for Sick Children, Belfast, UK – Stella419@hotmail.com*

Objectives: Anti-myelin oligodendrocyte glycoprotein (anti-MOG) antibodies have been identified in paediatric cases of demyelinating disease. Their relevance remains uncertain but MOG-positive acute disseminated encephalomyelitis (ADEM) may indicate a more pronounced systemic onset of symptoms and signify higher recurrence risk. We aimed to define the features of antibody-positive cases in our paediatric population. **Material and methods:** Case series of paediatric patients with monophasic or recurrent demyelinating episodes who demonstrated anti-MOG antibodies in serum. **Results:** We describe four children; three females, one male. All cases were serum anti-MOG antibody positive and aquaporin-4 antibody negative. Mean follow-up was 9.8 months (range 1–30 months). Mean age at onset was 6 years (range 5–7 years). All presented with ADEM which was monophasic in three cases. In the fourth, unilateral optic neuritis (ON) developed 8 weeks later and subsequently recurred after three months. Cranial Magnetic Resonance Imaging (MRI) was typical for ADEM in all, although initial scans were normal in three cases. Two cases had spinal cord lesions, one with widespread high T2-signal. All had cerebrospinal fluid (CSF) pleocytosis, with marked lymphocytosis in two, and one had markedly elevated CSF protein. CSF oligoclonal bands were absent in the three cases in which it was studied. Each received intravenous steroids at diagnosis of ADEM, followed by reducing doses of oral corticosteroid; this was also administered for each episode of ON in the polyphasic case. There was a good recovery in all cases. **Conclusions:** In this case series, anti-MOG antibody positivity was associated with monophasic ADEM in all but one case, which also had recurrent optic neuritis. All had a full re-

covery, suggesting that the antibody does not necessarily confer a poor short-term prognosis. Although anti-MOG antibody is a useful marker for autoimmune aetiology, it remains to be seen if it predicts recurrence or multiple sclerosis in the longer term.

O28 - 1989

Children in England with narcolepsy during the H1N1 (swine 'flu) pandemic: clinical features in those receiving AS03 adjuvanted pandemic A/H1N1 (2009) influenza vaccine and in unvaccinated cases

Winstone AM, Stellitano L, Verity CM, Shneerson JM, Andrews N, Stowe J, Miller E. *Addenbrookes Hospital, Cambridge, UK – annemarie.winstone@addenbrookes.nhs.uk*

Objectives: To retrospectively identify cases of narcolepsy aged 4 to 18 years in England with onset from January 2008 and investigate differences in clinical features between vaccinated and unvaccinated cases. **Material and methods:** Cases of narcolepsy aged 4 to 18 years with onset from January 2008 were identified by sleep centres and by paediatric neurologists in 16 English hospitals. Clinical information and sleep test results extracted from centre notes were reviewed by an expert panel. General practitioners provided vaccination and clinical histories. **Results:** Case notes for 245 children were reviewed; 75 had narcolepsy. Eleven were vaccinated before onset of symptoms. All 75 children presented with excessive daytime sleepiness. Presenting symptoms more frequently reported in the vaccinated cases were cataplexy, weight gain, behavioural problems, complex movement disorders, tongue protrusion and slurred speech. Other presenting symptoms were sleep-disturbance/nightmares, facial hypotonia, hypnagogic hallucinations, snoring, sleep paralysis, prolonged night time sleep, restless/painful legs, ptosis, ataxia, sleep automatisms and incontinence. Eventually all the vaccinated cases developed cataplexy compared to 38/64 (59%) of the unvaccinated cases. Investigations were as follows. Human leukocyte antigen (HLA) DQB1*0602 typing was performed in 6 vaccinated cases, all were positive. In 28 non-vaccinated cases HLA typing was done and 25 were positive. Cerebrospinal fluid orexin levels were measured in 2 vaccinated cases (both low) and 11 unvaccinated (9 low, 2 normal). Multiple sleep latency studies were performed in 9 vaccinated cases (all abnormal); they were performed in 56 unvaccinated cases (46 abnormal). **Conclusions:** We previously reported an increased risk of narcolepsy after A/H1N1 (2009) influenza vaccine. We have now analysed the clinical features of the cases. Some presenting symptoms were more frequently recorded in vaccinated cases who all developed cataplexy within the study period. Long term studies are needed to detect any differences in eventual outcome between vaccinated and unvaccinated cases.

O29 - 1951

Childhood encephalitis: epidemiological, clinical and radiological characteristics and their impact on the outcome

Liptai Z, Ujhelyi E, Mihaly I, Barsi P. *Szent Laszlo Hospital, Department of Paediatrics, Budapest, Hungary – zliptai@laszlokorhaz.hu*

Aim of the study: to estimate the frequency, etiologies and characteristics of childhood encephalitis and their impact on the outcome. **Patients and methods:** data of paediatric patients treated for encephalitis between 1998 and 2009 at Szent László Hospital were statistically analysed. **Results:** In the 12-year-period 178 children were treated for 179 episodes. 85% had infectious encephalitis (IE), 13% had acute disseminated encephalomyelitis (ADEM). The infectious agent was verified in 2/3 of cases. The commonest were herpes simplex virus (HSV): 16%, enterovirus: 38%, varicella-zoster virus (VZV): 11%. Prodromal ill-

ness was present in 65%. Focal deficits, confusion and severe disturbance of consciousness were more common in ADEM than in IE. Seizures occurred more often in HSV encephalitis. Focal deficits were more typical of VZV. CSF was abnormal in 85, EEG in 93%. Severe diffuse dysfunction occurred more often in ADEM than in IE. Periodic changes, focal and paroxysmal changes were more typical of HSV than of other etiologies. MRI was abnormal in 96% of ADEM and 53% of IE cases examined. 58% of all and 79% of ADEM patients required intensive care. HSV patients were more likely to require intensive care and for a longer duration, than patients with other etiologies. Mortality rate was 3%. Sequelae (26%) occurred more often after ADEM, following severely disturbed consciousness, seizure(s), severe diffuse dysfunction, focal, paroxysmal and periodic changes of the EEG and abnormal MRI. 14% developed epilepsy. Relapses occurred in 1 HSV and 2 ADEM patients. The most important predictors of unfavourable outcome were: ADEM, HSV-etiology, severely disturbed consciousness, focal seizures, paresis, pyramidal signs, paroxysmal EEG changes, cortical, subcortical abnormal signal on MRI. **Conclusion:** This large series of paediatric encephalitis patients is unique in terms of the high-ratio of successful epidemiological workup and of the correlations found between the acute phase and the outcome.

O30 - 1893

Guillain-Barré syndrome in UK children: H1N1 vaccinations, preceding infections and clinical features

Verity C. Addenbrookes Hospital, Cambridge, UK – christopher.verity@addenbrookes.nhs.uk

Objectives: To identify all new cases of Guillain-Barré syndrome (GBS) or Fisher syndrome (FS) in United Kingdom (UK) children in the 2 years following September 2009 and determine the proportion that was temporally associated with recent infections, with pandemic H1N1 (2009) strain influenza vaccination or with seasonal influenza vaccination. To report the clinical features of these cases. **Material and methods:** A prospective UK-wide epidemiological study using the British Paediatric Surveillance Unit (BPSU) system, including all children aged ≤ 16 years meeting the Brighton Collaboration criteria for GBS or FS. **Results:** We identified 112 children with GBS (66 boys and 46 girls) and 3 boys with FS in 2 years. The annual incidence rate of GBS in our patients <15 years old was 0.45/100,000, similar to other countries. Infection preceded the onset of symptoms in all but 20 of the 115 GBS/FS cases. In England 7 GBS cases received H1N1 (2009) vaccination and 3 others received seasonal vaccination within 6 months of symptom onset: no more than expected by chance. Most GBS cases were too weak to walk (90/112) and most (80) received intravenous immunoglobulin. 13 of the 112 GBS cases needed ventilation. About a third of GBS children had dysautonomia. 114/115 recovered sufficiently to go home. **Conclusions:** In 1976 a national immunization programme against swine influenza in the United States was discontinued because GBS was associated with vaccination. However we found that the majority of GBS and FS cases were temporally associated with previous infections, with no evidence of a temporal link with pandemic H1N1 (2009) strain vaccination in children. The outcome for GBS and FS after 6 months was better than reported in adult studies. **Acknowledgements:** Thanks to notifying paediatricians and the BPSU. Department of Health (DH) grant 019/0047: views expressed are not necessarily those of the DH.

Parallel session 6: Cerebral palsy

Chairs: Florian Heinen and Bernard Dan

O31 - 1568

Neonatal neuroimaging predicts recruitment of contralesional corticospinal tracts following perinatal brain injury

van der Aa NE, Verhage CH, Groenendaal F, Vermeulen RJ, de Bode S, van Nieuwenhuizen O, de Vries LS. Department of Neonatology, Wilhelmina Children's Hospital, Utrecht, The Netherlands – n.vanderaa@umcutrecht.nl

Objectives: Unilateral perinatal brain injury may result in recruitment of ipsilateral projections originating in the unaffected hemisphere and development of unilateral spastic cerebral palsy (USCP). The aim was to assess the predictive value of neonatal neuroimaging following perinatal brain injury for recruitment of ipsilateral corticospinal tracts. **Methods:** Neonatal magnetic resonance imaging and cranial ultrasound scans of 37 children (20 males, 17 females; median [range] gestational age 36 wk+4 [26+6–42wk+5] and birthweight 2312 ([770–5230]) g with unilateral perinatal arterial ischaemic stroke (n=23) or periventricular haemorrhagic infarction (n=14) were reviewed and scored for involvement of the corticospinal trajectory. Hand function was assessed using the Assisting Hand Assessment (AHA) and Transcranial Magnetic Stimulation (TMS) was performed (age range 7 years and 4 months – 18 years and 7 months) to determine the type of cortical motor organisation (normal, mixed or ipsilateral). Neuroimaging scores were used to predict TMS patterns. **Results:** Eighteen children developed USCP (49%), with ipsilateral corticospinal tract projections in 13 children (8 mixed, 5 ipsilateral). AHA scores decreased with increased ipsilateral projections. Asymmetry of the corticospinal tracts seen on neonatal MRI was predictive of development of USCP and recruitment of ipsilateral tracts (positive and negative predictive value of 73% and 91%). **Conclusion:** Neonatal neuroimaging can predict recruitment of ipsilateral corticospinal tracts. Early knowledge of the expected pattern of cortical motor organisation will allow early identification of children eligible for early therapy.

O32 - 1912

Brain volume reduction in young adults with perinatal hypoxic-ischaemic encephalopathy

Bregant T, Rados M, Vasung L, Zadnik V, Derganc M, Evans AC, Neubauer D, Kostovic I. Department of Pediatric Neurology, University Children's Hospital, University Medical Centre Ljubljana, Slovenia – tina.bregantdrmed@gmail.com

Objectives: A severe form of perinatal hypoxic-ischaemic encephalopathy (HIE) carries a high risk of perinatal death and severe neurological sequelae while in moderate and mild HIE only discrete cognitive disorders may occur. Imaging biomarkers for long term outcome in children with perinatal HIE are not known. **Material and methods:** MR imaging (3T Magnetom Trio Tim, Siemens) was performed in a cohort of 14 young adults (9 males, 5 females, mean age 22.1 \pm 0.7 years) with a history of mild or moderate perinatal HIE defined by Sarnat and Sarnat criteria. The control group consisted of healthy participants (9 males, 5 females, mean age 22.8 \pm 0.7 years). Volumetric analysis was done after the MR images processing using a fully automated CIVET pipeline. We measured gyrification indexes, total brain volume, volume of white and grey matter, and cerebrospinal fluid. We measured volumes, thickness and area of the cerebral cortex in the frontal, parietal, temporal, occipital lobe, and of the cingulate and parahippocampal gyrus, isthmus cinguli, and insula. **Results:** The HIE patient group showed smaller absolute volumetric data. Statistically significant ($p < 0.05$) reductions of

gyrification index in the right hemisphere, of cortical areas in the right temporal lobe and parahippocampal gyrus, of cortical volumes in the right temporal lobe and of cortical thickness in the right isthmus of the cingulate gyrus were found. Comparison between the healthy group and the HIE group of the same gender showed statistically significant changes in the male HIE patients, where a significant reduction was found also in whole brain volume; left parietal, bilateral temporal, and right parahippocampal gyrus cortical areas; and bilateral temporal lobe cortical volume. **Conclusions:** Our analysis showed general total brain volume reduction in HIE patients with predilection changes in the temporal lobes and parahippocampal gyrus.

O33 - 2123

Visual spatial perceptual profiles in children with developmental coordination disorder or in very premature children with cerebral palsy

Gonzalez Monge S. *Praticien Hospitalier, Lyon, France – sibylle.gonzalez-monge@chu-lyon.fr*

The visual-spatial function appears to be particularly sensitive to neuro-cognitive developmental disorders. This emphasizes the clinical importance of using tools to specifically test the visuo-spatial function during development. The aim of our study was to compare the visual spatial perceptual profiles in two groups of children with Developmental Coordination Disorder (DCD) or with Cerebral Palsy (CP) (i.e. without or with early cerebral lesions). We selected two groups of children aged 8 to 12 years old. Ten children were identified as having DCD following DSM-IV-TR criteria and a score below the 5% cut-off point on M-ABC-2 (Movement Assessment Battery for Children-Second Edition) and ten children with following criteria: diagnosis of Spastic Diplegia (SD), gestational age at birth was inferior to 33 weeks, diagnosis of Periventricular Leukomalacia documented by brain MRI. Each child had a full-scale IQ-score above 70 on WISC-IV (Wechsler Intelligence Scale for Children-Fourth Edition) and a low score on block design test (Perceptual Reasoning Index). All children were assessed with the DTVP-2 (Developmental Test of Visual Perception-Second Edition) measuring visual perceptual skills (NMVPQ, Non Motor Visual Perceptual Quotient) and visual motor integration skills (VMIQ, Visual Motor Integration Quotient). In 8 out of 10 very premature children with SD, concerning the DTVP profile, the VMIQ was lower than the NMVPQ and concerning MRI data, these children presented a posterior parietal white matter (or dorsal stream) involvement. The same DTVP's profile was obtained in 5 out of 10 children identified as having DCD and these results suggest that the dorsal stream could be involved, in the same way, in a neurocognitive developmental disorder without identified cerebral lesion. To conclude, the comparison of both neurocognitive developmental disorders could shed light on neuroanatomical bases of visual spatial perceptual impairment in children.

O34 - 1931

Innovative application of the motion graph deviation indexes for the quantification of the pre-post BTX – a upper limb movement changes

Darras N, Vanezis T, Tziomaki M, Pasparakis D, Papavasiliou A. *Elepap Gait Analysis and Motion Analysis Center, Athens, Greece – theon@otenet.gr*

The kinematic assessment of upper limb function requires the examination of a variety of tasks; this produces a very large set of data that is difficult to clinically analyze. We aimed to apply a new method that simplifies and enhances the quantitative assessment of upper limb performance pre and post Botulinum Toxin A (BTX-A) injection; this method has been previously

used in Gait Analysis and produces Motion Graph Deviation Indexes (MGDIs) that enable the examiner to summarize and directly compare graph information from different parameters and motions. **Methods:** Twenty Typically Developing subjects (age = 14.2 ± 6.6) were used for creating the Normal graphs. One patient with dystonia and two with spasticity were assessed pre and four weeks post BTX-A application. All subjects completed four “reach to grasp” and four gross motor tasks. The examiners were blind regarding injection sites and procedures. Kinematic calculations were based on the recommendations of the International Society of Biomechanics. MGDIs were calculated. Motion Indexes (MI) and Graph Indexes (GI) were created from the average MGDIs, representing the subject's deviation at a specific motion and at each graph respectively. Finally the Global Upper Limb Deviation Index was calculated from the averaged MI's demonstrating the overall subject deviation and four Body Level Indexes averaging the MGDIs of the Head-Trunk, Shoulder, Elbow and Wrist graphs of all motions. Pre-Post BTX-A index differences were calculated. The results were used to identify the Body Levels that showed changes on the Pre-Post BTX-A indexes. **Results:** The use of the four Body Level Indexes enabled the prediction of the areas that BTX-A was injected with 70–100% accuracy. **Conclusion:** This Upper Limb assessment protocol and the application of MGDIs were sensitive in recording and identifying the movement changes after BTX-A treatment.

O35 - 1861

Cerebral visual impairment and cerebral palsy: two sides of the same coin?

Fazzi E, Galli J, Micheletti S, Rossi A, Franzoni A. *Civil Hospital - Brescia D, Italy – elisa.fazzi@med.unibs.it*

Aim: the Cerebral Visual Impairment (CVI) (neurological disorder caused by damage to or malfunctioning of the retrogeniculate visual pathways) has been recognised as an important part of clinical manifestations in Cerebral palsy (CP). CP and CVI share a common origin; the literature shows that 60–70% of children with CP also have CVI. We set out to describe CVI in children with CP. A further aim was to establish whether different types of CP are associated with different patterns of visual involvement. **Methods:** 129 patients with CP and CVI underwent an assessment protocol including neurological examination, developmental (Griffiths Mental Development Scales50) and/or cognitive assessment (Wechsler Scales of Intelligence51), neuro-ophthalmological evaluation (using the Hirschberg Test of corneal reflexes 42), the Cover Test and the Piliaga Test 43 to detect strabismus; Teller Acuity Cards 44, Lea Symbols 45 or letter optotypes to evaluate visual acuity; Hiding Heidi Low Contrast “Face” Test 46 to determine contrast sensitivity; using a semirigid screen covered with black and white square patterns in front of the infant's face to test the optokinetic nystagmus 47, evaluating the behavioural reactions to the kinetic perimetry to assess the visual field 48 and Lang Stereotest 49 to verify stereopsis) and neuroradiological investigations. **Results:** Visual dysfunction in diplegia was characterised mainly by refractive errors (75% of cases), strabismus (90%), abnormal saccadic movements (86%), reduced visual acuity (82%). The subjects with hemiplegia showed strabismus (71%), refractive errors (88%); oculomotor involvement was less frequent (59%). This group had the largest percentage of patients with altered visual field (64%). Children with tetraplegia showed a severe neuro-ophthalmological profile, characterised by ocular abnormalities (98%), oculomotor dysfunction (100%) and reduced visual acuity (98%). **Interpretation:** Neuro-ophthalmological disorders are a main symptom in CP, associated with a distinct neuro-ophthalmological profile. Early and careful neuro-ophthalmological assessment of children with CP is essential for an accurate diagnosis and for personalised rehabilitation tools.

O36 - 2035

Clinical correlation of arcuate fasciculus lateralization in developmental dysphasia

Komárek V, Vydrová R, Kyněl M, Šanda J, Vránová M, Štírbová K, Kršek P. *Department of Child Neurology, Department of Radiology, Charles University Hospital Motol, Prague, Czech Republic – Vladimir.komarek@fnmotol.cz*

Objectives: In typically developing children aged 5–13 years, diffusion tensor imaging (DTI) demonstrated a relationship between arcuate fasciculus (AF) lateralization and cognitive abilities (receptive vocabulary scores and phonological processing tasks), suggesting that the left-lateralized arrangement of the AF plays an important role in language development as well as in pathophysiology of developmental dysphasia (DD). The aim of this study was to correlate DTI data with clinical severity of language impairment and with specific psychological tests. **Methods:** We performed DTI in 34 DD subjects. The group consisted of 11 (32%) girls and 23 (68%) boys (6.1–12.1 years old, median age 8.7 years). 11 children were evaluated with mild DD, 16 children with moderate DD and 7 children with severe DD. DTI parameters such as fractional anisotropy (FA), apparent diffusion coefficient (ADC), length, volume and count of fibres were established. AF volume laterality index (VLI) was calculated (Left AF–Right AF/Left AF+Right AF). Psychological assessment included examination of IQ, memory, verbal fluency, auditory and visual perception. Statistical analysis was performed using ANOVA. **Results:** Left AF was identified in 34 children and right AF was found in 32 subjects. VLI ≥ 0.2 corresponding with leftward AF laterality was found in 14 (41%) children, in 3 (21%) girls and in 11 (79%) males. Leftward AF laterality was found in 3 of 11 (27%) children with mild DD, in 6 of 16 (38%) with moderate DD and in 5 of 7 (71%) children with severe DD ($P=0.19$). Correlations between the DTI parameters (FA, ADC, VLI), neuropsychological scores and severity of DD were not statistically significant. **Conclusions:** Arcuate fasciculus laterality alone is not related to severity of DD. Altered development of other structures, extrema capsula fasciculus and uncinate fasciculus respectively, might play substantial role in specific language impairments.

O37 - 1898

Use of serious gaming to increase motivation of cerebral palsy children during rehabilitation

Bonnechère B, Jansen B, Omelina L, Da Silva L, Mougeat J, Heymans V, Vandeuren A, Rooze M, Van Sint Jan S. *Laboratory of Anatomy, Biomechanics and Organogenesis (LABO), Université Libre de Bruxelles, Belgium – bbonnech@ulb.ac.be*

Patient motivation is an important factor to take into consideration since patients, and more particularly young patient suffering of severe diseases such as Cerebral Palsy (CP), must adhere to a rehabilitation scheme as strict as possible. Patient motivation is the main key to a successful rehabilitation scheme. A main challenge is therefore to keep patients motivated enough despite the feelings they could have of “inefficiency”, “lack of progress”, “tiredness”, etc. Serious Gaming (SG) includes games that are developed for a particular purpose (e.g. rehabilitation) other than pure entertainment. Previous works studied the interplay between motivation, rehabilitation and SG. SG can be a good tool to increase children motivation but there is still a lack of evidence and studies are required to evaluate possibilities of SG for CP children. Six mini-games have been developed for the revalidation of CP children. Two different situations were assessed. During the first one (T1) 11 CP children (9.2 (2) years old GMFCS: 1.1 (0.4)) played the game 20 minutes per day during 5 consecutive days (daily use). For the second one (T2) 10 CP children (11.2 (3) years old GMFCS: 2 (0.8)) played the game 20 minutes per day twice a week during 4 weeks. For both T1 and T2 SG was added to con-

ventional rehabilitation. For T1 we used a visual analytic scale to evaluate enjoyment and pain during SG. Compared to conventional rehabilitation children, better enjoyed SG ($p=0.04$) and experienced less pain ($p=0.04$) during exercises. For T2 a quality of life questionnaire (Disabkids) was used. Children tended to improve (pre=38.7, post=40.5) but results are not significant ($p=0.07$). These first results suggests that SG can be used into conventional rehabilitation with positive influence on enjoyment and pain experience during exercises and may improve quality of life of CP children.

O38 - 1645

Brain lesions relate to gait pathology in children with unilateral and bilateral cerebral palsy

Van Gestel L, Ortibus E, Meyns P, De Cock P, Sunaert S, Feys H, Duysens J, Jaspers E, Desloovere K. *Department of Rehabilitation Sciences, Fac. of Kinesiology and Rehabilitation Sciences, KULeuven, Belgium – leen.vangestel@faber.kuleuven.be*

Objectives: To unravel the complex relations between the broad range of brain lesions in children with cerebral palsy (CP) and their characteristic primary motor deficits and gait pathologies. **Material and methods:** 51 children with CP (25 bilateral, 26 unilateral involvement) were enrolled. The following neurological parameters were evaluated qualitatively: corpus callosum (CC) (anterior, mid, posterior), cerebellum, basal ganglia (BG), and brainstem. Two groups of quantitative parameters were extracted: 1) integrity of periventricular/middle/subcortical white matter, summarized in sub- and global scores; 2) length and volume of the corpus callosum, volume of the lateral ventricles, and brainstem asymmetry. Gait pathology was evaluated by means of the Gait Profile Score (GPS). Primary motor deficits, more specifically lower limb muscle strength and spasticity, were evaluated by means of manual muscle testing and modified Ashworth scale respectively. Separate statistical analyses were conducted for the bilateral (BilG) and unilateral group (UniG). Spearman correlation coefficients, one-way ANOVA's and Mann-Whitney U tests ($p<0.05$) related neurological to motor parameters. **Results:** BilG: Spasticity correlated moderately with CC volume ($r=-0.46$) and BG-brainstem scores ($r=0.44$). Significantly higher spasticity scores were found for children with affected contra- and ipsilateral posterior limb of the internal capsule (PLIC). Muscle strength correlated moderately with BG-brainstem scores ($r=-0.56$) and was significantly lower with affected anterior body of the CC, or the contra- or ipsilateral PLIC. GPS scores correlated moderately with the total brain lesion scores ($r=0.53$) and with bilateral lesion scores of the middle white matter ($r=0.41$). Significantly higher GPS scores were found in children with affected subcortical white matter, contra- or ipsilateral PLIC. UniG: Spasticity correlated moderately with the integrity of the ipsilateral middle white matter ($r=0.45$), while the CC length correlated moderately with the GPS scores ($r=0.40$). **Conclusions:** This study highlights several potential relations between brain lesions and gait pathology in children with CP.

Thursday 26 September 2013

Parallel session 8: Neurogenetic disorders

Chairs: Marie Cecile Nassogne and Paolo Curatolo

O39 - 1826

Natural course of pontocerebellar hypoplasia type 2

Sánchez-Albisua I, Frölich S, Krägeloh-Mann I. University Children's Hospital, Tübingen, Germany – iciar.sanchez@med.uni-tuebingen.de

Introduction: Pontocerebellar hypoplasia Type 2 (PCH2) is a rare neurodegenerative autosomal recessive condition and defined on MRI by a small cerebellum and ventral pons. Ninety percent carry a p.A307S mutation in the TSEN54-gene. Clinical features are: mental retardation, microcephaly and dyskinesia. Clinical features haven't been detailed exhaustively and don't include the natural course. **Patients and methods:** Patients were recruited by contacting German patients' organizations. Inclusion criteria were imaging findings of PCH2 and a p.A307S mutation. Data from 33 patients were collected using physicians' reports and patient questionnaires. **Results.** – General symptoms: feeding difficulties (100%), sleep disorder (96%), apneas (67%) and recurrent infections (52%). Seventy-three percent of children were diagnosed with gastroesophageal reflux disease. A percutaneous endoscopic gastrostomy was necessary in 67% and a Nissen-funduplication in 36%. – Neurologic symptoms: Choreathetosis was present in 88% (62% with spasticity), 12% pure spasticity. Seizures occurred in 79%, status epilepticus in 39%. Epilepsy was drug resistant in 70%. Dystonic attacks occurred in 30%. – Neurodevelopmental data: All children made progress at a rudimentary level: consistent response to certain familiar objects (88%), fixing and following (76%), attempting to grasp objects (76%), moderate head control (73%), social smile (70%), rolling from prone to supine (58%), production of certain sounds to express approval/disapproval (55%), grasping and holding objects (24%), locomotion in the prone position (9%), sitting without support (9%). Ten percent lost achieved abilities on follow-up. – Anthropometric measurements: Weight, length and head circumference were in the normal range at birth and became abnormal, especially head circumference (–5.6 SD at age 5). **Conclusion:** Although PCH2 is considered a degenerative disorder, affected children can make some progress. Affected patients require a very intensive care.

O40 - 2159

Hypomyelinating leukodystrophy due to recessive mutations of GJC2 (connexin 47): clinical and radiological characteristics in 18 patients

Renaldo F, Tonduti D, Dorboz I, Masliah J, Giraud G, Elmaleh M, Orivoli S, Beraud-Majorel C, Drunat S, Chalard F, Barthez MA, Desguerre I, Quijano-Roy S, Rodriguez D, Boespflug-Tanguy O. Centre de Référence des Leucodystrophies, Service de Neuropédiatrie et Maladies Métaboliques; Hôpital Robert Debré, AP-HP, Paris, France – florenaldo@wanadoo.fr

Hypomyelinating leukoencephalopathies (HDL) are a heterogeneous group of childhood genetic disorders characterized by a reduced formation of myelin in the central nervous system. The prototypic early-onset hypomyelinating leukoencephalopathy is Pelizaeus–Merzbacher disease (PMD), an X-linked condition caused by mutations in the proteolipid protein (PLP) gene (Xq22). PLP1 mutations can also cause “pure” or “complicated” spastic paraplegia type 2 (SPG2), an allelic disorder at the same locus. Besides PMD, a growing number of Pelizaeus–Merzbacher-like disease (PMLD) are reported, not associated with PLP1 muta-

tions. Autosomal recessive mutations in GJC2 (GJA12, 1q42), encoding the connexin 47, can give rise to PMLD (HDL2) or spastic paraplegia type 44 (SPG44). We report initial and evolving characteristics in 18 GJC2-mutated patients. First we noted a large phenotypic variability, from the classic PMD-like phenotype to the much milder SPG form which can manifest in childhood or in adulthood. This important variability was also observed inside a large consanguineous family. Most of patients experienced early nystagmus as first symptom, associated with psychomotor delay although neurocognitive capacities were higher compared to PMD. The evolution was then marked by the occurrence of a progressive cerebello-spastic syndrome, extra-pyramidal symptoms in some patients, followed by motor and cognitive regression, sometimes loss of language skills, focal epilepsy, and frequently early optic atrophy. Evoked potentials showed more variable and moderate delayed central conduction times than in PMD. Nerve conduction velocities were normal. Magnetic resonance imaging (MRI) displayed diffuse hypomyelinating leukodystrophy associated with brainstem abnormalities in all patients. We found other peculiarities in a few patients. The clinical spectrum of GJC2 mutations is broader than PLP1 mutations with intra-family heterogeneity. Clinico-electrophysio-radiological specificities can make it possible to study GJC2 of first intention even among boys.

O41 - 1941

Mutation spectrum and clinical characteristics in hypomyelination with atrophy of the basal ganglia and cerebellum (H-ABC)

Hamilton EM, Vanderver A, Siriwardena K, Pinelli L, Schiffmann R, Blaser S, Naidu S, van Berckel CG, Polder E, Abbink TE, Wolf NI, van der Knaap MS. VUMC, Amsterdam, The Netherlands – e.hamilton@vumc.nl

Objectives: Hypomyelination with Atrophy of the Basal Ganglia and Cerebellum (H-ABC) is a rare hereditary leukoencephalopathy that was identified by MRI pattern analysis. 1 Exome sequencing in 11 H-ABC patients recently revealed the same de novo mutation in the TUBB4A gene, which encodes β -tubulin and is highly expressed in neuronal cells. 2 Mutations in TUBB4A are also associated with adult onset dystonias. We here describe the mutation spectrum, clinical phenotype and MRI characteristics in our cohort of 44 H-ABC patients. **Material and methods:** We initiated a cross-sectional observational study in our database of H-ABC patients. Sequential MRIs of patients were evaluated via a standard protocol. In all patients, DNA analysis and a clinical inventory were executed. **Results:** DNA analysis confirmed that the TUBB4A mutation, observed in the first 11 H-ABC patients, is by far the most common. Additionally, several other mutations were found. Preliminary results are suggestive of a genotype-phenotype correlation, with a phenotypic continuum extending from neonatal up to childhood disease onset, normal to delayed early development and slowly to more rapidly progressive neurological deterioration. Six patients have died (age 1.7–25 years). The oldest patient is now over 30 years. MRI showed disappearance of the putamen and a variable degree of cerebellar atrophy and cerebral atrophy, largely corresponding to the disease severity. Apart from hypomyelination, myelin loss was evident in some patients. **Conclusions:** H-ABC is an MRI based diagnosis and the current study further delineates the clinical course and mutation spectrum in this rare leukoencephalopathy. TUBB4A mutations are associated with different neurological disorders, sharing certain characteristics. H-ABC patients show a rather homogeneous phenotype with a distinctive MRI pattern and a variable disease severity. **References:** 1. van der Knaap MS, et al., AJNR 2002. 2. Simons C, et al., Am J Hum Genet. 2013

O42 - 1909

FOXP1 gene: phenotype–genotype relation in Spanish patients

Pineda Marfa M, O'Callaghan Gordo M, Gerotina Mora E, Quandt Herrera E, Rabaza Gairí M, Brandi Tarrau N, Cortés Saladelafont E, Roche Martínez A, Armstrong Morón J. *Fundació Hospital Sant Joan de Déu and CIBERER, ISCIII1, Servei Neuropediatria y genética molecular, Hospital Sant Joan de Deu 2, Barcelona, Spain – pineda@hsjdbbcn.org*

Introduction: Rett syndrome (RTT) is a neurodevelopmental disorder, of early onset, affecting almost exclusively girls. The disease has classical forms and atypical variants forms. Most cases are due to mutations in the MECP2 gene, but other genes had been described causing atypical forms of the disease: CDKL5 early epilepsy variant and FOXP1 congenital variant. FOXP1 (MIM 614364) is the first gene linked to autosomal RTT, located on chromosome 14q12. **Material and methods:** We have studied the FOXP1 gene by direct sequencing and MLPA (Probemix-P075, MRC-Holland) in patients RTT without MECP2 mutation and in patients with mental retardation and Rett-like clinical features. **Results:** we analyzed 211 patients with clinical presentation likely to have mutations in FOXP1 gene. We detected 9 patients: six of them had point mutations and three large rearrangements in FOXP1. At the moment of diagnosis the ages ranged from 1 to 9 years old and the gender was 4 males/5 females All had severe early postnatal encephalopathy with deceleration of head growth in the first months of life (1–9 months) with severe microcephaly from early childhood (–3ds/– 4ds), severe developmental delay, hypotonia, none of them has acquired independent walking and only 3 are able to seat unaided, absent language development, hand stereotypies, convergent strabismus, tongue protrusion, jerky arm movements, bruxism and epilepsy 5 patients. Brain imaging studies showed simplified gyral pattern, reduced white matter volume in frontal lobes and corpus callosum hypogenesis. **VIDEO. Conclusions:** Genetic etiologies of variant Rett syndrome are heterogeneous; screening the FOXP1 gene should be done not only in females, but also in male patients with clinical features of congenital phenotype Rett syndrome and in severe developmental encephalopathies. FOXP1 is not an X-linked gene and therefore there can be a higher incidence of mutation detection in RTT-like males than in MECP2 and CDKL5 genes.

O43 - 1896

The neurology of rhizomelic chondrodysplasia punctata

Bams-Mengerink AM, Koelman JHTM, Waterham H, Barth PG, Poll-The BT. *Academic Medical Centre, Amsterdam, The Netherlands – a.m.mengerink@amc.uva.nl*

Background: To describe the neurologic profiles of Rhizomelic chondrodysplasia punctata (RCDP), a peroxisomal disorder clinically characterized by skeletal abnormalities, congenital cataracts, severe growth and developmental impairments and immobility of joints. Defective plasmalogen biosynthesis is the main biochemical feature. **Methods:** Observational study including review of clinical and biochemical abnormalities, genotype, presence of seizures and neurophysiological studies of a cohort of 16 patients with RCDP. **Results:** Patients with the severe phenotype nearly failed to achieve any motor or cognitive skills, whereas patients with the milder phenotype had profound intellectual disability but were able to walk and had verbal communication skills. Eighty-eight percent of patients developed epileptic seizures. The age of onset paralleled the severity of the clinical and biochemical phenotype. Myoclonic jerks, followed by atypical absences were most frequently observed. All patients with clinical seizures had interictal encephalographic evidence of epilepsy. Visual evoked (VEP) and brain auditory potential (BAEP) studies showed initial normal latency times in 93% of patients. Deterioration of VEP occurred in a minority in both the severe

and the milder phenotype. BAEP and somatosensory evoked potentials (SSEP) were more likely to become abnormal in the severe phenotype. Plasmalogens were deficient in all patients. In the milder phenotype levels of plasmalogens were significantly higher in erythrocytes than in the severe phenotype. Phytanic acid levels ranged from normal to severely increased, but had no relation with the neurological phenotype. **Conclusion:** Neurodevelopmental deficits and age-related occurrence of seizures are characteristic of RCDP and are related to the rest-activity in plasmalogen biosynthesis. Evoked potential studies are more likely to become abnormal in the severe phenotype, but are of no predictive value in single cases of RCDP.

O44 - 1703

Deficiency of the E3 ubiquitin ligase TRIM2 causes early-onset axonal neuropathy

Ylikallio E, Pöyhönen R, Hilander T, Paetau A, Lönnqvist T, Tyynismaa H. *Research Programs Unit, Molecular Neurology, Biomedicum Helsinki, University of Helsinki, Helsinki, Finland – emil.ylikallio@helsinki.fi*

Purpose: To reveal the genetic etiology of an early-onset axonal neuropathy. **Patient:** Our patient is a 19-year-old female with severe neuropathy. She was born in a family with no consanguinity and had normal early development. At the age of 4 years she was sent to Children's Hospital in Helsinki because of muscle hypotonia. She was alert, but very lean with small muscle mass and muscle atrophy in hands and feet. The deep tendon reflexes were absent. ENMG showed polyneuropathy: in upper extremities the motor nerve conduction velocities were slow with increased distal latencies and low amplitude. The sensory amplitudes were low in upper extremities, and in lower extremities even the motor responses could not be measured. The sural nerve biopsy findings at the age of 5 years were consistent with an axonal neuropathy revealing a mild to moderate loss of prominently large myelinated fibers (MF), but no clear signs of active demyelination, hypertrophy or regeneration. In electron microscopy the axoplasm of slightly swollen large MF revealed prominent neurofilament content. **Genetic studies:** A whole-exome sequencing revealed compound heterozygous mutations: a missense mutation (c.680A>T) and a 1-bp deletion (c.1699delA) in the tripartite motif containing 2 (TRIM2) gene. The patient carried both the mutations whereas her father was heterozygous for the deletion and her mother for the missense mutation. TRIM2 is a RING finger protein that functions as an E3 ubiquitin ligase. The studies on fibroblasts showed that the mutations resulted in a severe reduction of TRIM2 in the patient's cells resembling a mouse model for Trim2 which has shown neurofilament disorganization in axons presumably because of deficient ubiquitination. Consistently, our patient's sural nerve biopsy showed axonal degeneration with disorganized accumulation of neurofilament. **Conclusion:** TRIM2 is a disease gene for early-onset, severe CMT2 with inefficient neurofilament degradation as a pathogenic mechanism.

O45 - 1612

RATE: randomised clinical trial of rapamycin in children with tuberous sclerosis complex and intractable epilepsy

Overwater IE, Rietman A, Bindels-de Heus GCB, Moll HA, Elgersma Y, Wit MCY. *Neurology, Neuroscience; ENCORE Expertise Centre for Neurodevelopmental Disorders, Rotterdam, The Netherlands – i.overwater@erasmusmc.nl*

Tuberous Sclerosis Complex (TSC) is caused by inactivating mutations in the TSC1 or TSC2 gene. Mutations in these genes cause disinhibition of the mTOR pathway, which is involved in several cellular pathways, including cell proliferation and control of synaptic plasticity. TSC patients suffer from hamartoma-

tous growths in various organs, including renal angiomyolipoma (AML). CNS manifestations include tubers, subependymal nodules and subependymal giant cell astrocytoma (SEGA). Up to 90% of TSC patients suffer from epilepsy, with 50% of patients intractable to anti-epileptic drugs. Recent clinical trials have shown a decrease in AML and SEGA volume upon treatment with mTOR inhibiting drugs. In animal models of TSC, mTOR inhibitors decrease seizures and improve EEG findings. Rapamycin (sirolimus) is an inhibitor of the mTOR pathway, and has been used in various animal and patient studies. In the TSC clinic of the ENCORE expertise center for neurodevelopmental disorders at the Erasmus MC-Sophia Children's Hospital, we are currently performing a randomized clinical trial into the effect of rapamycin on epilepsy in TSC patients. Eligible children, with a definite diagnosis of TSC and intractable epilepsy, participate in the trial during one year, and are randomised to receive add-on oral rapamycin treatment during the first or second six months of trial participation. Primary outcome of the trial is seizure frequency, assessed by an epilepsy diary kept by the parents. EEG and developmental examination are secondary outcomes, and are performed upon inclusion and after the first and second six months. Developmental examination includes mental, motor and behavioural functioning. To monitor safety, blood samples to determine rapamycin trough levels, renal and liver function and blood cell counts are taken regularly. Currently, 20 patients have been included in the RATE trial. Design, progression and preliminary results of the trial will be presented.

O46 - 1548

Long term follow-up of clinical and neurographical abnormalities in eight Croatian patients with triple A syndrome

Barisic N, Dumic M, Kusec V, Lehman I, Bunoza B, Grdjan P, Ivanja V. *Department of Pediatrics, University Hospital Centre Zagreb, University of Zagreb, School of Medicine, Zagreb, Croatia – barisic.nina@gmail.com*

Objective: To analyse long term follow up of neurological abnormalities (during 2 years to 23 years) in eight Croatian patients with triple A syndrome. **Background:** The triple A syndrome is caused by autosomal recessively inherited mutation in AAAS gene on chromosome 12q13 encoding the nuclear pore protein ALADIN. This multisystemic disease is characterized by achalasia, alacrimia, adrenal insufficiency and neurological impairment. **Design/Methods:** Clinical examination, electromyoneurography (EMNG) and molecular-genetic analysis were performed in eight patients with triple A syndrome (five males and three females). **Results:** At the time of diagnosis all patients (aged 2 years to 8 years) presented with alacrimia, latent or manifest adrenal insufficiency, anisocoria in 2, optic atrophy in 4, motor and sensory polyneuropathy on the first exam in 2 siblings, muscle weakness and hypotrophy of distal muscle groups, cavus feet, hyperreflexia but absent triceps surae jerks, talocrural joints contractures, tremor and dysmetria in 5 patients. First EMG findings were normal at the age 6–11 years in 6/8 patients. The follow up EMG showed chronic partial denervation in all patients. Spontaneous activity (fibrillations) was registered in 3/8, compound muscle action potentials (CMAP) were polyphasic in 6/8 patients. Absent or low CMAP amplitude (0–0.5 mV) was obtained in 6/8, decreased motor conduction velocity (29–40 m/s) in 8/8, absent F-wave potentials in 7/8, absent neural potentials in 5/8 and proximal conduction block in 5 patients. Mutation pSer263Pro was identified in 5 of 8 patients. One is homozygous and four are compound heterozygous for this mutation. Genotype/phenotype analysis confirmed lack of correlation in patients with triple A syndrome. **Conclusions:** Long term follow up neurography in patients with triple A syndrome showed progressive mixed motor and sensory polyneuropathy development with signs of pronounced demyelination and/or probably

secondary axonal damage. Molecular results support the hypothesis that the pSer263Pro mutation is founder mutation in Slavic population.

O47 - 1530

Outcome of surgical treatment of 64 TSC-associated subependymal giant cell astrocytomas

Kotulska K, Roszkowski M, Mandera M, Daszkiewicz P, Grajkowska W, Jurkiewicz E, Borkowska J, Jozwiak S. *The Childrens Memorial Health Institute, Warsaw, Poland – k.kotulska@czd.pl*

Objectives: Subependymal giant cell astrocytoma (SEGA) is a brain tumor associated with TSC. Nowadays there are two treatment options in SEGAs: surgery or mTOR inhibitor. The analysis of outcome of SEGA surgery may help characterize the patients who may benefit from pharmacotherapy. **Material and methods:** Sixty-four SEGA surgeries in 57 TSC patients, operated on between 1994 and 2011, in whom at least 12-month follow-up after surgery was known were included in the study. The indication for the surgery, tumor size, age of the patients, and post-surgical complications were analyzed. **Results:** Mean age of patients at surgery was 9.7 years (ranging from 6 weeks to 26 years). Mean follow up after surgery was 63.7 months (median 60 months). Thirty-seven (57.8%) tumors were operated on because the patients developed clinical symptoms, and 27 (42.2%) tumors were resected due to documented tumor growth and/or hydrocephalus revealed on neuroimaging. Surgery-related complications were reported in 0%, 46%, 83%, 81%, and 67% of patients with tumors maximum diameter below 2 cm, between 2 and 3 cm, between 3 and 4 cm, more than 4 cm, and bilateral SEGAs, respectively. Four patients (6.2% of all surgeries) died during the first week after surgery. Most common complications included: hemiparesis (22%), hydrocephalus (20%), haematoma (14%), and cognitive decline (6%). Complications were more common in children under the age of 3 years (83%) than in older patients (55%). Fifteen patients developed contralateral SEGA in 6–120 months after first surgery. **Conclusions:** Our study indicates that SEGA surgery is associated with significant risk, especially in cases of bilateral SEGAs, tumors bigger than 2 cm, and children below 3 years of age. Therefore, TSC patients should be thoroughly screened for SEGA growth, and early surgery should be considered in selected cases.

Parallel session 9: Varia

Chairs: Vladimir Komarek and Colin Kennedy

O48 - 1975

The presenting features of arterial ischaemic stroke in a population-based cohort

Mallick AA, Ganesan V, Kirkham FJ, Fallon P, Hedderly T, McShane T, Parker AP, Wassmer E, Wraight E, Amin S, Edwards HB, O'Callaghan FJK. *University of Bristol, UK – andrew.mallick@bristol.ac.uk*

Objectives: To describe the presenting features of childhood arterial ischaemic stroke (AIS) and analyse factors associated with such features. **Material and methods:** The cases notes of a population-based cohort of 96 children (aged >28 days to <16 years) residing in southern England who experienced AIS between July 2008 and June 2009 were analysed. Presenting features and risk factors were categorised according to schemes used by the International Pediatric Stroke Study. The commonly used adult stroke recognition tool, the FAST (Face Arm Speech Time) test was applied retrospectively. **Results:** Focal features (hemiparesis, facial weakness, speech disturbance, visual distur-

bance, and other focal features) were present in 85% of children, diffuse features (decreased conscious level, headache, vomiting, papilloedema, and other diffuse features) in 61% and seizures in 29%. A hemiparesis was present in 72% of children. 78% of children had a least one positive variable (facial weakness, arm weakness, or speech disturbance) on the FAST test. Diffuse features occurred more frequently with increasing age (odds ratio 1.14 [95%CI 1.03–1.26], $p=0.015$). Seizures were less likely with increasing age (OR 0.83 [95%CI 0.72–0.96], $p=0.012$). 75% of children under the age of 1 year had seizures at presentation. A positive FAST test was not associated with age. Diffuse features were independently associated with acute systemic risk factors (OR 5.36 [95%CI 1.72–16.7], $p=0.004$). Arteriopathy was independently associated with a reduced risk of seizures (OR 0.18 [95%CI 0.04–0.86], $p=0.031$). Children with acute systemic risk factors had reduced odds of a positive FAST test (OR 0.23 [95%CI 0.08–0.69], $p=0.009$). Presenting features did not significantly vary with gender. **Conclusions:** The presenting features of AIS in children are similar to those in adult AIS. However, presenting features vary according to age and underlying risk factors.

O49 - 2118

A clinical advisory board for a rare disease (Prader-Willi syndrome)

Blichfeldt S, Farholt S. Herlev University Hospital, Paediatric Department, Herlev, Denmark – s.blichfeldt@dadnet.dk

Prader-Willi Syndrome (PWS) is characterized by neonatal hypotonia, hypogonadism, growth retardation, mental retardation, hyperphagia from age 1–3, and a risk of morbid obesity and early death. Behavioral problems and later psychiatric diseases in adults are seen. PWS is caused by lack of paternal gene expression on chromosome 15q. Treatment is multidisciplinary and lifelong involving many different professionals. **Objectives:** To present the Danish Clinical Advisory Board for PWS (CABPWSDK) of 1991, supported by the Danish PWS association (PWSDK). **Method:** The CABPWSDK consists of professionals with an extensive experience in PWS. Members are pediatricians, psychiatrist, nurses, dietician, physiotherapist, special teachers, psychologist, social workers and social advisers included staff from the two national PWS centers. The group meets two times yearly beside e-mail contacts. Group members can be contacted directly by families and professionals. **Results:** The CABPWSDK advises about how to get support and treatment, about diagnostics and treatment possibilities. Articles on medical, social, and educational topics are written for the Danish PWS Newsletter. Group members teach at courses for families and professionals: medical personnel, teachers, daycare staff, caregivers for adults. The PWSDK edits leaflets on topics in PWS supported by the CABPWSDK. The regular contact in the CABPWSDK group secures continuous updating about PWS, about ongoing research and meetings in DK and abroad. The CABPWSDK can propose new projects supported by the PWSDK. **Conclusion:** The PWSDK and Danish families appreciate the work by the CABPWSDK, and group members find the contact to the PWSDK and the interdisciplinary contact important ensuring updated and qualified knowledge on PWS for the benefit of the patients. The described model is to be recommended.

O50 - 1933

Normative data of the 6-minute walk test in healthy boys aged 5–12 years and correlations with anthropometric variables and myometry

Goemans N, Klingels K, Boons S, Verstraete L, Peeters C, van den Hauwe M, Feys H, Buyse G. Child Neurology, University Hospitals Leuven, Leuven, Belgium – nathalie.goemans@uzleuven.be

Objectives: The aim of this study was to improve our insights on the 6-minute walk test (6MWT), an outcome measure currently used in clinical trials for ambulant Duchenne patients, by (1) generating normative data in healthy boys aged 5–12 years, and (2) describing the relation with anthropometric variables and myometry. **Material and methods:** Participants ($n=442$) were recruited in eight age categories between 5 and 12 years. Each boy walked 6 minutes (timed with stopwatch) along a 25 meters tape line. Maximal isometric contractions for knee flexion and extension were recorded with a hand-held myometer. **Results:** For the total group, the 6MWT distance was $582.2\text{m} \pm 88.2$ (mean \pm SD) with a mean velocity of 97m/min. The 6MWT distance increased significantly with age, from $478.0\text{m} \pm 44.1$ at age 5, to $650.0\text{m} \pm 76.8$ at age 12, with the steepest increase between 5 and 8 years. Percentile curves of the 6MWT were developed for age and height. Predicted values were calculated according to available reference equations (Geiger and Ben Saad), indicating an overestimation by those equations. Correlations with anthropometric variables were fair to good (age $r=0.62$, height $r=0.58$, weight $r=0.47$). Myometric variables (sum flexors, sum extensors, total sum) showed correlations of 0.46, 0.50, 0.52, respectively. Interestingly, when dividing into two age categories (5–8 years, 9–12 years), these range of correlations only applied to the younger age group, while in the older age group correlations were poor ($r=0.08$, 0.16, 0.15 respectively). **Conclusion:** The percentile curves according to age and height provide a useful tool in the assessment of ambulatory capacity in boys with variable diseases and more specifically in Duchenne patients. While significant correlations were found with anthropometric variables and myometry in the younger age group, further study is needed to define the additional factors influencing 6MWT, especially in the older age group.

O51 - 2115

Clinical presentation and genetic causes of Charcot Marie Tooth disease in a paediatric cohort

Niermeijer JMF, Rustenburg L, Van Ruissen F, Verhamme C, Baas F, Poll-The BT. Academic Medical Centre, University of Amsterdam, The Netherlands – j.f.niermeijer@amc.uva.nl

Introduction: Charcot-Marie-Tooth disease (CMT) is the overlapping term for a group of inherited neuropathies. To date more than 45 responsible genes have been described. With the increasing knowledge of the underlying genetic mechanisms, detailed descriptions of the different phenotypes become more important. **Methods:** A retrospective cohort study of children with CMT was performed at the department of paediatric neurology of the Academic Medical Centre Amsterdam, a tertiary referral centre for children with neuromuscular disorders. Patients were classified based on the clinical signs, family history, electrophysiological investigations and genetic testing results. **Results:** Forty-six children with CMT were included. In 23/46 patients NCS were performed. In 29/46 patients (63%) a genetic diagnosis was confirmed. 32 patients were classified as CMT1: 21 PMP22 duplications, 2 MPZ, 3 EGR2 and 1 GJB1 mutation. 14 patients were classified as CMT2. Only in 2/14 a genetic cause was identified yet: 1 GARS and 1 MFN2 mutation, the remainder is still under investigation. The median age of onset was 1.75 years (IQR 1.3 – 3.75 y). Gait disturbances were present in 52% and the most frequent presenting symptom. Three patients developed the first-

severe signs of CMT during a course of chemotherapy with vincristine. Only one patient in this cohort had mental retardation, although 5 others had behavioural or learning problems necessitating special schooling. Disease progression and clinical differences between the genetic subtypes will be described in detail. **Conclusion:** The age at first presentation in this cohort was more early than has been generally assumed. Children with CMT do very often present with the first symptoms during the first three years of life, and families at risk ask for genetic evaluation already early in life. There remains a substantial proportion of CMT2 patients without a genetic diagnosis. Additional sequencing is performed for these patients at this moment.

O52 - 2063

Spectrum of cerebellar and anterior horn cell degeneration caused by EXOSC3 mutations

Burglen L, Nguyen S, Cances C, Cuisset JM, Julia S, Metreau J, Lion-François L, Legall A, Amsallem D, Gelot A, Billette de Villemeur T, Rodriguez D. *Reference Center for Cerebellar Malformations and Congenital Diseases and Department of Genetics, AP-HP, Hôpital Trousseau and INSERM U676, Paris, France – lydie.burglen@trs.aphp.fr*

Pontocerebellar hypoplasia (PCH) associated with spinal cord anterior horn cell loss has been named PCH type 1 by Barth in 1993. PCH1 is an autosomal recessive disease characterized by an early-onset antenatal onset, with arthrogryposis and limited survival. Recently mutations of the EXOSC3 gene were reported in classical as well as in mildly affected PCH1 patients. **Objectives:** to describe the phenotype of patients affected with cerebellar and anterior horn cell degeneration caused by EXOSC3 mutations. **Patients and methods:** Clinical data and MRI from 8 patients affected with cerebellar and anterior horn cell degeneration related to EXOSC3 mutations were reviewed. **Results:** Two sibs and another patient fit the diagnosis of PCH1: they were affected from birth and presented with hypotonia, proximal muscular deficiency, respiratory and swallowing difficulties. Electromyogram showed neurogenic changes. In the familial case, PCH was evident on the MRI performed at 4 months in the older child but no change was noted at day 4 in the younger. Death occurred at, respectively, 11 months, 15 days and 4 months. In 2 patients, neuropathology showed a severe atrophy of the pons, cerebellum and anterior horn. Patients 4 to 7 presented with a progressive disease which began at 3–5 months. They had severe progressive hypotonia, proximal limb weakness and amyotrophy, nystagmus, spasticity, and increased tendon reflexes. MRI showed progressive cerebellar atrophy and/or cerebellar hypoplasia without brainstem involvement. Patient 8 had a non-progressive psychomotor retardation with PCH on MRI and he was able to sit in the first years of life. At age 10, he started to decline and presented with spastic paraplegia and proximal weakness, nystagmus and respiratory and swallowing difficulties. **Conclusion:** The gene EXOSC3 is a major PCH1 gene but is responsible for others, milder, phenotypes of cerebellar and anterior horn cell degeneration with cerebellar atrophy without brainstem involvement.

O53 - 1995

Long-term outcome after vegetative state due to near-drowning and quality of life of the families

Kluger G, Kirsch A, Hessenauer M, Lahl O, Steinbeis von Stülpnagel C. *Clinic for Neuropediatrics and Neurorehabilitation, Epilepsy Center for Children and Adolescents, Schöen Klinik Vogtareuth, Germany – gkluger@schoen-kliniken.de*

Objectives: Discussions between emergency medicine, intensive care, rehabilitation and palliative care concerning children in vegetative state lack information about the long-term prognosis

and quality of life (QoL) of their families. **Methods:** At two different time points, we investigated long-term outcome and QoL of the families of 85 children, who were in vegetative state 4 weeks after a near-drowning event, and who were transferred to our institution for early-phase rehabilitation in the years 1986–2001. Assessment 1 was performed in 2001 as anonymous questionnaire, assessment 2 in 2010–2011 as structured telephone interview with both parents separately. Additional interviews were carried out with one parent of children who survived concerning outcome according to Remi-Pro®. **Results:** Response rate of assessment 1: 53%; follow-up: 6 months – 15 years after the accident (mean: 5 years). Assessment 2 in 53/85 children (62%) and 99 parents with a mean follow-up of 15 years. **Outcome:** 14 children had died (26%), 5 were in sleep-wake level (9%), 10 in perception level (19%), 13 in communication level (24%), 2 in independence level (4%), 4 in group level (7%), and 5 in participation level (9%). Many parents reported massive and persisting feelings of guilt. When asked whether it would have been better that their child had died immediately after the accident despite resuscitation, 58/99 parents (59%) answered “no”. Independent of the outcome in their children the majority of parents reported a high level of satisfaction with their lives. **Conclusion:** Our results are in accordance with other investigations in chronic diseases of a non-linear relationship between physical health status and QoL. Our results can be useful for defining individual therapeutic goals and also support rehabilitation professionals in communicating confidence that long-term QoL of families with children in vegetative state due to acquired brain injuries is often good.

O54 - 1853

Manifestations of Cowden syndrome in childhood

Schieving JH, Padberg GWAM, Willemsen MAA. *Radboud University Hospital Nijmegen, Department of Pediatric Neurology Nijmegen, The Netherlands – j.schieving@neuro.umcn.nl*

Cowden syndrome (CS) is caused by a heterozygous germline mutation in the PTEN gene on chromosome 10. It is also called PTEN-hamartoma-tumor syndrome because of the high risk to develop benign and malignant tumors in thyroid, breast, endometrium, colon and urogenital tract mainly at adult age. Many attention has been paid to adults with CS, but little to children with this syndrome. We have seen 24 children with CS on our outpatient clinic of pediatric neurology and present their manifestations here. 50% of the children had an inherited mutation of one of the parents, the other 50% had a de novo mutation. All had birthweight above the 1st percentile, 50% even above the 2nd percentile. Head circumference was progressive in the first year of life and stabilized thereafter. All had also scaphocephaly. Gross motor milestones were delayed, but all children were walking independently at the age of three years. They all had hypotonia and suboptimal gross motor functioning. Verbal expression is a strong point of most children with CS. 40% of the children needed a special education school. Upper respiratory infections were common in infancy. Remarkable was the sweating during the night. Only one child developed a malignancy: an atypical meningioma.

O55 - 1566

Incidental white matter lesions in children presenting with headache

Bayram E, Topcu Y, Karaoglu P, Yis U, Cakmakci HG, Hiz SK. *Dokuz Eylul University Hospital, Division of Pediatric Neurology Izmir, Turkey – dr.erhanbayram@yahoo.com*

Aim: We aimed to describe the prevalence and significance of white matter lesions detected on magnetic resonance imaging in children with headache. **Material and methods:** Children who

were admitted with the complaint of headache and had a neuroimaging between December 2007 and June 2012 were included in the study. The patients with nonspecific white matter lesions were called for a control visit and current status of headache and neurologic findings were determined. **Results:** A total of 941 patients were included in the study. 61% of the patients had cranial neuroimaging. 8.2% had only cranial computed tomography, 7.5% had cranial cranial computed tomography and cranial magnetic resonance imaging and 84.3% had only cranial magnetic resonance imaging. The rate of incidental nonspecific white matter changes detected in our study group was 23/527 (4.4%) 14 (60.9%) had migraine without aura, eight (34.8%) had tension type headache and one (4.3%) had migraine with aura. All patients with nonspecific white matter changes on magnetic resonance imaging showed normal psychomotor development. The physical and neurologic examinations of all patients were normal. The mean clinical follow up period of the patients was 16.8 ± 17.3 months. No patients showed neurological deterioration during the follow up. The white matter lesions were supratentorial in all patients. The mean size of the lesions was 5.1 ± 4.5 mm. Repeated radiological evaluations were performed in 11 (47.8%) of the patients. No new white matter lesions were detected in control magnetic resonance imaging's during follow up. **Conclusion:** Non specific incidental white matter changes may be seen in children with headache. Normal clinical follow up the absence of evident benefits from repeated imaging studies, we suggest that repeated imaging studies are not warranted in every patient, and should be tailored according to clinical course.

O56 - 1721

The role of probabilistic tractography in the surgical treatment of pediatric brainstem gliomas

Máté A, Kis D, Vörös E, Barzó P. Department of Neurosurgery, University of Szeged, Szeged, Hungary – mateadree@gmail.com

Objective: Brainstem gliomas are often considered to be inoperable due to the high surgical risk. However even partial resection of the tumor may considerably increase the efficacy of radiotherapy and can extend survival. This is of special importance in the case of pediatric brainstem gliomas. The localization of the most important anatomical components of the brainstem may significantly decrease surgical risk. Probabilistic tractography is based on diffusion tensor magnetic resonance imaging and enables probabilistic mapping of white matter pathways. Our aim was to investigate whether probabilistic tractography is capable to segment the brainstem by its connections and localize the main ascending and descending pathways in healthy individuals and children with brainstem tumor. **Material and methods:** 10 children (age range: 5–17 years) with brainstem gliomas and 15 healthy volunteers (age range: 20–30 years) were included in the study. We performed segmentation of the pons and the midbrain (by their connections to the primary motor cortex, sensory and medial thalamus) and ran fiber tracking from the posterior limb of the internal capsule and the dorsolateral pons. **Results:** Our results revealed that segmentation of the brainstem by probabilistic tractography correlates well with brainstem anatomy. By fiber tracking we could localize motor, sensory and ascending reticular activating system pathways and unequivocally differentiate between expansive (n=6) and infiltrative (n=4) tumors. Navigation surgery was performed in 5 cases (2 subtotal and 3 partial resections). The patients' neurological status did not deteriorate postoperatively. **Conclusion:** According to our results, probabilistic tractography seems to be a promising tool in the preoperative investigation of pediatric brainstem gliomas.

Friday 27 September 2013

Parallel session 10: Movement disorders 2

Chairs: Mary King and Sameer Zuberi

O57 - 1880

Progressive ataxia, hyperkinetic movement disorder with myoclonic jerks and falls in a toddler: think of cerebral folate deficiency!

Toelle SP, Wille D, Schmitt B, Scheer I, Thöny B, Plecko B. University Children's Hospital Zurich, Division of Neurology, Switzerland – sandra.toelle@kispi.uzh.ch

Cerebral folate deficiency (CFD) is characterized by decreased concentrations of 5-methyltetrahydrofolate (5-MTHF) in CSF in the context of normal systemic folate metabolism. Mutations in the FOLR1 gene lead to a specific inability to transport 5-MTHF across the blood-brain barrier, resulting in progressive, severe neurological sequelae. A 5-year-old boy presented with progressive ataxia of trunk and limbs, a hyperkinetic movement disorder with myoclonic jerks, head stereotypies associated with abnormal eye movements, and daily attacks with sudden falls. These falls were to some extent triggered by body care as blowing his nose, washing his face or hands. They occurred up to more than 20 times per day, resembling myoclonic atstatic seizures with a rapid, brief flexion of the neck and the trunk and extension of the arms, reminiscent of infantile spasms. They lasted only 1–2 seconds but led to head injuries and were refractory to anticonvulsive treatment. The patients' cognitive and motor abilities deteriorated and he became very impulsive. MRI of the brain revealed hypomyelination and mild cerebellar atrophy, CT showed calcification within the basal ganglia (not visible on MRI), and 5-MTHF in the spinal fluid was measured 0.0 nmol/l whereas plasma folate was normal. The diagnosis of folate transporter deficiency was confirmed by identification of the homozygous nonsense mutation p.R204X in the FOLR1 gene, a mutation that was previously described. Treatment with oral and intravenous folinic acid resulted in impressive brain growth within months documented on imaging and obvious clinical improvement. Young children with ataxia, hyperkinetic movement disorder and seizures, typically combined with abnormal myelination should be screened for CFD, particularly in regard to the treatment option of this severe neurometabolic disorder. Calcifications within the basal ganglia can be a diagnostic finding not reported so far in the context of folate transporter deficiency.

O58 - 2017

Gabapentin can improve dystonia severity, transfers, sitting, sleep, mood and pain in children

Liow N, Marianczak J, Kirk E, Tomlin S, Lumsden D, Gimeno H, Kaminska M, Perides S, Lin JP. Complex Motor Disorders Service Children's Neurosciences Centre, Evelina Children's Hospital, Guy's and St. Thomas' NHS Foundation Trust, UK – natasha.liow@gmail.com

Objectives: This report examines the precedence and efficacy of gabapentin use with a literature review and retrospective cohort study. **Methods:** Pubmed and embase literature reviews examined gabapentin use in movement disorders, doses used, adverse effects and graded according to the Oxford CEBM Levels of Evidence criteria. Case-notes of children receiving gabapentin in the last four years were reviewed. Dystonia severity and functional levels were graded using the Dystonia Severity Assessment Plan (DSAP) and International Classification of Functioning, Disability and Health, Children & Youth version (ICF) respectively, before and after the use of gabapentin. ICF domains included seating tolerance, involuntary muscle contractions, sleep amount

and quality, and mood, which were graded on a scale from 0 (no impairment/difficulty) to 4 (complete impairment/difficulty). These grades were analysed using Wilcoxon signed-rank tests. **Results:** 41 reports described the use of gabapentin in the treatment of movement disorders. Highest levels of evidence were found in the treatment of Restless Leg Syndrome: a recent meta-analysis found improvement of symptoms over placebo. Positive reports were also seen in orthostatic tremor, essential tremor and dystonia but limited evidence for gabapentin use in children with dystonia and chorea. 49 children were identified aged 2–18 years. A significant decrease in DSAP ratings was seen following gabapentin treatment (mean before: 2.73, post: 1.68, $Z=-4.682$, $p<0.01$). All selected ICF category means and median values improved significantly, with a median gabapentin dose of 51.5mg/kg/day (SD: 37.0) compared to a median dose of 23.7mg/kg/day (SD: 13.1) in 15 children receiving gabapentin for neuropathic pain. No unexpected side-effects were reported at this higher dose. **Conclusion:** Gabapentin appears to improve dystonia severity, transfers, sleep amount and quality, sitting tolerance, agreeableness/mood, tone, involuntary contractions and pain. Median doses for successful management of dystonia was twice that needed for neuropathic pain in children, however, further research is required.

O59 - 1906

Alternating hemiplegia and ATP1A3 gene: evolution of 12 cases into adulthood. Genotype–Phenotype correlations

Ramirez-Camacho A, Panagiotakaki E, Poncelin D, Nicole S, Lesca G, Arzimanoglou A. *Epilepsy, Sleep and Paediatric Neurophysiology Department, Femme Mère Enfant Hospital, University Hospitals of Lyon (HCL), France – aliaraca@hotmail.com*

Introduction: Mutations in ATP1A3 gene as the aetiology of 75% of cases of alternating hemiplegia of childhood (AHC) is a recent major discovery. Natural history and evolution of the disease into adulthood remain topics of debate and of future research. **Objectives:** To assess evolution 6 years after the last clinical update of French patients, previously included in the European Network for Research on Alternating Hemiplegia (ENRAH) Database. **Methods:** Patients were contacted through the French Parents Association (AFHA) and they were examined and filmed during its annual meeting. **Results:** At this occasion 18 patients were re-evaluated (12 adults, 6 children) and 6 cases (all children) were new. Median age of the 12 adult patients was 27.5 years (18–38 years). In contrast with hemiplegic attacks, 50% of the adult patients presented with an increase in frequency of the dystonic attacks that became their main type of paroxysmal phenomena. Five patients experienced severe status epilepticus frequently time-related to gait deterioration. Half of the cohort had lost the ability to walk independently and were wheel chair-bound. Only one of them was not epileptic. Seven of twelve patients had a stable clinical course after 6 years while three patients considered “to still make some progress”. Mutations in ATP1A3 gene were identified in nine patients, two had no mutations and genetic analysis is in process in one patient. **Conclusion:** Our previous results (Panagiotakaki et al, 2010) suggested individual variability in patients with AHC, but a rather steady clinical course in adults when studied as a group. Longer follow-up of this cohort of adult patients shows that motor regression could be frequent, notably in patients with status epilepticus. In light of the discovery of ATP1A3 gene mutations as the aetiology of AHC, genotype-phenotype correlations will be presented and discussed.

O60 - 1707

Ataxia and areflexia precede progressive myoclonus ataxia in young children with GOSR2 mutation

van Egmond ME, Verschuuren-Bemelmans CC, Nibbeling EA, Elting JW, Sival DA, Brouwer OF, de Vries JJ, Kremer HP, Sinke RJ, Tijssen MA, de Koning TJ. *Department of Neurology, University of Groningen, University Medical Center Groningen, The Netherlands – m.e.van.egmond@umcg.nl*

Objectives: Progressive myoclonus ataxia is a descriptive diagnosis characterized by myoclonus, ataxia and infrequent seizures. Possible underlying etiologies include Unverricht-Lundborg disease and mitochondrial encephalopathy, but often the etiology cannot be determined. Recently, a homozygous mutation in the GOSR2 gene (c.430G>T, p.Gly144Trp) was reported in twelve patients with childhood-onset progressive ataxia and myoclonus, denominated as progressive myoclonus epilepsy. The aim of this study is to provide longitudinal clinical descriptions of the natural history, video documentation, neuroimaging and neurophysiological data of five Dutch patients with GOSR2 mutations. **Material and methods:** We evaluated five patients with cortical myoclonus, ataxia and areflexia caused by GOSR2 mutations. **Results:** All five patients (aged 7–26 years) had the same homozygous mutation in GOSR2. All originated from the northern Netherlands and showed a remarkably homogeneous phenotype with ataxia, areflexia, myoclonus and relatively mild epilepsy. Four patients presented with symptoms of unsteady gait and clumsiness between 2 and 3 years of age. Areflexia and ataxia preceded the multifocal myoclonus and generalized myoclonic seizures. Myoclonus and ataxia have been relentlessly progressive over the years. Electroencephalography showed cortical spikes preceding myoclonic jerks and a prominent photoconvulsive response, indicating cortical reflex myoclonus. Electromyography revealed signs of sensory neuronopathy and/or anterior horn cell involvement. **Conclusions:** We present new, longitudinal data of the evolution of the GOSR2 phenotype from infancy to adulthood. So far, GOSR2 mutations have been considered in the differential diagnosis of patients with progressive myoclonus epilepsy. Based on the presented data, we would advise to consider mutation analysis of GOSR2 in children and adolescents with progressive myoclonus ataxia as well as in young children with progressive ataxia and areflexia, a clinical picture resembling Friedreich's ataxia.

O61 - 1802

Tyrosine hydroxylase deficiency. The Greek experience

Pons R, Syrengelas D, Gkika A, Dinopoulos A, Orfanou I, Serrano M, Artuch R, Youroukos S. *Agia Sofia Hospital, Athens, Greece – roserpons@med.uoa.gr*

Objectives: The objective of this video presentation is to illustrate the evolution of the motor development of 4 patients with tyrosine hydroxylase deficiency. **Material and methods:** All patients were diagnosed based on CSF biogenic amine analysis and sequencing analysis of the TH gene that revealed a homozygous pathogenic mutation in exon 6 (c.707T>C). All patients were started with L-Dopa at 0.5–1 mg/kg/d. Doses were gradually increased according to tolerance and clinical response. The Gross Motor Function Measure was performed at several points in time. **Results:** All patients showed improvements in motor development that were objectively quantified on the Gross Motor Function Measure. Patients showed L-dopa induced dyskinesias of variable intensity and they were managed mainly by a slow and gradual increase of the L-dopa dose. Two patients were also managed with amantadine. **Conclusions:** Tyrosine hydroxylase deficiency is a treatable disease. L-dopa induced dyskinesias probably due to dopamine receptor hypersensitivity are toler-

able with a slow titration of the L-dopa dosing together with amantadine in some cases.

Parallel session 11: Neurometabolic disorders

Chairs: Rudy Van Coster and Marjo van der Knaap

O62 - 1673

The natural history of late infantile CLN2 disease: striking homogeneity of clinical progression in two independently obtained large clinical cohorts

Schulz A, Nickel M, Downs M, Mezey J, Landy H, Sondhi D, Jacoby D, Wittes J, Crystal R, Kohlschütter A. *Children's Hospital, University Medical Center Hamburg-Eppendorf, Hamburg, Germany – anschulz@uke.de*

Late infantile CLN2 disease (CLN2) is a lysosomal storage disease caused by deficient tripeptidyl-peptidase 1 activity and characterized by progressive psychomotor and language decline. The clinical course was originally described quantitatively in a patient cohort using a disease-specific rating scale. Recently, this cohort has been expanded to 29 genetically confirmed patients. This new study focused on (i) first symptoms to support early diagnosis, (ii) prospective longitudinal data acquisition covering a period of 26 years (1986 to 2012), and (iii) quantification of rate of decline as a means to measure disease progression. Results of the study showed the following: (1) Early symptoms of CLN2 comprise delayed language acquisition and seizures (73% of patients; median age of onset 37 months). (2) Disease progression was measured longitudinally by the sums of the 3-point motor and language subscales of the Hamburg-LINCL score. In this cohort, onset of neurological decline occurred at a median of 39 months of age (lower to upper quartile 35–44 months; range 14–84 months). Onset of symptoms leads to a rapid, progressive clinical decline with a linearized mean rate of decline of 2.2 units/year ($SD \pm 1.1$). Slowly progressing patients were uncommon and mostly related to unusual genotypes. The age-specific level of functioning was similar in an independent dataset of 62 observations in 43 patients from the Weill Cornell CLN2 cohort. Further, quantification of CNS MRI parameters of the Weill Cornell subjects showed similar status. This analysis of CLN2 natural history shows a high degree of homogeneity in the population across time and geography and supports the use of such data as natural history controls in future therapeutic studies. The data underscore the rapid decline in this disease, and therefore the importance of early diagnosis for potential therapies. CLN2 should be considered in young children with new onset seizures of uncertain etiology.

O63 - 1788

Diagnosing the tip of an iceberg in a potentially treatable neurometabolic disorder: cerebral creatine deficiency syndromes

Haliloglu G, Oguz KK, Onol S, Tokatli A, Coskun T, Topcu M. *Hacettepe University Children's Hospital, Department of Pediatric Neurology, Turkey – gtuncer@hacettepe.edu.tr*

Cerebral creatine deficiency syndromes (CCDS) include autosomal recessively inherited synthesis defects (GAMT and AGAT deficiency), and X-linked creatine transporter defect (CRTR). These disorders are characterized by mental retardation, expressive aphasia, autistic behaviour, epilepsy, and movement disorders, and represent a group of neurometabolic diseases, which are potentially treatable. We would like to present clinical and neuroimaging features of 6 children diagnosed with GAMT deficiency, from 5 unrelated families, with long term follow-up (2–6 y) on oral creatine supplementation therapy. In our cohort (F: 2, M: 4)

mean age at diagnosis was 11.5 months (6–18 months), mean age at diagnosis was 6.2 y (17 months–11y). Delay in developmental milestones/retardation, autistic spectrum disorder, stereotypical movements, and speech delay were present in all of the patients, and febrile seizures (n= 3), hypoxic insult at birth (n= 2), hypotonia (n= 2), movement disorder (n= 1), indirect hyperbilirubinemia (n= 1), epileptic encephalopathy (n= 1) were additional features. There were increased urinary guanidinoacetate levels (tandem-MS) (n= 6), basal ganglia involvement (n= 4), cerebral creatine deficiency demonstrated by MRS (n= 6), and diagnosis was confirmed by GAMT mutations (n= 5). Neuroimaging findings including basal ganglia involvement and lack of creatine peaks were normalized on 6th month of oral creatine supplementation. Epilepsy, behavioural features, movement disorder responded well to treatment, and time lag between onset of symptoms and age at diagnosis correlated with degree of mental retardation and expressive language (n= 4). Developmental and expressive language delay, hypotonia, seizures, movement disorder, autistic behaviour are core features of CCDS, and this potentially treatable neurometabolic disease should be included in the differential diagnosis. MR-spectroscopy serves as a valuable tool for both diagnosis and monitorization of therapy.

O64 - 1920

Zellweger spectrum manifestations in adulthood

Berendse K, Engelen M, Wanders RJA, Waterham HR. *Poll-The BT. Department of Paediatric Neurology, Emma Children's Hospital, Academic Medical Center, Amsterdam, The Netherlands – k.berendse@amc.uva.nl*

Background: Zellweger spectrum disorders (ZSDs) are peroxisomal biogenesis disorders (PBDs) and represent a continuum of different phenotypes. This spectrum is clinically characterized by a variable severity of global neurological involvement, dysmorphism, visual impairment, sensorineural deafness and other systemic manifestations. ZSD patients with severe disease manifestations usually do not survive their first-year of life and patients with a milder phenotype can survive into their first or early second decade. Common biochemical markers in plasma are elevated very long chain fatty acids, bile acid intermediates and branched-chain fatty acids. Furthermore there is an impairment in the plasmalogen biosynthesis. As a result of improved biochemical and clinical characterization, more patients with milder forms of ZSDs are diagnosed. Furthermore, as a consequence of improved health care, more patients will survive and reach adulthood. Currently mutations in PEX-1, -2, -3, -6 and -10 are already associated with milder clinical phenotypes. However an overview of clinical manifestations in adult ZSD patients is currently lacking. **Objective:** To give an overview of the clinical and biochemical spectrum in adult ZSD patients. **Methods:** This retrospective study included 10 ZSD patients, regularly followed-up by our hospital teams for neurological and non-neurological symptoms. **Results:** In our cohort, all patients had a severe visual- and hearing- impairment. Verbal communication was possible in 7/10 and the majority is able to walk independently. Surprisingly, none of the patients had epilepsy. A cerebellar syndrome and pyramidal signs were seen in 3 patients and 5 suffered from peripheral polyneuropathy. Normal MRI was seen in 2/10. We only noted progressive leukoencephalopathy in 1 patient. In some patients, we also noticed normalization of abnormal peroxisomal markers in plasma (e.g. C29 and pipecolic acid). **Conclusion:** Relatively mild ZSDs with prolonged survival is not uncommon in ZSDs. In addition, mild patients can present with normal peroxisomal markers.

O65 - 1997

Hematopoietic stem cell transplantation in juvenile metachromatic leukodystrophy

Groeschel S, Bley A, Kühl JS, Kehrer C, Müller I, Kohlschütter A, Weschke B, Krägeloh-Mann I. *Department of Pediatric Neurology & Developmental Medicine, University Children's Hospital, Tübingen, Germany – samuel.groeschel@med.uni-tuebingen.de*

Objective: Hematopoietic stem cell transplantation (HSCT) is thought to result in endogenous and continuous enzyme replacement in metachromatic leukodystrophy (MLD), a rare neurometabolic disorder. Former anecdotal HSCT reports indicated inconclusive results due to the variable natural course of later onset forms. **Patients and methods:** 23 patients with juvenile MLD had undergone HSCT in 3 German centers between 1991 and 2011. Their motor and cognitive functions as well as MRI changes were compared to 25 untreated MLD patients. “Stable disease” was defined as losing not more than one level in gross motor function (GMFC-MLD) and less than 15 IQ points (1 SD). **Results:** Among HSCT patients, 4 children died from transplant-related mortality; two patients with rapid MLD progression at HSCT deceased after 1.5 and 8.6 years. Although survival rates after HSCT did not differ from the non-treated group, neurological outcome was improved. Patients transplanted in the presymptomatic and early symptomatic stage were more likely to show “stable disease” (not significant, $p=0.1$, chi square). MRI severity scores at HSCT were significantly lower in patients with “stable disease” than in those who deteriorated ($p=0.007$, M-W-test). In comparison to untreated controls, HSCT patients with “stable disease” had lower MRI scores at their last exam ($p=0.013$, M-W-test). More importantly, 65% of untreated patients progressed to GMFC-MLD level 5 (only head control possible) 10 years after disease onset, whereas all of the HSCT patients with “stable disease” retained the ability to sit independently (level 3 or better) ($p=0.025$, log-rank test). **Conclusions:** Children with juvenile MLD have a reasonable chance to show “stable disease” after HSCT when transplanted at an early stage with limited MRI changes. These patients have a better motor outcome and MRI scores compared to untreated patients. However, benefit and risk have to be carefully balanced considering the relevant transplant-related mortality.

O66 - 1608

Hypomyelination and congenital cataract: three additional patients carrying novel mutations

Biancheri R, Traverso M, Rossi A, Gazzero E, Assereto S, Baldassari S, Fruscione F, Abdalla EM, Fassad MR, Ruffinazzi G, Savasta S, Zara F, Minetti C. *Department of Neuroscience, Istituto Giannina Gaslini, Genova, Italy – roberta@biancheri.com*

Objectives: to describe three additional patients affected by Hypomyelination and congenital cataract (HCC, OMIM #610532) carrying novel mutations in the FAM126A gene. HCC is a rare autosomal recessive disorder characterized by congenital cataract, progressive neurologic impairment, and myelin deficiency in the central and peripheral nervous system (Zara F et al, 2006; Biancheri R et al, 2007). **Material and methods:** a 19-month-old girl from Morocco (patient #1) and two female siblings aged 7 and 4 years respectively from Egypt (patients #2 and #3) underwent clinical, neurophysiological, neuroradiologic and molecular studies. **Results:** Patient #1 showed bilateral congenital cataract and mild developmental delay. Nerve conduction velocity studies were normal. Brain MRI showed diffuse supratentorial hypomyelination. Molecular analysis identified the homozygous variant c.169T>C determining the substitution of cysteine with arginine in position 57 of the protein. Patients #2 and #3 showed congenital cataract and developmental delay, being unable to walk without support. Pyramidal and cerebellar signs were evi-

dent at neurological examination and peripheral nervous system involvement was depicted by neurophysiological studies. Brain MRI showed diffuse supratentorial hypomyelination with superimposed areas of increased water content. Molecular analysis identified a microdeletion c.100-101delAA which causing a premature stop (p.Lys33Glufs*17) in the protein. **Conclusions:** The clinical picture of the first patient is consistent with a mild form of HCC. Interestingly, this is the second patient in whom peripheral nervous system was not involved. It is likely that the identified missense mutation has less detrimental effects if compared with splice-site mutations or deletions. On the other hand, the phenotype of the siblings is consistent with the classical HCC form. This report further confirms that HCC is not uncommon in the Mediterranean area. The peculiar clinical and magnetic resonance findings are useful to properly address molecular investigations to obtain the correct diagnosis.

O67 - 2165

Phenotypical variation in vanishing white matter disease

van der Lei HDW, Gerver JAM, van Berkel CGM, van der Knaap MS. *Child Neurology, VU University Medical Center, Amsterdam, The Netherlands – h.vanderlei@vumc.nl*

Objective: Vanishing white matter (VWM) is an autosomal-recessive leukoencephalopathy characterized by slowly progressive ataxia and spasticity with additional stress-provoked episodes of rapid deterioration. VWM is caused by mutations in the genes encoding eukaryotic initiation factor 2B, which is pivotal in protein translation. The disease onset, clinical severity and disease course of VWM patients vary greatly. Although VWM was initially recognized as a disorder of young children, it has become clear that the variation in disease severity is large. Severe forms start in the antenatal or early infantile period and lead to early demise. Much milder variants start in adolescence or adulthood and are characterized by slow disease progression. Large studies on phenotypical variation are scarce. **Methods:** We performed a large cross-sectional observational study and included all available patients from our genetically confirmed VWM patient database. We used clinical questionnaires on robust parameters to collect information on disease course. **Results:** From our database of 228 patients with VWM, 5 patients were excluded because of co-morbidity. 102 patients were female. Mean age of first symptoms was 7.5 years (range 0–54.0). Mean age at diagnosis was 14.4 years (range 0–59.3). Mean age of death (54 patients) was 9.1 years (range 0.1–39). We divided the population into four age of onset categories; antenatal-infantile ($0 \leq 2$ years), early-juvenile ($2 \leq 6$ years), late-juvenile ($6 \leq 18$ years), and adult onset (>18 years). Young patients had a more severe disease course characterized with earlier fatality, loss of independent walking, vision and speech, more involvement of other organs, epilepsy, and higher occurrence of coma episodes. The younger the more sensitive to stress. Female patients were older and had milder disease. **Conclusions:** The clinical variation in VWM is extremely wide. The younger the first neurological symptoms appear, the more severe the disease course is. Females tend to have less severe disease.

O68 - 2091

Neurological phenotypes in Niemann-Pick type C disease: unraveling an overlooked neurometabolic disorder

Lourenço CM, Van der Linden V, Bonfim D, Ribeiro E, Marques Jr W. *University of Sao Paulo, Sao Paulo, Brazil – charlesgenetica@gmail.com*

Objective: Niemann-Pick type C disease (NP-C) is a rare inborn error of metabolism caused by defective intracellular transport of cholesterol. It can present with a wide range of neurologic

findings, some of them quite non-specific. This study discusses the neurological features of NP-C. **Design:** Retrospective cohort study. **Method:** A retrospective study, with review of neuroimaging and neurophysiological data, was carried out of Brazilian NP-C patients diagnosed in the last 6 years. **Results:** Thirty-eight patients were included in the study, in 25/38 NP-C was confirmed by filipin staining (13 patients required molecular analysis). The following clinical types were seen seen: perinatal (5), infantile (15) and juvenile (18). Prolonged neonatal jaundice was a common feature and 3 patients were diagnosed with “neonatal hepatitis”. Patients with the perinatal form usually had hypotonia as the main feature, followed later by spasticity. Infantile patients usually had a “symptom-free” period, followed by relentless neurodegeneration: cerebellar ataxia, dystonia, learning disabilities and behavior changes were commonly seen in this group. Juvenile patients, presented mostly with progressive psychiatric changes and extrapyramidal features. Ocular abnormalities were seen in 30 patients (mostly, vertical supranuclear gaze paralysis). Leukoencephalopathy and progressive cerebral/cerebellar atrophy were the main MRI features. Gelastic cataplexy, although present only in a subset of the infantile/juvenile patients, is a relatively specific finding for NP-C. **Conclusion:** Neurological manifestations in NP-C patients are extremely variable, even in the same family. Better understanding of the natural history of the disease is crucial for evaluation of potential therapeutic approaches in such devastating disorder.

O69 - 1973

MRI in the diagnosis of peroxisomal disorders when laboratory tests fail

van der Knaap MS, Ferdinandusse S, Vanderver A. *Child Neurology, VU University Medical Center, Amsterdam, The Netherlands* – ms.vanderknaap@vumc.nl

Objectives: Peroxisomal blood tests are generally considered to be conclusive. We observed several patients with a clinical and MRI phenotype suggestive of a peroxisomal defect, but no convincing abnormalities in peroxisomal blood tests. Brain MRI showed typical abnormalities as observed in different variants of peroxisomal disorders. Our aim was to evaluate the accuracy of this MRI diagnosis with further peroxisomal and molecular testing. **Material and methods:** We searched our database of unclassified leukoencephalopathies and found 18 such patients. We collected clinical data and scored available MRIs of these patients. We performed further peroxisomal studies in fibroblasts, including immunofluorescence microscopy analysis with antibodies against catalase, a peroxisomal matrix enzyme. We performed complementation analysis. We analyzed the suspected genes. **Results:** We confirmed the diagnosis of Zellweger spectrum disorder in 3 patients, D-bifunctional protein deficiency in 3 patients, and Refsum disease in the others. The clinical findings were within the spectrum known for these diagnoses. In the early onset peroxisomal disorders, sequential MRIs showed that the abnormalities started in the hilus of the dentate nucleus and superior cerebellar peduncles. Subsequently, the cerebellar white matter and brain stem tracts were affected, followed by the parieto-occipital white matter, splenium of the corpus callosum and posterior limb of the internal capsule. Eventually, all cerebral white matter became abnormal. The thalamus was typically affected as well. In patients with Refsum disease the cerebellar white matter was affected. **Conclusions:** If MRI reveals abnormalities suggestive of peroxisomal defects, negative peroxisomal blood tests do not exclude the diagnosis. DNA analysis of suspected genes or further tests in fibroblasts should be performed, most importantly immunofluorescence microscopy analysis with antibodies against catalase to stain peroxisomes.

O70 - 1720

Brain volumetry and clinical scoring in patients with CLN2 disease: a diagnostic tool to monitor disease progression

Löbel U, Nickel M, Nestrasil I, Sedlacik J, Kohlschütter A, Schulz A. *Department of Diagnostic and Interventional Neuroradiology, University Medical Center Hamburg-Eppendorf, Hamburg, Germany* – u.loebel@uke.de

Objectives: Brain atrophy due to neuronal loss is a striking feature of patients with late-infantile neuronal ceroid lipofuscinosis (CLN2), one of the most common degenerative brain disorders in childhood. A precise and quantitative description of disease progression is urgently needed in order to establish an evaluation tool for future experimental treatments. We measured the longitudinal development of gray matter (GM), white matter (WM) and CSF volumes and correlated those with the clinical course. **Material and methods:** Twenty-one MRIs of eight patients (3 male; 5 female; mean age, 6.9 ± 2.5 years) with genetically confirmed CLN2 were performed on a 1.5T scanner using a 3D T1-weighted magnetization-prepared rapid gradient-echo (MP-RAGE) sequence using the following parameters: TR/TE/TI/flip angle = 1900/2.97/1100 ms/15°; FOV, 256 mm; matrix, 256×176 ; slice thickness, 1 mm; 160 slices with whole brain coverage. Volumetric segmentation of the brain was performed with the Freesurfer image analysis suite. The clinical severity was assessed by the Hamburg late-infantile NCL-score, a disease-specific scoring system. **Results:** The volumes of overall supratentorial brain tissue, supratentorial cortical GM, volume of basal ganglia and thalami, cerebellar GM and cerebellar WM significantly decreased with age ($P < 0.01$), while the volume of the lateral ventricles increased ($P = 0.03$). Supratentorial WM volume did not correlate with age. A strong correlation with clinical scoring existed for all GM regions ($P < 0.01$) and for CSF volume ($P = 0.011$). **Conclusions:** Patients with CLN2 showed a highly homogeneous decline of GM and WM, and an increase of CSF volumes. The correlation of MRI parameters with age and the clinical score was stronger for the GM volumes as for CSF volumes. Decline of cortical GM volume seems to be the most sensitive parameter for assessment of disease progression and represents a potential sensitive outcome measure for evaluation of future therapies.

O71 - 2078

Brain gene therapy for metachromatic leukodystrophy

Sevin C, Roujeau T, Piguet F, Sondhi D, Colle MA, Raoul S, Deschamps JY, Bouquet C. *Inserm U986 Paris, Hopital Bicêtre, France* – caroline.sevin@inserm.fr

Metachromatic Leukodystrophy (MLD) is a lethal neurodegenerative disease caused by deficiency of Arylsulfatase A (ARSA). The most severe late-infantile form starts around 1–2 years, leading to death within a few years, without available treatment. Among potential therapeutic interventions, brain gene therapy could ensure rapid and sustained delivery of ARSA enzyme in the brain, a prerequisite to arrest the neurodegenerative process in due time. We have demonstrated efficiency and safety of intracerebral delivery of adeno-associated-vector serotype rh.10 encoding human ARSA (AAVrh.10/ARSA) in MLD mice. Particularly, sulfatide isoforms that accumulate specifically in oligodendrocytes of MLD mice were normalized after treatment. We have optimized and validated, in non-human primates, the neurosurgical procedure to allow simultaneous infusion of vector at 12 different brain sites, and demonstrated that the injection of AAVrh.10/ARSA (10EXP11 viral particles/hemisphere) results in significant ARSA overexpression in normal monkey, without any side effect. Toxicological studies have been achieved and we have obtained authorizations from regulatory agencies to move towards phase I/II tolerance and efficiency clinical trial that is opened for recruitment. This trial will enroll five children (age between 6 months

and 4 years) with early-onset forms of MLD, following specific clinical, neurocognitive and radiological criteria. AAVrh.10/ARSA vector will be administrated to 12 locations in the CNS, guided by brain imaging. Safety and efficiency parameters will be evaluated up to 2 years, a period that will be sufficient enough to assess the potential therapeutic efficiency of brain gene therapy in rapidly progressing forms of MLD.

Parallel session 12: Fetal and neonatal neurology

Chairs: Marc D'Hooghe and Linda De Vries

O72 - 1702

Concordance between head circumference growth and neurological impairment among four clinical presentations of microcephaly

Coronado R, Giraldo J, Macaya A, Roig M. *Hospital de Terrassa, Catalonia, Spain* – rcoronado@comb.cat

Our aim was to investigate correlations between head circumference (HC) growth and neurological impairment among four different clinical presentations of microcephaly in pediatric patients. HC charts of 3,269 patients from a tertiary paediatric neurology section were reviewed and 136 microcephalic participants were selected. Standardized HC Minimum, HC Drop and HC Catch-up variables were defined. Children with evidence of Severe Learning Disability (IQ below 70) and/or significant Cerebral Palsy (GMF-CS III or higher) were classified within the Neurologically Impaired Group and the rest of participants within the Normal-Mildly Impaired Group. Using the Head Growth Function $C = HC \text{ Minimum} + HC \text{ Drop}$, with a cut-off level of $C = -4.28$ SD, we analyzed the agreement between the function prediction and the actual neurological status in four clinical groups: Idiopathic, Familial, Syndromic and Symptomatic. We discuss the differences found in the concordance between function prediction and neurological outcome for every clinical presentation of microcephaly. Our results are helpful to refine the clinical use of HC charts in order to anticipate Neurological Impairment in microcephalic infants and children.

O73 - 1935

SBA and control muscle ultrasound density from pre- to postnatal life

Verbeek RJ, Sollie KM, Mulder PB, van der Hoeven JH, Hoving EW, Sentner CP, Sival DA. *Dept. of Neurology, UMC Groningen, University of Groningen, Groningen, The Netherlands* – r.j.verbeek@umcg.nl

Objectives: In spina bifida aperta (SBA), the “second-hit of damage” refers to delayed neurological damage superimposed upon the congenital myelomeningocele (MMC). Neuro-protective treatment strategies aim to reduce this, but potential neuromuscular gain is still unclear, partly by the lack of comparable quantitative indicators. We reasoned that longitudinal muscle ultrasound density (MUD) could non-invasively elucidate alterations in segmental neuromuscular integrity. However, longitudinal fetal MUD outcomes are still unknown, so far. In SBA and control children, we aimed to assess and compare MUD from pre- to postnatal life. **Material and methods:** In 30 SBA [MMC Th8-S1 (median L4)] and 20 control children we cross-sectionally compared MUD of biceps, quadriceps, tibial anterior and calf muscles during the 1st; 2nd and 3rd trimester of pregnancy and subsequently during 0, 6 and 12 months postnatal age. **Results:** 12 of 30 SBA-patients died (9 fetuses by planned terminated pregnancy; 3 neonates by the consequences of devastating hydrocephalus). Both SBA and control children revealed an intra-individual MUD increase from the first trimester of pregnancy until the sixth month after birth

[median MUD increase: 51% and 31% in SBA and controls, resp.] and stabilized, thereafter. Comparing fetal-MUD between SBA and controls, revealed significantly higher SBA-MUD outcomes from the 1st to 3rd trimester of pregnancy (caudal to the MMC; $p < .05$). Comparing postnatal-MUD between SBA and controls, also revealed significantly higher SBA-MUD outcomes from birth to 1 year (caudal to the MMC; $p < .05$). **Conclusions:** From the first trimester of pregnancy to 1 year of follow-up, SBA MUD caudal to the MMC is increased compared to controls. This may implicate that the muscle ultrasound technique is applicable for longitudinal comparison between innovative fetal treatment strategies. Future analysis of individual MUD trajectories may reveal whether the technique could also be applied for individual neuromuscular surveillance.

O74 - 2025

Benefits of universal newborn screening for permanent childhood hearing impairment to reading comprehension in adolescence: early confirmation of deafness matters

Kennedy CR, Pimperton H, Chorozoglou M, Kreppner J, Mahon H, Powers SG, Peacock J, Stevenson JE, Terleksi M, Worsfold SM, Yuen HM. *Southampton General Hospital, Southampton, UK* – crk1@soton.ac.uk

Objectives: To determine the effect of universal newborn hearing screening (UNHS) and early confirmation of permanent childhood hearing impairment (PCHI) on reading and language in adolescence. **Material and methods:** Long-term follow-up study of a large group of deaf teenagers and a comparison group of normally hearing children all of whom were previously involved in population-based studies of UNHS when they were born in 1992-97 and also had assessment of language and reading at primary school age.^{1,2} The primary outcome was scores on the York Assessment of Reading for Comprehension (YARC) analysed in a regression model that adjusted for the effects of maternal education, non-verbal ability (Raven's progressive matrices score) and severity of PCHI. Language comprehension and expression were also assessed. Scores were expressed as z scores where the mean (SD) score in the comparison group was 0 (1). **Results:** Reading comprehension z-scores at mean (SD) age of 17.1 (1.45) years in 67 of 98 (68%) of those previously assessed at primary school age, including 15 with cochlear implantation, were significantly higher in those whose PCHI had been confirmed at age <9 months than in those with later confirmed PCHI (group means - 0.63, -1.86 respectively; adjusted group mean difference = 1.07, 95% CI = 0.33 to 1.81, $p = 0.005$). This pattern of findings was attributable to the subgroup treated with hearing aids and was not seen for the subgroup who had received cochlear implants. Language outcomes showed similar patterns of inter-group differences. **Conclusions:** This unique study shows continuation of benefit into adolescence in aided children with bilateral PCHI from confirmation of deafness prior to age 9 months. Other factors seem more salient in determining the reading and language outcomes of cochlear implantees.

O75 - 1987

Specific impairment of functional connectivity between language regions in former early preterms

Wilke M, Hauser T-K, Krägeloh-Mann I, Lidzba K. *Department of Pediatric Neurology & Developmental Medicine, University Children's Hospital Tübingen, Germany* – marko.wilke@med.uni-tuebingen.de

Objectives: Prematurity is associated with a high risk for an adverse neurodevelopmental outcome; particularly in children born ≤ 32 weeks of gestation. In recent years, the importance of neurocognitive deficits has been increasingly recognized. Among these, language has consistently been shown to be affected. It has

the advantage that it can be well-characterized using both neuropsychological testing and non-invasive imaging approaches, such as functional magnetic resonance imaging (fMRI). **Material and methods:** We here report on a study comparing former early preterm born children and adolescents (PT, $n = 29$, 20M) and typically developing children (TD, $n = 19$, 7M), using conventional MRI group analyses as well as task-based and resting-state functional connectivity analyses. **Results:** We found only small regions with significantly different activation on the group level (PT > TD) but significantly stronger connectivity between functionally-defined superior temporal lobe (STL) language regions in TD participants. There were also significant differences in local and global network efficiency (TD > PT). Surprisingly, there was a stronger connectivity of STL regions with non-STL regions both intra- and interhemispherically in PT participants, suggesting the presence of both reduced and increased connectivity in the language network of former preterms. Very similar results were obtained when using task-based vs. resting state functional connectivity approaches. Finally, lateralization of functional connectivity correlated with verbal comprehension abilities, suggesting that a more bilateral language comprehension representation in the brain is associated with better performance. **Conclusions:** Our results suggest the existence and persistence of abnormal connectivity patterns; they are discussed in the context of normal brain and language development. They underline the importance of interhemispheric crosstalk for the development of language comprehension in former early preterms.

O76 - 1901

Neurodevelopmental outcomes of newborns requiring a brain MRI: a retrospective study

Papandreou A, Poulton C, Kermode R, Ramesh CA. West Hertfordshire Hospitals NHS Trust, Watford General Hospital, Watford, UK – apostolis_papandreou@hotmail.com

Objectives: To assess neurodevelopment of babies requiring an MRI brain in the neonatal period. **Material and methods:** A retrospective study was performed. All neonates ($n=84$), born in a UK district general hospital and requiring an MRI brain from January 2001 to December 2009 were included. Neurodevelopmental status around the age of 2 years was assessed, either in a tertiary centre (using the Griffiths developmental assessment tool) or locally by community and/or acute paediatric consultants. Babies lost to follow up before the corrected age of 12 months were not included in our results analysis. **Results:** 70/84 notes were reviewed. 74% had a final neurodevelopmental assessment at a corrected age equal or greater than 18months. 14% ($n=10/70$) were lost to follow up before 12months corrected age. Neurodevelopmental outcomes were correlated with clinical examination at discharge, with imaging and EEG findings. 16% of patients with normal examination at discharge had moderate/severe delay. Conversely, 73% patients with abnormal neurological examination had developmental delay (18% mild, 55% moderate/severe) during final assessment. 28% of patients with abnormal cranial ultrasound scans had mild delay and 28% had moderate/severe delay. A normal MRI brain was associated with normal neurodevelopment in 100% of cases. An abnormal MRI was associated with mild delay in 30% and moderate/severe delay in 30% of cases. An abnormal neonatal EEG was associated with 50% moderate/severe developmental delay. An abnormal MRI paired with an abnormal EEG report was associated with moderate/severe delay in 60% of patients. **Conclusions:** Neurological condition at discharge correlates well with final outcomes. Cranial ultrasound abnormalities do not necessarily predict developmental delay. A normal MRI is a very strong predictor of normal neurodevelopment. An abnormal MRI is associated with moderate to severe delay in 30% of cases, percentage which is increased to 60% when paired with an abnormal EEG.

O77 - 1605

Thrombophilic genes polymorphisms in children with perinatal brain injury

Baranov DA, Lvova OA, Kuznetsov NN, Kovtun OP, Plaxina AN, Kolmogortseva VD. City's Perinatal Center, Russia – medicus_br33@rambler.ru

Aim: To estimate the role of inherited thrombophilia in newborns with hypoxic- ischemic encephalopathy (HIE) and intraventricular hemorrhage (IVH). **Material and methods:** A double center case-control study. We screened 49 full-term and preterm infants with HIE/IVH and 57 term- and sex matched healthy control group for 7 single nucleotide polymorphisms (SNPs) of hemostasis' and folic acid cycle's enzymes' genes with the help of polymerase real-time chain reaction. **Results:** Almost all the neonates had the thrombophilic SNPs in homozygous or heterozygous state 2.76 ± 1.0 vs 1.88 ± 0.8 . Only 2 infants (control group) had no gene's defects. One SNP had been identified in 6 vs 18 cases ($p=0.01$), two – 13 vs 22 ($p=0.1$), three – 18 vs 15 ($p=0.1$), four ($n=11$) and five ($n=1$) SNPs had only neonates with HIE/IVH ($p=0.001$). 16 patients had FGB:G-455A polymorphism versus 7 in control group (OR=3.46, 95% confidence interval (CI) 1.3–9.5; $p=0.01$). Prothrombin gene heterozygosity in normal controls (1.8%) did not statistically differ from HIE/IVH cases (6.1%) ($p=0.2$). We also observed F5: G1691A 5 vs 0 ($p=0.018$); ITGA2: C807T 29 vs 23 (OR=2.14, 95% CI 1.0–4.7; $p=0.04$); ITGA2: TT in homozygous state 8 vs 0 ($p=0.001$); ITGB: T1565C 20 vs. 16 (OR=2.19, 95% CI 1.0–4.9; $p=0.01$); PAI-1: -675 4G4G in homozygous state 15 vs 6 (OR=3.75, 95% CI 1.3–10.9; $p=0.009$); MTHFR: C677T 25 vs 17 (OR=2.45, 95% CI 1.1–5.5; $p=0.02$). **Conclusion:** The incident of severe thrombophilic SNPs (FGB: G-455A, F5: G1691A, ITGA2: C807T, ITGB: T1565C, MTHFR: C677T) among neonates with HIE/IVH is higher than in control group. The carrier state of these SNPs increases the chance to develop perinatal HIE/IVH twice and more.

O78 - 1870

Neuro-imaging and neurodevelopmental outcome in preterm infants with a periventricular haemorrhagic infarction located in the temporal and frontal lobe

Soltirovska Salamon A, Groenendaal F, Van Haastert IC, Rademaker CM, Benders MJ, Koopman-Elseboom C, de Vries L. Department of Neonatology, Wilhelmina Children's Hospital, University Medical Centre, Utrecht, The Netherlands – anetasol@yahoo.com

Objectives: The neurodevelopmental outcome of preterm infants with periventricular haemorrhagic infarction (PVHI) has overall been reported as poor. The spatial relationship between the site of the PVHI and the corticospinal tracts is important for predicting motor outcome. No studies have compared the outcomes of infants with PVHI located in the temporal or frontal lobe. The aim of this study was to compare clinical, neuroimaging characteristics and neurodevelopmental outcome in preterm infants with a PVHI located in the temporal and frontal periventricular white matter. **Methods:** retrospective hospital based study of preterm infants with a gestational age <34 weeks with a frontal ($n=22$) and temporal ($n=12$) PVHI. The clinical course, neuroimaging studies (cranial ultrasound and/or MRI) and neurodevelopmental outcomes were reviewed. Adverse outcome was defined as moderately or severely abnormal neurological examination during the last visit, presence of cerebral palsy, epilepsy, hearing or visual impairment and/or an abnormal development between 24 and 36 months (Griffiths' developmental quotient ≤ 85). **Results:** infants with a temporal PVHI were significantly more at risk of an adverse outcome compared with those with a frontal PVHI ($p=0.006$). One infant with a temporal lobe PVHI developed ipsilateral CP due to a parietal PVHI on the contralateral side. Cognitive impairment was noted in one third of the infants in both groups.

A significantly larger proportion of infants with a temporal PVHI developed visual impairment and/or behavioural problems (50% and 70% respectively) compared to those with a frontal PVHI (9% and 13% respectively). **Conclusion:** PVHI located in the temporal and frontal lobe is almost invariably related to a normal motor outcome, but carries a risk for cognitive, behavioural and visual problems. Preterm infants with temporal lobe PVHI are more at risk of an adverse outcome than those with frontal lobe PVHI.

O79 - 1599

Prognostic value of conventional EEG in asphyxiated term newborns treated with hypothermia: experience in 20 cases

Aeby A, Khabbache K, Van Overmeire B, Vermeylen D, Van Bogaert P. *Pediatric Neurology, Erasme-Hospital, Belgium – ULB. alec.aeby@ulb.ac.be*

Introduction: Perinatal hypoxic ischemic encephalopathy (HIE) is an important cause of mortality and neurologic morbidity in the term newborn. Hypothermia has shown to reduce death and neurologic impairment in several studies on HIE infants. Numerous studies have shown that conventional EEG performed at 24 h of life has a very robust prognostic value in HIE managed without hypothermia. Nevertheless, the prognostic value of conventional EEG in HIE treated with hypothermia is uncertain. **Objectives:** To identify the prognosis value of conventional EEG in the first 20 HIE newborns treated with hypothermia at Erasme Hospital. **Methods:** We reviewed the medical records, MRI, electroencephalograms and outcome data of the twenty HIE newborns that were managed with hypothermia in our service between 2008 and 2012. Bad neurological outcome was defined as Bayley III score <70 at 2 years or cerebral palsy or moderate (parasagittal brain injury) to severe (basal ganglia lesions) brain injury on early (day 4) brain MRI. EEG was graded according to Murray classification (Grade 0 to 4). **Results:** Eight infants died (40%), amongst which two had a brain MRI that revealed severe brain injury. Amongst the 12 survivors, 11 had a normal neurological examination or Bayley III score and one had a cerebral palsy. All had a brain MRI, which was normal or mildly abnormal in eleven patient and moderately abnormal in one patient. All twenty patients showed significant abnormalities in the first EEG (Murray score ≥ 1). Death or bad neurological outcome was associated with the persistence of Murray score ≥ 2 at 48 hours. A normalization of the EEG (Grade 0–1) in the first 48 hours was always associated with a good prognosis. **Conclusions:** Our study shows that conventional EEG performed at 48 hours in newborns with HIE undergoing therapeutic hypothermia provides prognostic information about neurologic outcome.

O80 - 1570

Cognitive outcome in childhood following unilateral perinatal brain injury

van der Aa NE, van Buuren LM, Dekker HC, Vermeulen RJ, van Nieuwenhuizen O, van Schooneveld MMJ, de Vries LS. *Department of Neonatology, Wilhelmina Children's Hospital, Utrecht, The Netherlands – n.vanderaa@umcutrecht.nl*

Objectives: To assess cognitive outcome in children with periventricular haemorrhagic infarction (PVHI) or perinatal arterial ischemic stroke (PAIS) and relate these findings with early developmental outcome and neonatal MRI findings. **Methods:** A neuropsychological assessment was performed in 50 children with unilateral PVHI (n=21) or PAIS (n=29) at a median age of 11y 9mo (range 6–20 years) and included tests for intelligence, verbal memory, visual-motor integration, word comprehension, attention, reaction times and executive function. The Griffiths' scales were used for early developmental assessment at 24 months

(range 18–32 months). **Results:** In children with PVHI, both the early Griffiths' scores (mean 87, 95%CI 83–92) and the Full Scale IQ (FSIQ) scores at school age (mean 86, 95%CI 78–94) were below the test mean of 100. In the PAIS group, early Griffiths' scores were within the normal range (mean 98, 95%CI 93–104) but at school-age FSIQ scores were below average (mean 87, 95%CI 80–94). In children with PVHI, FSIQ scores correlated with the level of maternal education and were lower following ventricular dilatation, whereas involvement of basal ganglia and thalami and postneonatal epilepsy were associated with lower cognitive outcome in PAIS children. **Conclusion:** Cognitive outcome following PVHI or PAIS is below average, but still within one SD for most children. Prediction of cognitive outcome remains challenging, but some early predictors can be recognised.

Parallel session 14: Learning disabilities, ADHD and autism

Chairs: Patrick Berquin and Sergiusz Jozwiak

O81 - 1871

Motor cortical inhibition in ADHD: modulation of the transcranial magnetic stimulation-evoked N100 during a go/nogo task

D'Agati E, Hoegl T, Dippel G, Curatolo P, Bender S, Kratz O, Moll GH, Heinrich H. *University Hospital of Erlangen, Germany, Tor Vergata University, Rome, Italy – elisadagati@gmail.com*

Objectives: The N100 component, evoked by transcranial magnetic stimulation (TMS) and electroencephalography (EEG) is associated with the activation of inhibitory cortical circuits and has recently been suggested as a potential marker of inhibition in Attention Deficit Hyperactivity Disorder (ADHD). In healthy subjects, the TMS-evoked N100 decreases during motor response preparation and movement execution and increases during response inhibition. This study is the first investigating modulation of the TMS-evoked N100 at stages of response preparation, activation, execution and inhibition in ADHD patients during a go/nogo task. The aim of the present study was to investigate the modulation of the TMS-evoked N100 at stages. **Material and methods:** 18 children with ADHD and 19 typically developing children, aged 10 to 14 years, all right handed were assessed. TMS was delivered over the left motor cortex, the TMS-N100 was measured at electrode P3. The TMS-evoked N100 was determined at rest and at different time points (50 ms before S2; 150, 300 and 500 ms after S2) in a cued go/nogo task (S1-S2 paradigm). Correlations between the TMS-evoked N100 measures, MEP-related TMS measures (e.g., short-interval intracortical inhibition) and performance measures were calculated. **Results:** Though the TMS-evoked N100 was not found to be significantly reduced at rest in the ADHD group, a smaller increase in go trials and a smaller decrease after inhibiting a response compared to typically developing children were observed. In go trials, a lower TMS-evoked N100 was associated with a smaller variability of reaction times. **Conclusions:** A reduced modulation of the TMS-evoked N100 amplitude at response execution and inhibition during a go/nogo task, extends the picture of inhibition deficits at the cortical level in ADHD underlining the relevance of the TMS-evoked N100. Findings suggest a functional involvement of the mechanisms underlying the TMS-evoked N100 at the motor output stage.

O82 - 1582

Preliminary data on the use of cigarettes, alcohol and drugs in a follow-up study of adolescents with Tourette syndrome

Groth C, Debes N, Skov L. *Pediatric Department, Herlev University Hospital, Denmark – camilla.groth.jakobsen@gmail.com*

Background and aim: Tourette Syndrome (TS) and co-morbid symptoms often have psychosocial and educational consequences for the young. Adolescents with inadequately treated TS are at risk of developing abuse of cigarettes, alcohol and drugs. This abuse stems from the belief that it may dampen the tics and co-morbid symptoms. Here, we examined the use of cigarettes, alcohol and drugs in adolescents with TS and its correlation with severity of tics. **Methods:** We included 116 adolescents with TS (age 16–20 years) and used structured interviews to assess the use of cigarettes, alcohol and drugs and the Yale Global Tic Severity Scale Score to assess the severity of the tics. Data from the Danish National Youth Health profile from 2011 were used as background population. **Results:** The mean age of the included TS adolescents was 18.43 years and 81% were male. Compared with data from the Danish National Youth Health profile, fewer TS adolescents used alcohol and fewer TS adolescents had a weekly alcohol consumption above 20 units. More TS adolescent were daily smokers of cigarettes (28.5%) than in the background population (16.2%). One fourth (27.3%) of the TS cigarette smokers felt an effect of smoking on tic. Cannabis was more frequently smoked (within 4 weeks) by the TS adolescents (15.5%) than their national counterparts (6.2%). Of the TS-cohort 4.3% had abused one or more hard drugs previously. Smokers and frequent users of drugs had a tendency towards higher Global Tic Scores. **Conclusion:** Compared with the Danish background population, more TS adolescents are smokers of cigarettes and cannabis but fewer drink alcohol. Professionals need to be aware of the risk of abuse among TS adolescents. No clear correlation exists on the use of cigarettes, alcohol and drugs and the severity of tics.

O83 - 2038

Do rolandic spikes on EEG at ADHD assessment influence on ADHD subtype and the use of methylphenidate for ADHD?

Socanski D, Herigstad A. *Stavanger University Hospital, Norway – socanski@hotmail.com*

There are some relationships between attention-deficit/hyperactivity disorder (ADHD) and rolandic spikes (RS) on EEG. RS occur in children with ADHD and may contribute to the occurrence of ADHD symptoms in some cases. **Purpose:** The aim of the present study was to investigate whether RS on EEG at ADHD assessment influence on the occurrence of ADHD subtype and the use of methylphenidate (MPH) for ADHD. **Method:** A retrospective study of 607 ADHD children (82.4% male), aged between 5 and 14 years, who were diagnosed between January 2000 and December 2005 was performed. At least one routine awake EEG was recorded on 517 patients and 39 patients had EEG with epileptiform abnormalities (EA). The group with RS (group one) was compared to control groups; group two (patients with EA without RS) and group three (patients without EA). The three groups were followed-up for one year. Measure outcomes were: ADHD subtype and the use of MPH for ADHD. **Results:** The group with RS consisted of 9 patients, 2 of them had previous history of epilepsy. Group two (patients with EA without RS), consisted of 30 patients, 10 of them had previous epilepsy. Of the 30 patients without EA (group three), nobody had previous epilepsy. ADHD combined subtype was diagnosed in the vast majority of cases in all groups. MPH was used similarly in groups (89%, group one; 87%, group two; 83%, group three). There was no statistic difference between groups with and without RS where MPH was used as medication for ADHD. The previous epilepsy co-morbidity and

occurrence of RSs were not a reason for not treating ADHD. **Conclusions:** The study suggested that RS occurrence at ADHD assessment does not influence on ADHD subtype occurrence and the use of MPH during 12 months follow-up.

O84 - 1965

Improving motor learning in a rat model of ADHD

Soderlund GBW, Bergquist F. *Norway – goran.soderlund@hisf.no*

Introduction and objectives: Counterintuitively, acoustic white noise improves performance in inattentive persons, e.g. with ADHD. Such noise benefit may involve stochastic resonance, where a certain amount of noise improves suboptimal performance. The moderate brain arousal model predicts that low dopamine ADHD subjects require more noise than control subjects for optimal performance. Like people with ADHD, the spontaneously hypertensive (SH) rat displays hyperactivity, impaired attention and impaired motor skills. The effect of white acoustic noise and methylphenidate on motor learning and spontaneous motor activity was investigated in the SH rat. **Methods:** Charles River SH rats (SHR/NCr1) and Wistar (WIS/SCA) rats were trained in a skilled reaching task (Montoya) and a gross motor coordination task (Rotarod acceleration) for ten days. Spontaneous open field locomotor activity was recorded. The independent variables were: noise (75 dBA), silence (35–40 dBA), methylphenidate (4 mg/kg i.p.), and vehicle (0.9% NaCl i.p.). **Results:** Noise but not methylphenidate, improved skilled reach learning in the SH rat. Learning was unaffected by treatments in Wistar rats. SH rats only performed at 50% of Wistar rat performance on the Rotarod but performance was improved to normal by both noise and methylphenidate. SH rats displayed open field hyperactivity, which was attenuated by methylphenidate but not by noise. **Discussion:** Auditory noise has a strong positive effect on skilled motor learning in the ADHD phenotype rat, but not in a control strain. The effect of noise differs in several important aspects from the effect of methylphenidate, indicating different action mechanisms that could be capitalized clinically.

O85 - 1992

Cortico-vocal coherence in autism spectrum disorders

Suarez Garcia S, Clumeck C, Bourguignon M, Wens V, Op De Beeck M, Marty B, Soncarrieu M, Deconinck N, Delvenne V, Goldman S, Van Bogaert P, De Tège X. *Université Libre de Bruxelles, Laboratoire de Cartographie Fonctionnelle du Cerveau, Belgium – ssuarezg@ulb.ac.be*

Introduction: The cortico-vocal coherence (CVC) measures the coupling between the reader's voice and the listener's cortical activity. Significant coupling typically occurs at about 0.5 Hz between the time-course of the reader's voice and listener's cortical neuromagnetic signals with local coherence maxima located at the right posterior superior temporal sulcus (pSTS) and gyrus. This phenomenon seems to reflect the processing of rhythmic prosody at the sentence level. The integrity of prosody perception is still a controversial question in autism spectrum disorder (ASD) population. Neuroimaging studies have pointed out the key role of the STS in the pathophysiology of ASD. We investigated, using magnetoencephalography (MEG), the CVC phenomenon in ASD Patients. **Methods:** Seven ASD patients (6 males and 1 female aged 13–20 years), diagnosed with Asperger Syndrome (n=4) or Autism (n=3) based on DSM-IV criteria and the Autism Diagnostic Observation Schedule (ADOS) were recruited. Cortical neuromagnetic signals were recorded using a whole-scalp MEG while patients listened to a text continuously read by a French speaking male (live) and female (recording) during five minutes. In the live voice condition, the voice's fundamental frequency was recorded by a three-axis accelerometer attached to the reader's throat. We

recorded also cortical activity in a rest condition. Coherence, which is an extension of Pearson correlation coefficient, was computed between the reader's voice time-course and listener's MEG signals. Coherent neural sources were subsequently reconstructed using Dynamic Imaging of Coherent Source. **Results:** Significant CVC was found in all patients in the two conditions with coherent sources located at the right STS (life voice) and at the right middle temporal gyrus (recorded voice). **Conclusions:** These results suggest the existence of preserved CVC in patients with ASD. This finding supports the existence of preserved neural processing of rhythmic prosody at the sentence level in ASD patients.

O86 - 1830

Cognitive functions in school-children with frontal or temporal epilepsy – long term study

Mazurkiewicz-Beldzinska M, Kondracka J, Szmuda M, Matheisel A. *Department of Developmental Neurology Medical University of Gdańsk, Poland – mmazur@gumed.edu.pl*

Purpose: In order to compare the cognitive functions in school-children with temporal (TLE) versus frontal lobe epilepsy (FLE) and control group from the time of diagnosis through the long term follow up the following study was performed. **Method:** 61 children with TLE 56 children with FLE and 60 healthy subjects were included in study. The applied test battery consisted of measures assessing both intelligence as well as executive and motor skills. All children had MRI and EEG recordings (usually in 3- 6 months intervals). The follow up took from 3 to 7 years (mean 5.2 years). At the time of diagnosis and in 12–15 months intervals the neuropsychological assessment was done and the results were correlated with the number of seizures, treatment and EEG changes. **Results:** There was no significant difference in global IQ scores between the groups at the time of diagnosis. Later during the study we observed the lower IQ performance in FLE group with poor control of seizures. Children with FLE had significantly lower scores in nonverbal memory tasks, presented higher attention deficit and slower performance speed at the time of diagnosis and through the whole study. The TLE group performed significantly worse as compared with control group in verbal learning and performance speed with no differences in attention. That changed during the study where we observed negative effect on attention and aggravation in deficits in verbal and also in nonverbal memory tasks. **Conclusion:** The children with new onset FLE present with more severe cognitive and attention problems compared with TLE group, however the TLE group performance changed during time. The strong correlation between the focus localization but also type of treatment end seizure control was found and will be discussed.

O87 - 1771

Long-term simvastatin treatment for cognition and daily life in children with neurofibromatosis type 1: results from the NF1-SIMCODA trial

van der Vaart T, Plasschaert E, Rietman AB, Renard M, Oostenbrink R, Vogels A, de Wit MC, Descheemaeker MJ, Vergouwe Y, Catsman-Berrevoets CE, Legius E, Elgersma Y, Moll HA. *Department of Neuroscience; Department of Paediatrics; ENCORE Expertise Centre for Neurodevelopmental Disorders, Erasmus MC, Rotterdam, The Netherlands – m.vandervaat@erasmusmc.nl*

Background: Neurofibromatosis type 1 (NF1) is a common single-gene neurocognitive disorder characterized by neurocutaneous symptoms, lower IQ, internalizing behavioural problems and attention deficits. In Nf1-mice, loss of neurofibromin increases RAS-activity and reduces synaptic plasticity in the brain. Statin-induced HMG-CoA-reductase inhibition by statins prevented

RAS-activation, restored plasticity, learning and attention in Nf1-mice. Short-term simvastatin administration to NF1 patients was inconclusive. A trial with longer treatment duration and use of clinically relevant outcome measures was needed. The NF1-SIMCODA trial aims at detecting the effects of long-term simvastatin on cognition and daily life in children with NF1. **Methods:** Individuals from the Netherlands and Belgium aged 8–15 years with genetically confirmed diagnosis of NF1, not using stimulant medication were eligible for this 12-month randomized double-blind placebo-controlled clinical trial. Intervention consisted of 20–40 mg/d simvastatin or placebo. Primary outcomes were IQ (Wechsler Intelligence Scales for Children-III-NL) and parent reports on internalizing behavioural problems and attention problems (Child Behavioural Checklist) after 12 months of treatment. **Results:** We randomised 84 participants between March 9, 2010 and March 6, 2012. Data acquisition has been completed in March 5, 2013. Median age of participants was 11.5 years (range 7.9–16.0) and average IQ at baseline was 83.3 (SD 15.6). **Conclusions:** The effect of simvastatin on IQ and behaviour in children with Neurofibromatosis type 1 will be presented at the European Paediatric Neurology Society congress in Brussels. (Trial identifier: trialregister.nl number, NTR2150.)

O88 - 1682

Effects of methylphenidate on functional networks activation in children with attention deficit hyperactivity disorder

Berquin P, Querne L, Service de Fall S, Delignières A, Simonnot A, Le Moing A-G. *Service de Neuropédiatrie & GRAMFC U1105, CHU Amiens, France – patrick.berquin@u-picardie.fr*

Background: Many fMRI studies in ADHD had focused on frontal regions known to be a site of action of methylphenidate and be involved in executive, control and inhibitory functions. New approach shifts the focus from regional brain abnormalities to dysfunction in distributed network organization. The objective was to study how the methylphenidate modifies in children with ADHD the activations of functional networks during visuospatial processing. **Methods:** Eleven drug-naïve ADHD children and 11 typically developing (TD) children performed a flanker task during magnetic resonance imaging. The ADHD-group was scanned twice, before initiation of methylphenidate and one month afterwards with methylphenidate (extended-release formulation). The functional sequence consisted of successive conflict/unconflicting blocks. Brain activity for visuomotor conflict was imaged by contrasting hemodynamic activity during conflict versus unconflicting blocks. **Results:** Prior to methylphenidate, the ADHD-group showed bilateral activations in visual and dorsal-attentional (only the posterior part) networks and in several regions of the default-mode network. In contrast, the TD-group showed bilateral activation in the fronto-parietal network. With methylphenidate, activations in the ADHD-group were reduced in both visual and default-mode networks. Methylphenidate also initiated activations in the anterior part of the dorsal-attentional network and in the right hemispheric part of the fronto-parietal network. **Conclusions:** Our results suggest that ADHD children engaged different networks than TD children for performed visuomotor conflict. Hyperactivation of the visual, dorsal-attentional and default-mode networks could be compensatory mechanisms and/or be consecutive to a default of inhibitory control normally exerted by the fronto-parietal network. Methylphenidate by improving partially the activation of the fronto-parietal network may improve in turn inhibitory control on visual and default-mode networks. The dorsal attentional network remained activated, suggesting that attentional networks compensate the incomplete activation of the fronto-parietal network.

O89 - 1600

Language development at 2 years is correlated to brain microstructure in the left superior temporal gyrus at term equivalent age: a diffusion tensor imaging study

Aeby A, De Tiège X, David P, Balériaux D, Van Overmeire B, Metens T, Van Bogaert P. *Pediatric Neurology and Laboratoire de Cartographie Fonctionnelle du Cerveau UNI (Université Libre de Bruxelles - ULB Neuroscience Institute) Erasme-Hospital, Belgium – alec.aeby@ulb.ac.be*

This study aims at testing the hypothesis that neurodevelopmental abilities at age 2 years are related with local brain microstructure of preterm infants at term equivalent age. Forty-one preterm infants underwent brain MRI with diffusion tensor imaging sequences to measure mean diffusivity (MD), fractional anisotropy (FA), longitudinal and transverse diffusivity ($\lambda_{//}$ and λ_{\perp}) at term equivalent age. Neurodevelopment was assessed at 2 years corrected age using the Bayley III scale. A voxel-based analysis approach, statistical parametric mapping (SPM8), was used to correlate changes of the Bayley III scores with the regional distribution of MD, FA, $\lambda_{//}$ and λ_{\perp} . We found that language abilities are negatively correlated to MD, $\lambda_{//}$ and λ_{\perp} in the left superior temporal gyrus in preterm infants. These findings suggest that higher MD, $\lambda_{//}$ and λ_{\perp} values at term-equivalent age in the left superior temporal gyrus are associated with poorer language scores in later childhood. Consequently, it highlights the key role of the left superior temporal gyrus for the development of language abilities in children. Further studies are needed to assess on an individual basis and on the long term the prognostic value of brain DTI at term equivalent age for the development of language.

Parallel session 15: Epilepsy

Chairs: Sameer Zuberi and Oebele Brouwer

O90 - 2157

Treatment of electrical status epilepticus in sleep (ESES): a systematic review and meta-analysis

Van den Munckhof B, Van Dee V, Liukkonen E, Sagi L, Loddenkemper T, Sánchez Fernández I, Braun KPJ, Jansen FE. *Rudolf Magnus Institute of Neuroscience, Department of Paediatric Neurology, University Medical Center, Utrecht, The Netherlands – B.vandenMunckhof@umcutrecht.nl*

Purpose: Epileptic encephalopathy with ESES is a rare pediatric epilepsy syndrome with significant aggravation of interictal epileptiform discharges in sleep and acquired impairment of cognition or behavior. The aim of treatment of ESES syndrome is to improve cognitive outcome. However, it is unknown which treatment is most effective. The aim of this meta-analysis is to create an overview of the current evidence for different treatment regimens in children with ESES syndrome. **Methods:** A broad literature search using Pubmed and Embase was performed. Articles were selected if they contained original treatment data of patients with ESES syndrome. Authors were contacted to gain additional information. Individual patient- data were collected, coded and checked by a second investigator. **Results:** The literature search yielded 1663 articles. After excluding duplicates and applying in- and exclusion criteria 109 articles remained that described 727 treatments in 493 patients. Treatment with conventional anti-epileptic drugs (AED, n = 335) caused any (i.e. cognitive or EEG) improvement in 50% of patients, cognitive improvement in 38% and EEG-improvement in 43%. Benzodiazepines (n=133) caused any improvement in 71%, cognitive improvement in 50% and EEG improvement in 61%. Steroids yielded any improvement in 84%, cognitive improvement in 85% and EEG improvement

in 78%. Surgery (n=62) resulted in any improvement in 89%, cognitive improvement in 84% and EEG improvement in 82%. A subgroup analysis of studies that included consecutively treated patients only (n=309) showed significantly lower treatment effectiveness for AED and benzodiazepines (any improvement in 17% and 55% respectively). **Conclusion:** This meta-analysis suggests superior effectiveness of steroids and surgery in epileptic encephalopathy with ESES. However, most studies were small and retrospective. Furthermore, the substantially lower success rates in the subgroup- analysis of consecutively treated patients suggest an important publication bias. Our findings emphasize the urgent need for a randomized controlled trial in patients with ESES syndrome.

O91 - 1581

Compensatory visual system adaptations after hemispherectomy in children

Koenraads Y, van der Linden DCP, van Schooneveld MMJ, Imhof SM, Porro GL, Braun KPJ. *Department of Ophthalmology, Rudolf Magnus Institute of Neuroscience, University Medical Center Utrecht, Utrecht, The Netherlands – Y.Koenraads@umcutrecht.nl*

Objectives: Several case-reports have suggested that an anomalous head posture (AHP) and exotropia on the side of the visual field (VF) defect may compensate for homonymous hemianopia. The aim of this study was to determine the prevalence of these compensatory mechanisms in children who underwent hemispherectomy. **Material and methods:** Patient files from all children who underwent hemispherectomy and had a postoperative ophthalmological examination in the UMC Utrecht up to October 2012 were retrospectively reviewed. The prevalence of the possible compensatory mechanisms (dynamic AHP and manifest or intermittent exotropia both directed towards the side of the VF defect) was determined. Subsequently, clinical characteristics were compared between patients who did, and those who did not develop compensatory adaptations. To account for the potential effect of insufficient follow-up time, children with no adaptations reported were only included in the study if follow-up duration was at least two years. **Results:** 45 children (21 ♂ and 24 ♀) underwent a hemispherectomy (22 right and 23 left) at a median age of 2.1 yr (range 0.2–14.3 yr). Median ophthalmological follow-up was 2.4 yr (range 0.1–14.8 yr). AHP and exotropia on the side of the VF defect were found in 53% and 40% of children respectively. The latter occurred significantly more often in children who underwent right-sided hemispherectomy. There was no significant difference in age at surgery, etiology of epilepsy, seizure freedom, developmental scale, fixation, visual acuity, spherical equivalent or optic disc between the groups. **Conclusions:** This study shows that functional adaptations to compensate for homonymous hemianopia – i.e. AHP and exotropia – both occur frequently after hemispherectomy in children. Dynamic head posturing and exotropia of the eye on the side of the VF defect may be part of a coping strategy to maximize the visual field. Surgical treatment of exotropia should then be avoided.

O92 - 2108

The classification of epilepsies using the ILAE revised terminology and concepts for organization of seizures and epilepsies and ICD-10 – challenges in clinical practice

Iliescu C, Barca D, Budisteanu M, Burloiu C, Butoianu N, Minciu I, Motoescu C, Tarta-Arsene O, Craiu D. *“Carol Davila” University of Medicine, Department of Neurology, Pediatric Neurology, Neurosurgery, Psychiatry - Pediatric Neurology Clinic No.II, Bucharest; Al. Obregia Hospital, Bucharest, Romania – iliescu_catrinel@yahoo.com*

Objectives: Epilepsies classification is important in clinical practice but different systems are used in the same time and the

results might be inaccurate. New concepts were proposed but controversies exist and misunderstanding of terms persist in publications. The aim is to present our results and challenges we faced in applying the ILAE revised terminology and concepts for organization of epilepsies and to compare these with the data obtained with ICD-10, which is used in daily practice. **Material and methods:** we searched our Epilepsy Registry and selected the cases admitted with a new diagnosis of epilepsy from our pediatric neurology clinic, during 2 consecutive months. We grouped the patients according with WHO age groups: infants (<1 year), children (1–9 years old) and adolescents (from 10 years until 17 years old – upper age limit for pediatric specialties in our country). We used the history, clinical and complementary data for classifying the epilepsies and the ICD-10 codes from files. **Results:** 51 patients under 18 years old were included. A diagnosis of electroclinical syndrome was possible in 28 (55%). Cause was defined in 20 of all patients (39%), and was unknown in 31. All 15 patients with an electroclinical syndrome and cause unknown were in fact “idiopathic” if using present classification, and 16 patients (31%) were with unknown cause and undefined prognosis. ICD-10 classification offered few useful data for clinical practice. **Conclusions:** the ILAE revised terminology and concepts for epilepsies organization is useful. Still some terms are unclear and misunderstandings possible. Age grouping being different among publications, we propose that a standardized organization to be used and upper limit for pediatric age to be unified in studies, for useful analysis. ICD should be in accordance with the new concepts for a more accurate analysis on a National and European level

O93 - 2003

Different aspects in the evaluation of vagus nerve stimulation efficacy among children with therapy-refractory epilepsy

Orosz I, Buck E, Sperner J, Thyen U. *Department of Neuropediatrics, Children's Hospital, University of Lübeck, Germany – Iren.Orosz@uksh.de*

Objectives: Efficacy of vagus nerve stimulation (VNS) among children with therapy-refractory epilepsy has been reported to be around 30–40% in most studies, although clinical experience shows that there are more patients who profit from VNS. Our goal was to examine the impact of VNS therapy not only on seizure frequency, but also on different other and so far underreported factors in children with recalcitrant epilepsy. **Material and methods:** 75 children (mean age at VNS implantation 10.9±4.9 years, range 2.3 - 21.8 years) with treatment-resistant epilepsy implanted with a VNS system at the University of Lübeck, Germany, during the last decade were retrospectively analyzed. Patients were followed up to 11.4 years after VNS system implantation. Data were retrieved from patient charts and seizure diaries. Response was defined as ≥50% seizure reduction after VNS. **Results:** One year after implantation, the rate of responders and seizure-free patients was 29.3% and 4%, respectively. At most recent follow-up (mean 3.7 years, range 1.0 – 11.4 years), this rate was 37.3% and 13.3%, respectively. Significantly higher number of responders was observed with VNS output currents between 1.75 mA and 2.25 mA. At the last recording, 56% of patients had positive magnet effects, i.e. disruption of seizures. However, among these children there were up to 71.4% non-responders according to seizure frequency analyses. By assessment of quality of life, most evident variables that improved with VNS therapy were mood, vigilance, and concentration. The longest seizure-free time (days per month) was significantly increased during the whole follow-up period. There was a significant decrease in number of hospital admissions and a trend towards a reduced number of stati epileptici 10 years before and after VNS. **Conclusions:** This implies that VNS in epileptic children has a broad spectrum of favourable effects, not being confined to reduction of seizure frequency.

O94 - 1758

Cardiac and respiratory autonomic dysfunction in childhood epilepsy

Jansen K, Varon C, Van Huffel S, Lagae L. *Pediatric neurology, University Hospitals Leuven, Belgium – katrien.jansen@uzleuven.be*

Objectives: Epilepsy is a neurological condition characterized by recurrent seizures. Since the autonomic nervous system has an important representation in the brain, autonomic disturbances can be part of the disease. Acute cardiac and respiratory changes can be seen due to involvement of autonomic control centers in seizure activity. Heart rate variability is an excellent tool to provide insight in the functionality of the autonomic nervous system. Our aim is to investigate the effect of epilepsy on the central autonomic nervous system by measuring heart rate, respiration and heart rate variability. **Methods:** Long-term EEG was recorded in childhood epilepsy patients including autonomic parameters. Heart rate was measured in 80 focal and generalized seizures. Respiration was measured in 20 focal and generalized seizures. Interictally, heart rate variability was assessed in 13 patients with West syndrome and 17 refractory epilepsy patients and compared to control subjects. Respiration was measured in 10 patients with West syndrome, 10 with temporal lobe epilepsy and 10 with absence epilepsy and compared to controls. **Results:** Ictal tachycardia was clear in patients with focal seizures, but not in generalized seizures. In temporal lobe seizures, lower breathing frequencies with risk of apnea were noted. Interictally, a depressed heart rate variability was seen with a significant reduction in vagal tone during slow wave sleep after a longer disease course in patients with refractory epilepsy and West syndrome. In patients with West syndrome but also in absence epilepsy, respiratory control was altered in between seizures, early after onset of the disease. **Conclusions:** We were able to show that cardiac as well as respiratory autonomic changes are present in childhood epilepsy. Respiration is altered earlier in the course of the disease compared to the cardiovascular system. Heart rate variability can be used as a biomarker for chronic autonomic dysfunction in patients with epilepsy.

O95 - 1739

Severe myoclonic epilepsy in infancy: clinical and neuropsychological analysis according to age at diagnosis of SMEI

El M'Kaddem B, Christiaens F, van Rijckevorsel F, Nassogne MC. *Université catholique de Louvain, Cliniques universitaires Saint-Luc, Bruxelles, Belgium – bouchra.elmkaddem@uclouvain.be*

Introduction: Severe myoclonic epilepsy of infancy (SMEI) is a rare epileptic encephalopathy characterized by drug-resistant febrile and afebrile generalized or unilateral convulsive seizures. Cognitive deterioration becomes evident from the second year of life. Sodium channel SCN1A gene mutations have been found in 40–70% of patient with typical SMEI. **Objectives:** Clinical follow-up, neuropsychological outcomes, control of seizures and antiepileptic treatments between different groups were analysed according to age at diagnosis of SMEI. **Material and methods:** A retrospective study realised in patients with SMEI and positive mutations of SCN1A, at Hospital Saint Luc. Medical records of 19 patients were reviewed to collect information regarding general characteristics, age at onset, type and duration of seizures, status epilepticus, neuropsychological features, and genetic analysis. Antiepileptic treatment before and after genetic confirmation of SMEI was also noted. Patients were categorized according to the age at diagnosis of SMEI into three groups: Group 1 (3 patients diagnosed between 24–31 years old), Group 2 (8 patients diagnosed between 6–18 years old) and Group 3 (8 patients diagnosed between 6 – 24 months). **Results:** Epilepsy characteristics do not differ among the different groups at its onset. Later seizure con-

trol was more difficult to obtain in Groups 1 and 2; Group 2 being the one with the greatest seizure frequency. Patients in Group 1 and 2 received at least 4–6 antiepileptic drugs and most of them were treated by currently contraindicated drugs. 66% of patients in Group 1 and 25% of patients in Group 2 have severe cognitive impairment. **Conclusions:** Seizure control in SMEI is difficult and cognitive prognosis remains poor. It appears that antiepileptic treatment according to new international recommendations leads to a better epileptic and cognitive development. For this reason, a prompt clinical and genetic diagnosis is necessary to provide an adequate treatment.

O96 - 1638

Electrical status epilepticus in sleep (ESES): etiology, clinical picture and course

Aleksandrova I, Bojinova V, Dimova P. *Clinic of Child Neurology, "St. Naum" University Hospital of Neurology and Psychiatry, Sofia, Bulgaria – iliyana_abv.bg*

Objectives: To analyze the etiology, clinical manifestations and disease course in children with electrical status epilepticus in sleep (ESES). **Material and methods:** We retrospectively analyzed the data of 60 children with ESES treated from 2006 to 2012. **Results:** Thirty eight patients had an atypical evolution of idiopathic focal childhood epilepsy with 33 of them being long-term followed up. The mean age of seizure onset was 5 years with a mean age of ESES manifestation of 7 years. Initially, almost all children had focal seizures with or without secondary generalization. At the time of ESES manifestation 44.7% experienced new seizure types (atonic, myoclonic or atypical absences); 63.2% had increase in seizure frequency; and 44.7% had either cognitive deterioration or behavioral problems. The clinical features in two patients were consistent with acquired anterior opercular syndrome. In one case the epilepsy had a very aggressive course evolving to CSWS-related encephalopathy. Twenty two patients had symptomatic epilepsy due to: cortical malformation (n=4), ante- or perinatal ischemic lesions (n=12), tuberous sclerosis, angioma, congenital toxoplasmosis, meningoencephalitis, stroke and microdeletion syndrome (each in one case). The epilepsy onset in this group was at a younger age (mean 2 years). Twenty-one children were long-term followed up. Seizure remission was achieved in 24/33 idiopathic cases. Improvement, or normalization, of EEG was achieved in 13/33 (40%) of them, while 20/33 (60%) had relapsing ESES. The evolution in the symptomatic group was unfavorable – 19/21 (90.5%) had relapsing or persistent ESES, and 16/21 (76%) continued to have seizures. **Conclusion:** With regard to the seizures, the outcome of ESES in idiopathic cases is good, yet many patients remained with cognitive or behavioral impairment. Thus, early recognition and appropriate treatment is essential for the prognosis. The underlying etiology seems to have a major impact, since patients with symptomatic epilepsy have a worse outcome.

O97 - 1635

Treatment of electrical status epilepticus in sleep (ESES): efficacy and unsolved questions

Dimova P, Alexandrova I, Bojinova V. *Clinic of Child Neurology, "St. Naum" University Hospital of Neurology and Psychiatry, Sofia, Bulgaria – psdimova@gmail.com*

Objectives: To analyze the treatment and its efficacy in children with electrical status epilepticus in sleep (ESES). **Material and**

methods: We retrospectively reviewed the data of 60 children with ESES treated from 2006 to 2012. **Results:** In our cohort patients with idiopathic focal epilepsy predominated (38 vs 22 children with symptomatic epilepsy). They showed a later epilepsy and ESES onset and more benign disease course. A permanent remission of seizures and improvement, or normalization, of ESES was achieved with the initial treatment in 39.4% (13/33) of the idiopathic group. Best results were seen on therapy with: 1) corticosteroids in combination with ethosuximide [ESM] (n=2), levetiracetam [LEV] (n=3), clonazepam [CZP] and LEV (n=1) or lamotrigine [LTG] (n=1); 2) LEV alone (n=3) or in combination with valproate [VPA] (n=1) and CZP (n=1); 3) Sulthiame [STM] (n=1). Twenty out of 33 patients (60.9%) showed relapsing ESES. Later in the disease course seizure remission was achieved in 11/20 patients by: 1) corticosteroids alone (n=2) or in combination with LEV (n=1), ESM (n=1), CZP (n=1), Nitrazepam (n=1); 2) LEV (n=3); 3) STM (n=1); 4) ESM (n=1). The patients with symptomatic epilepsy had more unfavorable evolution as 19/21 (90.5%) had persistent or relapsing ESES with only transient improvement with various therapeutic approaches, and only 5 children (24%) became seizure-free. **Conclusion:** ESES is characterized by a significant therapeutic refractoriness, especially in symptomatic epilepsies. The most effective anticonvulsants in our study are LEV, benzodiazepines, STM and ESM. Corticosteroids, however, show the most pronounced and long-lasting effect, but only when used in appropriate doses and for sufficient period of time considering the risk of serious side effects. Large prospective studies are needed to establish guidelines for the treatment strategy in ESES.

O98 - 1979

Intravenous methylprednisolone for the treatment of infantile spasms

Aburahma A, Al-Sharqawi S. *Jordan – samahk72@yahoo.com*

Purpose: this is a description of the clinical experience of utilizing intravenous (IV) pulse methylprednisolone for the treatment of infantile spasms. **Methods:** a retrospective study utilizing chart reviews of all patients who presented with infantile spasms and were treated with IV pulse methylprednisolone between July 2007 and April 2013. Patients were identified through identifying all patients with a hypsarrhythmia pattern on EEG during that period of time. Data was collected regarding clinical presentation of patients, EEG results, neuroimaging, laboratory findings, presumed underlying cause of the spasms, response to treatment with pulse methylprednisolone, and complications of therapy. **Results:** Twenty nine patients were identified. All patients with infantile spasms were treated with IV methylprednisolone as ACTH is not available in Jordan. As EEG was utilized for identification of infants, all showed a hypsarrhythmia pattern. Twenty two patients had an abnormal MRI, most commonly congenital brain malformations, followed by evidence of perinatal brain injury. All patients received IV pulse methylprednisolone therapy at a dose of 20–30mg/kg/day for 5 days, followed by outpatient oral prednisone taper. Oral Ranitidine was given during steroid therapy. Twenty one patients showed complete cessation of the spasms during the hospital stay. Four patients showed reduction in severity and frequency of spasms. None of the patients had any serious adverse effects that necessitated cessation of therapy. **Conclusion:** IV methylprednisolone is an effective, safe, inexpensive, and easy to administer therapeutic option for infants with infantile spasms. More studies are required to evaluate this therapy in a controlled manner and to evaluate the long term outcome of these infants.

SELECTED POSTER PRESENTATIONS

Wednesday 25 September 2013

PP1. Cerebral palsy, neonatology, stroke

Chair: Lars Palm

PP1.0 - 1848

The reparative effects of neural stem cells in neonatal hypoxic ischemic injury are not influenced by host gender

Ashwal S, Ghosh N, Turenius C, Dulcich M, Denham CM, Tone B, Hartman R, Snyder EY, Obenaus A. *Department of Pediatrics, Loma Linda University School of Medicine, Loma Linda, California, USA – sashwal@llu.edu*

Background: Gender is increasingly recognized as an important influence on brain development, disease susceptibility, and response to pharmacologic and rehabilitative treatments. In regenerative medicine, it remains entirely unknown whether there is an interaction between transplanted stem cells and host gender that might bias efficacy and safety in some patients but not others. **Methods:** As proof-of-concept, we examined the role of recipient gender in a rat pup model of neonatal hypoxic-ischemic injury (HII) treated with human neural stem cells (hNSCs). Into the cerebral ventricles of rats subjected to HII, we implanted female hNSCs, labeled with superparamagnetic iron-oxide (SPIO) particles, and serially monitored HII evolution (by magnetic resonance imaging [MRI], histopathology, behavioral testing) and hNSC fate (migration, replication, viability). **Results:** Recipient gender after hNSC implantation did not influence the volume or location of ischemic injury (1, 30, or 90d post-implantation) or behavior (at 90d). SPIO labeling did not influence HII evolution. Independent of gender, hNSC implantation appeared to have its greatest benefit on mild and moderate rather than severe HII lesions. Lesion volumes in pups with mild/moderate injuries receiving hNSCs remained stable over the 90d observation period rather than increasing as is the natural history for such lesions. Treatment, however, did not prevent the gradual increase in lesion volume in pups with severe HII. **Conclusions:** Our results suggest that hNSC treatment would be equally safe and effective for male and female human newborns with mild-to-moderate HII.

PP1.1 - 1847

Hypothermia after rat pup hypoxia/ischemia: effects on cytokines, signaling molecules and core/penumbra volumes

Yuan X, Ghosh N, McFadden B, Tone B, Tian HR, Snyder EY, Obenaus A, Ashwal S. *Department of Pediatrics, Loma Linda University School of Medicine, Loma Linda, California, USA – sashwal@llu.edu*

Objective: Hypothermia (HT) is standard of care for neonates with hypoxic ischemic injury (HII). Because of its modest effect, additional translational studies are needed to maximize neuroprotection, specifically when HT is combined with other treatments (e.g., stem cells). **Methods:** Unilateral HII (carotid occlusion, 8% O₂) was induced in 10d rat pups and followed by 24 hours of HT (30°C; n=18) or normothermia (NT, 35°C; n=15). MRI, neurological testing (righting reflex) and cytokine/signaling molecule profiles (Luminex/ELISA) were collected pre-HII and at 0, 24, 48, 72 hrs post HII. **Results:** Compared to NT, HT pups had less weight loss (33.5%) at 24hr and faster righting reflexes (43%) at 0–48hr post HII. Compared to NT, HT reduced MRI measures of HII including the rat pup severity score (64%) & HII volumes (total lesion, 69%; ischemic core, 79% & penumbra, 63%) between 0 and 48 hrs. HT reduced expression of inflammatory cytokines (interleukin-

1 β , p<0.05). Interferon- γ , tumor necrosis factor- α and monocyte chemoattractant protein-1 expression were lower in the HT than in the NT group (although not statistically significant) indicating less inflammation in the HT group. Stromal cell-derived factor-1 α levels were not modified (p<0.81) suggesting that HT does not affect stem cell signaling molecules. Interestingly, at 72hrs post HII (48hrs post HT) there was an increase in cytokine levels that was associated with increased HII injury volumes and a reduced righting reflex, suggesting a rebound effect. Our data demonstrate that HT reduces inflammatory cytokines without altering stem cell signaling within 0–48 hrs post HII, thus increasing the HT treatment window.

PP1.2 - 1727

Susceptibility of hippocampal neurons to hypothermia during development

Chae SA, Seo KA, Kim SH, Lee NM. *Departments of Pediatrics, College of Medicine, Chung-Ang University, Korea – kidbrain@korea.com*

Objectives: This study evaluated the extent of damage due to hypothermia in the mature and immature brain. **Methods and material:** Organotypic hippocampal cultures were prepared from 7 day old rat pups. Hippocampal tissue cultures at 7 and 14 days in vitro (DIV) were used to represent the immature and mature brain, respectively. The cultures were exposed at 25°C for 0, 10, 30, and 60 min (n=30 in each subgroup). Propidium iodide fluorescent images were captured 24 and 48 hrs after hypothermic injury. Damaged areas of the Cornu Ammonis 1 (CA1), CA3, and dentate gyrus (DG) were measured using image analysis. **Results:** At 7 DIV, the tissues exposed to cold injury for 60 min showed increased damage in CA1 (P<0.001) and CA3 (P=0.005) compared to the control group at 48 hr. Increased damage to DG was observed at 24 (P=0.008) and 48 hrs (P=0.011). The 14 DIV tissues did not demonstrate any significant differences compared with the control group, except for the tissues exposed for 30 min in which DG showed less damage at 48 hr than the control group (P=0.048). In tissues at 7 DIV, CA1 (P=0.040) and DG (P=0.013) showed differences in the duration of cold exposure. **Conclusions:** The immature brain is more vulnerable to hypothermic injury than the mature brain.

PP1.3 - 1950

Learning walking coordination through dynamic recurrent neural network in children with bilateral cerebral palsy

Hoellinger T, Cheron G, Dan B. *Laboratory of Neurophysiology and Movement Biomechanics, Université Libre de Bruxelles, Brussels, Belgium – hoellint@gmail.com*

The existence of dedicated neuronal modules such as those organized in the cerebral cortex, thalamus, basal ganglia, cerebellum or spinal cord raises the question of how these functional modules are coordinated for appropriate motor behavior. Study of human locomotion offers an interesting field for addressing this central question. We describe the use of a dynamic recurrent neural network (DRNN) mimicking the natural oscillatory behavior of human locomotion for reproducing the planar co-variation rule in both legs at different walking speeds. Neural network learning was based on sinusoidal signals integrating frequency and amplitude features of the first three harmonics of the sagittal elevation angles of the thigh, shank and foot of each lower limb. We verified the biological plausibility of the neural networks in healthy subjects and children with spastic bilateral cerebral palsy (GMFCSI-II). Best results were obtained with oscillations extracted from the first three harmonics in comparison to oscillations outside the harmonic frequency peaks. We show application of this approach and discuss implications for neu-

rophysiological understanding of the central pattern generator processing relevant oscillation signals and integrated management programs in cerebral palsy.

PP1.4 - 1932

Botulinum toxin A in the treatment of cerebral palsy: stability of doses and inter-session intervals across time for different patient groups

Nikaina I, Foska K, Mitsou G, Papavasiliou A. *Department of Neurology, Pendeli Children's Hospital, Athens, Greece – theon@otenet.gr*

Aim: To review the experience with botulinum toxin A (BoNT-A) of a paediatric multidisciplinary cerebral palsy clinic and test stability of doses and inter-session intervals in different patient groups. **Methods:** Children and adolescents, younger than 18 years old with Spastic Cerebral Palsy (SCP) who received BoNT-A injections were included in this study. Onabotulinumtoxin A and Abobotulinumtoxin A were used for multi-level upper and/or lower limb injections, repeated as needed at >4 months intervals. Data on the dosage scheme, the frequency of the injections and the duration of the treatment along with patients' demographic data were collected. **Results:** 454 patients with a mean age of 5.3 years (\pm 3.6) received 1515 BoNT-A sessions. Total doses/kg of BoNT-A were stable across sessions ($p=0.244$) but they were higher in children bilaterally ($p<0.001$) and more severely involved ($p<0.001$). In children with bilateral SCP doses/kg demonstrated an increasing trend with time ($p=0.030$). Children older than 4 years were injected with similar doses/kg as compared to the younger ones ($p=0.109$), but unlike younger patients their doses/kg decreased with time ($p=0.024$). doses/kg in lower limbs were stable across time in both unilateral and bilateral SCP ($p=0.177$ and $p=0.609$, respectively). In bilateral SCP doses/kg were higher in severely affected ($p=0.020$) and older patients ($p=0.003$); in unilateral SCP, children older than 4 years had lower doses/kg in their lower limbs ($p=0.061$) versus the younger ones, with a decreasing trend as time evolved ($p=0.016$). doses/kg in upper limbs were stable across time in both unilateral and bilateral SCP ($p=0.807$ and $p=0.106$, respectively). Inter-session intervals were longer as time evolved ($p=0.003$), when Onabotulinumtoxin A was used ($p=0.019$) and in older children ($p=0.001$). **Conclusion:** Age at treatment onset interfered with doses and intervals. Stability of doses/kg injected and elongation of inter-session intervals excluded secondary unresponsiveness to BoNT-A due to antibodies.

PP1.5 - 1899

Management and interpretation of medical data related to cerebral palsy: the ICT4Rehab project

Bonnechère B, Wermenbol V, Dan B, Salvia P, Le Borgne Y, Bontempi G, Vansummeren S, Sholukha V, Moiseev F, Jansen B, Rooze M, Van Sint Jan S. *Laboratory of Anatomy, Biomechanics and Organogenesis (LABO), Université Libre de Bruxelles, Belgium – bbonnech@ulb.ac.be*

Cerebral palsy (CP) is a complex disorder and the aetiology is probably one of the primary causes why different approaches are sometimes adopted in different hospitals for patient data management (anamnesis, clinical trials and functional analysis), and the decision-making over the best treatment approach to offer to the patients. This variety of approaches is a problem for information and data exchange. The project ICT4Rehab (www.ICT4Rehab.org) is a multidisciplinary project funded by the Brussels region. ICT4Rehab develops a shared technology platform that addresses some of the above-mentioned problems. The platform offers hospitals the ability to store the data of their patients on a shared server data. A secured access then allows

comparing the data of a particular patient with groups of patients (e.g. two groups of patients suffering for different pathologies within the same hospital, group a patient presenting the same pathologies from two different centres to compare methodology) or normal populations. This comparison is performed by data mining methods. The representation of data within the platform is based using today biomechanical and clinical standards. Serious gaming data are also integrated into the system. Clinical needs from several Belgian clinical centres have been gathered within a common shared technological structures developed by the project. Currently, patient files from three Brussels hospitals can be accessed by common statistical and reporting tools. Data integration of more hospitals is planned for the near future. The paradigm behind the ICT4Rehab project can be relatively extended to other efforts (for example, to connect to the creation of a central CP register in Europe (<http://www.scpnetwork.eu/>). Such shared information will allow producing more meaningful statistical results and facilitate consensus mechanism. The ICT4Rehab project seeks to expand its user group by inviting all motivated clinicians to test the structure of data sharing and mining tools developed by the project.

PP1.6 - 1680

Clinical patterns of secondary dystonia and choreoathetosis in dyskinetic CP

Monbaliu E, Ortibus E, Prinzie P, De Cock P, Klingels K, Heyrman L, Feys H. *KU Leuven, Department of Rehabilitation Sciences, Belgium; DC GID(t)S, Dominiek Savio Institute, Belgium – Elegast.Monbaliu@faber.kuleuven.be*

Objectives: A better understanding of the clinical dystonia and choreoathetosis patterns in relation to motor classifications and brain lesions is essential to targeted therapy interventions. Therefore this study aimed: (1) to map dystonia and choreoathetosis across twelve body regions during voluntary asked activities and during rest; (2) to relate them with motor classifications; (3) to examine their relationship to lesions in the thalamus and basal ganglia. **Material and methods:** Fifty-five participants with dyskinetic CP (mean age 14 years 6 months, SD 4 years 1 month; age range 6–22 years) were evaluated using the Dyskinesia Impairment Scale (DIS), measuring both dystonia and choreoathetosis, the Gross Motor Function Classification System (GMFCS) and the Manual Ability Classification System (MACS). Non-parametric statistics (Wilcoxon signed-rank test and Spearman's rank correlation) were used to analyze clinical patterns and to relate them with the motor classifications. The Mann-Whitney U test was used to compare dystonia and choreoathetosis to the brain lesions. **Results:** Dystonia and choreoathetosis were simultaneously present across all body regions but participants showed significantly more dystonia than choreoathetosis (mean percentage 70.2% versus 26.7%, $p<0.01$). Also, dystonia and choreoathetosis were significantly higher during activity than at rest. Spearman correlations between the GMFCS and MACS with the DIS scores were high for dystonia, respectively 0.70 and 0.65. We found no significant correlations for choreoathetosis ($r_s=0.17$ and 0.21). Finally, participants with pure thalamus and basal ganglia lesions clearly showed higher scores for choreoathetosis ($p=0.03$), but not for dystonia ($p=0.44$). **Conclusions:** In dyskinetic CP, dystonia and choreoathetosis are simultaneously present but with a higher dominance of dystonia. Higher scores for dystonia were clearly associated with more severe motor disability suggesting that dystonia, rather than choreoathetosis, has a larger impact on motor functions. Finally, pure thalamus and basal ganglia lesions seem to be particularly associated with choreoathetosis.

PP1.7 - 1983**Quality of life one year after arterial ischaemic stroke in a population-based cohort**

Mallick AA, Ganesan V, Kirkham FJ, Fallon P, Hedderly T, McShane T, Parker AP, Wassmer E, Wraige E, Amin S, Edwards HB, O'Callaghan FJK. *University of Bristol, United Kingdom* – andrew.mallick@bristol.ac.uk

Objectives: To assess the quality of life (QoL) of children after arterial ischaemic stroke (AIS) and analyse factors associated with impaired QoL. **Material and methods:** A population-based cohort of 96 children (aged >28 days to <16 years) residing in southern England with AIS onset between July 2008 and June 2009 were followed-up at one year post AIS. QoL was assessed using the Pediatric Quality of Life Inventory (PedsQL). Children were also assessed using the Pediatric Stroke Outcome Measure (PSOM) and the Pediatric Stroke Recurrence and Recovery Questionnaire (RRQ) which have both been validated for use in paediatric stroke. Cognitive outcome was also assessed using a short form of the Wechsler Intelligence Scale for Children (WISC). **Results:** Parental-proxy PedsQL scores were available for 62 children and child self-reported PedsQL scores were available for 34 children. The mean total-scale PedsQL score by parental-proxy was 75.5 (SD 20.2) which was significantly below the UK norm for healthy children (84.6, $p=0.0008$). The mean total-scale PedsQL score by self-report was 83.0 (SD 15.7) which was not significantly different from the UK norm (83.9, $p=0.72$). Increasing total PSOM scores (greater neurological impairment) was associated with lower parental ($p<0.0001$) and self-reported ($p<0.0001$) PedsQL scores. Higher WISC scores were associated with higher parental ($p=0.005$) and self-reported ($p=0.001$) PedsQL scores. In a multivariate analysis PSOM sensorimotor deficits (but not other PSOM domains), female gender, and the presence of recurrent headache were all independently associated with lower parental-proxy PedsQL scores. **Conclusions:** Parental-proxy QoL scores are reduced one year after AIS but child self-reported scores are not. The presence of sensorimotor deficits is the most important predictor of reduced QoL.

PP1.8 - 1980**Psychomotor development in children with posthaemorrhagic ventricular dilatation**

Laroche S, Hollander R, Ceulemans B. *University Hospital Antwerp, Belgium* – sabrina.laroche@uza.be

Psychomotor development in children with posthaemorrhagic ventricular dilatation. Laroche S., Hollander R., Ceulemans B., departments of Neonatal Intensive Care and Paediatric Neurology of University Hospital Antwerp. **Objective:** Follow-up study of posthaemorrhagic ventricular dilatation in a neonatal intensive care unit. **Methods:** We studied 47 children (period 2000–2010) with posthaemorrhagic ventricular dilatation retrospectively. Thirty-one of them had a gestational age (GA) below 32 weeks, 10 between 32 and 37 weeks, and 6 were born term. Patients with congenital anomalies (2), postneonatal CNS damage (1) and those lost to follow-up (1) were excluded. In the neonatal unit patients were followed with brain ultrasound. After hospital discharge their psychomotor development was assessed regularly. **Results:** We used Levene indices to make therapeutic decisions. In 17 patients the ventricular dilatation stabilised without intervention. We could stabilise 6 of the preterm neonates with a GA below 32 weeks with evacuating lumbar punctures only. In 6 patients the ventricular dilatation resolved using a subcutaneous reservoir. Twelve neonates needed a ventriculoperitoneal shunt. Two of the term neonates were treated with an external drain. There was an incidence of shuntinfections of 15%; *Staphylococcus epidermidis* was the main cause (62%). A central motor problem was seen in 12 (28%) of the chil-

dren: 5 hemiplegias, 3 quadriplegias, 2 diplegias, and in another 2 hypotonia dominated the clinical picture. All but three of our patients with cerebral palsy walked independently around the age of 2.5 years. The incidence and severity of central motor problems was the highest in the group with a GA between 32 and 37 weeks. A mental developmental index below 70 was seen in 5 children (11%). Characteristics of autism spectrum disorder were diagnosed in 7 (15%). **Conclusion:** Only 12 out of 43 patients with posthaemorrhagic ventricular dilatation needed a ventriculoperitoneal shunt. Global outcome seems acceptable.

PP2. Epilepsy 1

Chair: Peter Baxter

PP2.0 - 2107**A new approach to genetic diagnosis in early infantile epileptic encephalopathy and severe neurodevelopmental delay using a gene panel**

Mctague A, Scott RH, Moody H, Meyer E, Drury S, Fielding S, Trump N, Morrogh D, Lench NJ, Kurian MA. *Neurosciences Unit, UCL-Institute of Child Health, London, United Kingdom* – a.mctague@ucl.ac.uk

Objective: The early infantile epileptic encephalopathy (EIEE) syndromes are a heterogeneous group of conditions characterised by intractable seizures and developmental delay or regression. An increasing number of genetic causes are recognized; however genetic heterogeneity and phenotypic pleiotropy are common, rendering single gene testing impractical, time consuming and costly. We describe a pilot study of a new approach to genetic diagnosis using a multiple gene panel. **Methods:** Our gene panel included 29 genes associated with EIEE and developmental delay (including those cited on OMIM as EIEE 1–13). For detection of small copy number variants, we utilised Roche Nimblegen custom design software to create an exon-level 135K comparative genomic hybridization (CGH) array. In addition, Custom HaloPLEX sequence capture (Agilent) and Illumina sequencing was undertaken using a MiSeq platform. We tested 48 children with severe developmental delay and early onset seizures. All had been pre-screened with diagnostic microarray and methylation studies for Angelman's syndrome, where appropriate. **Results:** Data quality was high (greater than 30x-fold sequence data coverage, 90% of targeted coding bases) and no false positive calls were made. Mutations were identified in 5 patients (10%) and included nonsense mutations and deletions in a number of genes including MECP2 (2 patients), CDKL5, SLC9A6 and EHMT1. **Conclusions:** We report a multiple gene panel which has combined targeted, exon-level array CGH with next-generation sequencing technology to screen 29 disease causing genes in a cohort of patients with early onset seizures and neurodevelopmental delay. This diagnostic approach is likely to abolish the need for sequential gene testing in this group of disorders, and will no doubt improve genetic diagnosis (and likely provide earlier diagnosis) in this disparate range of conditions, thereby allowing better prognostication and genetic counselling for patients and their families.

PP2.1 - 1874**Ohtahara syndrome in two half siblings due to a novel SCN2A mutation**

Zerem Sheinman A, Halevy A, Michaeli-Yossef Y, Goldberg-Stern H, Blumkin L, Kivity S, Saitsu H, Lev D, Leshinsky-Silver E, Lerman-Sagie T. *Pediatric Neurology Unit, Metabolic Neurogenetic Service, Wolfson Medical Center, Holon, Israel* – ayeletzerem@gmail.com

Objective: Ohtahara syndrome (OS) is a devastating early in-

fantile epileptic encephalopathy characterized by early onset of tonic spasms, intractable seizures, suppression-burst pattern on EEG and severe psychomotor retardation. De novo mutations in STXBP1 and ARX are major causes. SCN2A gene encodes the α 1-subunit of the neuronal voltage-gated sodium channel. Mutations in SCN2A have been reported to cause benign epileptic syndromes, such as benign familial neonatal- infantile seizures, which are inherited from an affected parent. In contrast, several de novo SCN2A mutations have been reported to cause more severe epileptic phenotypes such as Dravet syndrome. The objective of this report is to describe a gonadal mosaicism of SCN2A mutations in two half siblings with Ohtahara syndrome. **Material and methods:** We describe a patient with classic OS who presented on the first day of life with refractory tonic seizures. A suppression- burst pattern evolved later in life to modified hypersarrhythmia. The patient developed severe progressive microcephaly ($-6SD$), profound mental retardation and spasticity and never achieved any developmental milestones. He died at the age of 5 years. The patient's DNA was screened for SCN2A mutations by high resolution melt analysis. The mutation was confirmed by Sanger sequencing. **Results:** The patient was found to have a novel missense mutation (c.4007C>A p.S1336Y). The parents were negative for the mutation. The father has another son from a different mother presenting as OS. The sibling with OS carries the same mutation; thus suggesting a diagnosis of paternal gonadal mosaicism. **Conclusions:** The broad clinical spectrum of SCN2A mutations should include Ohtahara syndrome. This is the first report of familial OS due to germline mosaicism. It has important consequences for genetic counseling when SCN2A mutations appear to occur de novo.

PP2.2 - 2026

Novel compound heterozygous mutations in TBC1D24 cause familial malignant migrating partial seizures of infancy

Milh M, Falace A, Villeneuve N, Vanni N, Cacciagli P, Assereto S, Nabbout R, Benfenati F, Zara F, Chabrol B, Villard L, Fassio A. INSERM U 910 and APHM Service de Neurologie pédiatrique, Marseille, France – mathieu.milh@ap-hm.fr

Early-onset epileptic encephalopathies (EOEEs) are a group of rare devastating epileptic syndromes of infancy characterized by severe drug resistant seizures and electroencephalographic abnormalities. The current study aims to determine the genetic etiology of a familial form of EOEE fulfilling the diagnosis criteria for malignant migrating partial seizures in infancy (MMPSI). We identified two inherited novel mutations in TBC1D24 in two affected siblings. Mutations severely impaired TBC1D24 expression and function, which is critical for maturation of neuronal circuits. The screening of TBC1D24 in an additional set of 8 MMPSI patients was negative. TBC1D24 loss of function has been associated to idiopathic infantile myoclonic epilepsy, as well as to drug resistant early onset epilepsy with intellectual disability. Here we describe a familial form of MMPSI due to mutation in TBC1D24, revealing a devastating epileptic phenotype associated with TBC1D24 dysfunction.

PP2.3 - 2143

Clinical and neuroimaging features of patients with ESES

Yüksel D, Ozkan M, Aksoy A, Kaya Ü. Dr. Sami Ulus Children's Health and Diseases Training and Research Hospital, Ankara, Turkey – drdeniz_yuksel@yahoo.com.tr

Objective: "Electrical status epilepticus during slow wave sleep" (ESES) is characterised by the electroencephalographic pattern of continuous spike waves during slow wave sleep (CSWS) and variable neuropsychological impairments. The aim of this study was to evaluate the clinical and neuroimaging features of ESES

and to investigate possible risk factors. **Methods:** In a retrospective study, we analysed the demographic and clinical data and waking after sleep EEG slow waves of 16 patients with ESES. The patients showed continuous spike waves ($>85\%$) associated with regression of cognitive functions. **Results:** The mean age was 9.37 ± 3.15 (range 3–15 years), 7 male and 9 female patients who had been diagnosed with ESES were enrolled in the study. The age at the onset of their first seizure was 2.93 ± 2.48 (range 0–10 years), the mean age at the onset of the ESES clinic was 7.5 ± 2.78 (range 2–13 years). Their respective medical histories showed 2 patients with a prematurity, 3 patients with perinatal asphyxia, 2 patients with congenital cytomegalovirus infections, 2 patients with neonatal convulsions, 1 patients with neonatal stroke, 1 patients with intrauterine growth retardation, and 2 patients with febrile convulsions. Our neurological examination revealed 8 patients (50%) with microcephaly, 13 patients (81%) with mental retardation, 6 patients (37%) with cerebral palsy, 5 patients with speech delay, and 2 patients with ataxia. Brain magnetic resonance imaging findings showed malformations of cortical development (schizencephaly, lissencephaly, cortical dysplasia), corpus callosum agenesis, periventricular leukomalacia, cortical atrophy, thalamic lesions, calcifications, hypoxic ischemic lesions, stroke, and only five patients had normal results. Except three patients the remaining patients underwent antiepileptic drug polytherapy. **Conclusions:** Early and effective therapy aiming to decrease the duration of ESES may also help prevent permanent neuropsychological impairment, though no consensus exists as to the optimal treatment.

PP2.4 - 2121

Recurrent status epilepticus and dystonia caused by a mutation in SCN8A

Peake D, Anderson J, Anderson C, McKee S. Paediatric Neurology Department, Royal Belfast Hospital for Sick Children, United Kingdom – shane.mckee@belfasttrust.hscni.net

Introduction: Several voltage-gated sodium-channel genes have been implicated in seizure disorders, including SCN1A, SCN2A, SCN3A, and SCN9. SCN8A encodes the neuronal sodium channel NaV1.6 that is highly abundant in the CNS, and recently linked with infantile epileptic encephalopathy. We present a 16 year-old female with a severe epileptic encephalopathy associated with an SCN8A mutation detected by whole-exome sequencing. **Case report:** The proband presented at age 8 months with clustering of frequent myoclonic seizures - up to 50/day, not associated with fever or illness. Subsequent recurrent generalised tonic clonic seizures and frequent episodes of status epilepticus (from age 1y) resulted in >25 admissions to hospital, often involving PICU. Later seizures (refractory to treatment) were more typical of clustering of focal motor, tonic and atonic seizures. The last EEG showed slow spike-and-wave discharge superimposed on abnormal, slow background, frequency 1.5–2.0Hz (Lennox-Gastaut). Several neuroimaging studies (MRI & CT) between 8m and 16y were normal. There was no period of normal development; neurological examination revealed a normocephalic child with central hypotonia, generalised limb dystonia and contractures. There were no dysmorphic features other than small, cold hands and feet. Death occurred at 16 years following a period of hospital admission with intractable seizures and acute chest infection on a background of increasing respiratory compromise. Karyotype and microarray-CGH were normal. Whole-exome sequencing revealed a de novo heterozygous missense mutation p.G1625R in SCN8A. **Conclusion:** Further cases of SCN8A-associated early infantile epileptic encephalopathy will almost certainly come to light via exome sequencing, and help clarify the phenotypic spectrum and management options.

PP2.5 - 2056**The role of ictal subtraction SPECT for the diagnosis of focal cortical dysplasia in an infant**

Kara B, Maras H, Yalcin EU, Aktan F, Demirbas F, Anik Y, Ciftci EA, Gorur GD. *Kocaeli University Medical Faculty, Department of Pediatrics, Division of Child Neurology, Kocaeli, Turkey – bkuskudar@gmail.com*

Infantile epileptic encephalopathies cause global developmental and intellectual retardation without effective treatment. Cortical dysplasias are an important cause of infantile epileptic encephalopathy, because surgical treatment of the epileptic foci may improve the prognosis. Cortical dysplasias cannot be shown with cranial magnetic resonance imaging in every patient, and PET and/or SPECT have been shown to be valuable tests in the detection of seizure foci. In the literature, ictal subtraction SPECT appears to be more sensitive than other tests. 4-month-old girl was reported for hypomotor and complex focal seizures, and nystagmus-like eye movements. Seizures could not be controlled despite different antiepileptics. Interictal electroencephalograms (EEG) showed bilateral occipital epileptiform activity. Cranial magnetic resonance imaging was normal. During video EEG monitorization, a lot of seizures were recorded, and all of them were from the occipital lobes, especially left. PET analysis was not informative. Ictal SPECT showed left occipital parasagittal hyperperfusion area, and perfusion of this area returned to normal with interictal SPECT. A new cranial magnetic resonance imaging was ordered, and we observed thin cortex (2.7 mm) and insufficient sulcation at the left parasagittal occipital lobe compatible with ictal SPECT. The diagnosis of the patient was intractable epilepsy due to focal cortical dysplasia, and now she is being evaluated for surgical treatment. Ictal subtraction SPECT can provide important information in the detection of seizure foci and preoperative evaluation of medically intractable epilepsy.

PP2.6 - 2050**Crossed cerebellar diaschisis with non-refractory epilepsy**

Monier A, Aouni S, Dan B. *Clinique de Neurologie, Hôpital Universitaire des Enfants Reine Fabiola, ULB, Brussels, Belgium – anne.monier@huderf.be*

We report a 5 year-old boy who presented with iterative generalized seizures lasting for 24 hours with febrile otitis media. He had previously suffered one status epilepticus episode at 18 month and one short-lasting seizure at 4 years, with normal brain MRI. He also presented a mild coordination disorder. On presentation, MRI showed left fronto-occipital gliotic lesions with normal diffusion-weighted images and MRA. EEG showed moderate left fronto-parietal epileptiform activity. After acute management, the child was rapidly seizure-free. Two-year follow-up revealed no seizure under valproic acid, mild right upper limb paresis, coordination disorder and executive dysfunction, necessitating integration in a special school. Repeat brain MRI (after 1 and 2 years) showed an increase of the white matter lesions and significant atrophy of the right cerebellar hemisphere, with normal MRA. EEG shows sustained epileptiform activity in the left fronto-parietal region and no continuous spikes and waves syndrome during sleep. This evolution is consistent with crossed cerebellar diaschisis (CDD), a rare condition where a cerebellar lesion develops remote from a contralateral supratentorial primary site of injury, presumably due to loss of afferentation in the corticopontocerebellar tract connecting the two areas. Metabolic depression, retrograde degeneration and excitotoxicity are the main suggested mechanisms. In children, most cases are related to encephalitis and tumor, rarely to stroke, migraine and refractory focal epilepsy. The present report suggests that CDD can occur without clinical seizure, potentially due to remaining focal

epileptiform activity. In our patient, it is highly probable that the slowly progressive white matter injury of unknown origin potentiates the phenomenon. Whether epileptic subclinical activity should be treated more aggressively remains questionable.

PP2.7 - 2032**Benign familial infantile epilepsy due to PRRT2 gene mutation without paroxysmal kinesigenic dyskinesia**

Maras H, Kara B, Yalcin EU, Iseri SU, Ozbek U. *Kocaeli University Medical Faculty, Department of Pediatrics, Division of Child Neurology, Kocaeli, Turkey – hulyamaras@gmail.com*

Mutations of PRRT2, which encodes “proline-rich transmembrane protein 2”, have been identified in patients with benign familial infantile seizures (BFIS), infantile convulsions with choreoathetosis (ICCA) syndrome and familial paroxysmal kinesigenic dyskinesia (PKD). All these phenotypes had autosomal dominant inheritance. PRRT2 is a presynaptic protein, and likely has a role for exocytosis and neurotransmitter release. Recent studies show that PRRT2 gene mutation is the most common cause of BFIS. 6-month-old boy had hypomotor seizures. His brother, maternal aunt, and maternal uncle also had seizure history in infancy. All patients had normal neurologic development. Seizures of the index patient and his brother were controlled with phenobarbital, maternal aunt and maternal uncle of the index patient were free of seizures, and had no history of antiepileptic medication. BFIS was diagnosed due to seizures beginning in infancy and normal neurologic development. PRRT2 gene mutation was observed in the affected patients. All affected patients were reevaluated for paroxysmal kinesigenic dyskinesia, but there were no history or clinical evidence of dyskinesia. PRRT2 should be the first gene to screen in patients with BFIS. Paroxysmal kinesigenic dyskinesia may not accompany in all patients with PRRT2 mutations.

PP2.8 - 1767**Safety of adjunctive zonisamide in paediatric epilepsy patients: results from a pooled analysis of 17 studies**

Giorgi L, Patten A. *Eisai Limited, Hatfield, Herts, UK – mandrews@mxmcommunications.com*

Objective: To assess the safety of adjunctive zonisamide in paediatric epilepsy patients. A pooled analysis of 17 studies (including four randomised, double-blind trials) was conducted. Safety population comprised patients aged ≤ 16 years receiving ≥ 1 study drug dose. Assessments included treatment-emergent adverse events (TEAEs), clinical laboratory parameters, vital signs and electrocardiography. Analysis included 398 patients (< 12 years, $n=191$; 12–16 years, $n=207$). All but seven received zonisamide as adjunctive therapy. Mean zonisamide dose was 253 mg/day and mean exposure duration was 319 days. Most TEAEs were of mild or moderate intensity; the most frequently reported treatment-related TEAEs ($\geq 5\%$) being decreased appetite (13.7%), somnolence (12.3%), fatigue (9.6%), irritability (7.5%) and lethargy (5.5%) in patients aged 6–11 years, and decreased appetite (15.9%), fatigue (10.1%), somnolence (8.7%), weight decreased (7.7%), dizziness (7.7%), headache (6.8%) and insomnia (5.3%) in patients aged 12–16 years. Incidence of serious zonisamide-related TEAEs was 3.5% overall. Seven patients experienced TEAEs resulting in death, two of which were judged as related to zonisamide treatment (status epilepticus, possibly related; multi-system organ failure, definitely related). One case of death (SUDEP) in a placebo-treated patient occurred in Study E2090-E044-317. However, this study was excluded from the pooled analysis, having not met the entry criterion of including ≥ 3 zonisamide-exposed paediatric patients. TEAEs led to discontinuation of 10.3% patients; most commonly, lethargy (1.0%) and fatigue (1.0%). 28 patients (7.0%) had TEAEs of decreased weight and 78 (19.6%) had

TEAEs of decreased appetite. There were no reports of Stevens Johnson Syndrome or toxic epidermal necrolysis. Twenty-eight patients had decreased bicarbonate levels and two had TEAEs of decreased bicarbonate. No changes in vital signs of clinical concern were observed and there were no reports of clinically significant electrocardiogram abnormalities with zonisamide treatment. No new or unexpected safety findings emerged when zonisamide was used as adjunctive treatment in paediatric patients.

PP2.9 - 2030

Intelligence two years after epilepsy surgery in children

Viggedal G, Olsson I, Carlsson G, Rydenhag B, Uvebrant P. Sahlgrenska University Hospital, Gothenburg, Sweden, Department of Paediatrics, Institute of Clinical Sciences at the Sahlgrenska Academy, Gothenburg University, Gothenburg, Sweden, Department of Neuropediatrics, Medical Center of Schleswig-Holstein, Sweden – gerd.viggedal@vgregion.se

Objectives: To evaluate cognitive functions before and two years after surgery in a consecutive series of paediatric patients. Specific objectives were to relate cognitive effects to seizure outcome and to explore the effect on IQ in children with a low pre-operative IQ. **Material and method:** Ninety-four children underwent epilepsy surgery in the years 1987 to 2006 at Sahlgrenska University Hospital in Gothenburg and had complete pre- and postoperative assessments of intelligence. The Swedish versions of the Griffiths' Developmental Scales and the Wechsler scales were used to assess intelligence. **Results:** Higher or unchanged full-scale IQ and verbal IQ scores two years after surgery were recorded in 43 (46%) of the 94 children, and 51 (54%) had higher or unchanged performance IQ. Before surgery 49 (52%) had an average full-scale IQ (>69), 17 (18%) had mild learning disabilities (IQ 50 to 69) and 28 (30%) severe learning disabilities (IQ<50). Sixty-five of the children (69%) had at least a 75% reduction in seizure frequency and 47 (50%) became seizure-free. A significant difference in median levels of change in full-scale IQ, verbal IQ and performance IQ was found between the seizure-free and not seizure-free children two years after surgery. A higher or unchanged full-scale IQ was found in four of the ten seizure-free and in six (33%) of 18 not seizure-free children with severe learning disabilities. Six (86%) of 7 seizure-free children with a mild learning disabilities had a higher or unchanged full-scale IQ, compared with three of the ten not seizure-free. Eighteen (60%) of 30 seizure-free children with an average IQ had a higher or unchanged full-scale IQ compared with six (32%) of the 19 not seizure-free children. **Conclusion:** Seizure freedom is the most important factor for the prognosis of cognitive development, regardless of the intellectual level of the child before surgery.

PP3. Neuromuscular and movement disorders

Chair: Michèl Willemsen

PP3.0 - 2024

Congenital myopathy associated with mutations in skeletal muscle alpha-actin gene (ACTA1)

Coppens S, Dan B. Belgium – sacoppen@ulb.ac.be

Objectives: To describe the clinical and histopathological presentation of ACTA1 congenital myopathy. **Material and methods:** We reviewed the history, clinical examination, muscular histopathology and genetics results in three patients with a genetically proven or suspected ACTA1 congenital myopathy. **Results:** The first two patients have a very similar clinical presentation with severe hypotonia at birth, high-arched palate, facial weakness,

prominent neck flexion weakness, scoliosis and nocturnal hypoventilation requiring nocturnal non-invasive ventilation, and delayed motor milestones but eventual acquisition of independent walking. Muscle pathology was non-specific in one patient and showed congenital fiber-type disproportion in the other one. A dominant, de novo, missense mutation was identified in ACTA1 gene in both patients: c.16G>A in the first and c.925C>T in the second one. The third patient showed a severe fetal presentation with polyhydramnios and akinesia, and severe neonatal respiratory insufficiency causing death soon after birth. Muscle pathology showed a severe myofibrillary disorganisation with large accumulations of thin myofilaments, that are highly suggestive of actin myopathy. Genetic search for ACTA1 mutation is still in progress in this third patient. **Conclusion:** ACTA1 mutations are a common cause of congenital myopathy associated with various muscle pathology types, with two specific patterns: actin myopathy and intranuclear rods. Mutations sites occur all along the gene and explain the important variety in the clinical presentation that ranges from a severe neonatal form with akinesia and respiratory insufficiency requiring mechanical ventilation to a milder form compatible with life into adulthood. The striking feature in the latter patients is the importance of the axial, facial, bulbar and respiratory weakness contrasting with the relative preservation of limb strength, compatible with independent walking.

PP3.1 - 1795

Muscular dystrophies and congenital myopathies in childhood. Incidence and frequency of individual subtypes diagnosed in a thirty year period

Thorarinsdottir BK, Tulinius M, Darin N. Gothenburg, Sweden – brynja.thorarinsdottir@vgregion.se

Muscular dystrophies and congenital myopathies often produce a similar clinical picture of muscle weakness and atrophy. Population studies that include muscular dystrophies and congenital myopathies are rare, it is not well studied how common these disorders are. The aim of the study was to identify all the patients diagnosed with muscular dystrophies and congenital myopathies in childhood over a thirty year period, between 1979 and 2009, and to describe the cumulative childhood incidence of these disorders. The geographic area studied was the region of western Sweden. We analyzed registers from local and regional pediatric hospitals and local and regional child rehabilitation centers, registers of muscle biopsies, neurophysiologic examinations and genetic analyses. The total number of identified cases were 207 patients. 139 patients with muscular dystrophies that were divided into 63 patients with Duchenne muscular dystrophy, 14 with Becker muscular dystrophy, 21 with limb-girdle muscular dystrophy, 15 with facioscapulohumeral muscular dystrophy, 3 with Emery-Dreifuss muscular dystrophy and 23 with congenital muscular dystrophy. 68 patients were diagnosed with congenital myopathy. The cumulative childhood incidence of Duchenne muscular dystrophy and congenital muscular dystrophy are similar to what have been found in previous studies from Sweden. The incidence of congenital myopathy is higher. In this group the majority of patients had unspecific muscle morphological findings.

PP3.2 - 1699

The effect of steroids on puberty in Duchenne muscular dystrophy

Dooley JM, Bobbitt SA. Nova Scotia, Canada – jdooley@dal.ca

Steroids have greatly enhanced the quality of life and longevity of patients with Duchenne muscular dystrophy (DMD) but often with associated side effects. All patients with DMD from the

Canadian Province of Nova Scotia are followed in our Neuromuscular clinic at Dalhousie University in Halifax. We assessed the pubertal development of our patients who were 14 years or older and had been treated with deflazacort as their only glucocorticoid. Puberty was classified as delayed if the patient was 14 years or older and had testicular volume of less than 4 cc. Gonadotropin Releasing Hormone (GnRH) stimulation testing was performed, with LH and FSH measured before and 40 minutes following administration of a GnRH agonist. Half (6 of 12) of the boys who were treated with deflazacort as their only glucocorticoid had pubertal delay. There was no difference in the age of onset, dose or duration of deflazacort therapy between those who did and did not have delayed puberty. Deflazacort was used for 5–16 years among those with pubertal delay and for 8–15 years for those with normal puberty. Delayed puberty should be included and studied in future trials that address different doses and schedules of deflazacort therapy in DMD.

PP3.3 - 1808

Disease-related symptoms and activities of daily living: a novel survey of patients with nonsense mutation Duchenne muscular dystrophy

Reha A, Barth J, Elfring GL, Spiegel R. South Plainfield, New Jersey, USA – areha@ptcbio.com

Objectives: Health-related quality of life in Duchenne muscular dystrophy (DMD) is not well understood, and there is a need for a sensitive disease-specific questionnaire. We developed a survey of symptoms and activities of daily living (ADL) which we piloted in an ongoing open-label study of ataluren in nonsense mutation DMD. We describe the survey design and provide a preliminary summary of baseline data in 18 patients. Substantial additional data will be available at the time of the EPNS meeting. **Material and methods:** The survey is administered by site personnel to the same respondent (patient/parent/caregiver) throughout the study. At baseline (prior to initiation of ataluren treatment), information is collected on disease-related symptoms/ADL (classified into six pre-specified categories). Respondents then rate any changes in these symptoms/ADL on a 5-point Likert scale at each 12-week visit during the study. **Results:** Patients representing various degrees of ambulatory disability were included. Physical functioning was the most commonly identified category at baseline (32 times by 14 patients), followed by general energy level (9 times; 9 patients) and cognition/school functioning (6 times; 6 patients). Sleep and emotional/social functioning were each identified by two patients, and “other” by one. Walking, climbing stairs and standing up were the most common aspects of physical functioning reported at baseline. Concentration and school performance featured in the cognition/school functioning category. **Conclusions:** Patient/caregiver reports are an essential component in the clinical assessment of DMD. We have developed a survey to allow patients/caregivers to self-identify specific ADL affected by DMD and assess response to treatment. This is intended to aid in the construction of a new instrument sensitive to detect changes in ADL/disease symptoms. The survey is being piloted in an ongoing open-label ataluren trial in nmDMD and will be used in a pivotal Phase 3 randomized study to complement functional outcome measures.

PP3.4 - 1800

Ryanodine myopathies without central cores

Rocha J, Taipa R, Melo Pires M, Oliveira J, Santos MR, Santos M. Neurology Department - Hospital de Braga, Portugal – manuela.a.santos@gmail.com

Objectives: Myopathies related to Ryanodine Receptor 1 (RYR1) mutations are one of the most frequent and their classical histo-

logical presentation is central core myopathy. Clinical variability and hystopathological overlap with other myopathies is increasingly recognized, promoting diagnostic difficulties. Here we report 3 cases of RYR1 myopathies without central cores and highlight their clinical particularities. **Material and methods:** Patients were selected from clinical database with the following criteria: congenital myopathies without cores and RYR1 mutation. We identified three unrelated patients. **Results:** Female, 15 years-old, with maternal family history of limb weakness. She had lower limb weakness complaints from age of 5, presenting a progressive scoliosis since the age of 10. She presented a mild proximal tetraparesis with axial and facial involvement. Muscle biopsy revealed marked type 1 fiber predominance. Female, 18 years-old, with history of easy fatigue. She developed a progressively worsening of muscle weakness and rapidly progressive scoliosis from age 11, with need of surgical treatment at 14 and need of BIPAP. She presented mild proximal tetraparesis and severe axial involvement. Muscle biopsy revealed abnormal fiber size variation, mild endomysial fibrosis, areas of increased adipose tissue and type 1 fiber predominance. Male, 11 years-old, with muscle weakness since age 2 with slowly progressive course. At the age of 10 he had facial paresis with slight disphonia, moderate tetraparesis mainly proximal and in lower limbs. Muscle biopsy showed fiber typing uniformity with oxidative enzymes. Different RYR1 mutations were identified in all patients. **Conclusions:** These cases illustrate early-onset myopathies, progressing later in childhood, two with a predominant axial involvement. Hystopathological examination revealed either a uniformity of fiber type or a clear predominance of type 1 fibers without central cores. These cases reinforce the need to recognize the hystopathological variability of RYR1 myopathies, stressing the lack of clinical correlation with histological non-specific finding.

PP3.5 - 1554

Multidisciplinary approach to rare diseases – Friedreich's ataxia

Malenica M, Kukuruzovic M, Krakar G, Cvitanovic-Sojat L. University Hospital Centre Sestre Milosrdnice, Pediatrics Clinic, Department of Neuropediatrics, Croatia – mgnjdic@yahoo.com

Aim: To emphasize the need for multidisciplinary approach in determining the diagnosis and in treatment of children with Friedreich's ataxia (FA)- autosomal recessive neurodegenerative disease. **Case report:** A female 15.5 years old girl with uneventful family history and normal psychomotor development was admitted due to clumsiness. She previously received an ortosis due to thoracic scoliosis. During her stay we noticed mild ataxia, tremor, and nystagmus with neurographical finding of complete loss of sensory potentials with demyelination signs and borderline speed of conduction on lower extremities. DNA analysis determined a full mutation of frataxin on chromosome 9. Heart ultrasonography confirmed concentric hypertrophic cardiomyopathy. Continuous measuring of systemic pressure diagnosed hypertension with high risk for damage of target organs. There was no other cause of hypertension so it was most likely a consequence of hypertrophic cardiomyopathy. With ACE inhibitor therapy she achieved pressure normalization. She is receiving support therapy with idebenon, coenzyme Q10, and vitamin E. She receives physical therapy following spine surgery due to scoliosis. Besides regular visits to pediatric neurology specialist she is also seeing a cardiologist, ENT specialist, ophthalmologist, and psychologist. Her neurological status is according to International Cooperative Ataxia Rating scale deteriorating despite support therapy. **Conclusion:** Out case emphasizes the need for continuous multidisciplinary approach to patients with FA which in our patient so far includes a pediatric neurology specialist, pediatric cardiology specialist, pediatric nephrology specialist, physical therapy specialist, ENT specialist, ophthalmologist, and psychologist.

PP3.6 - 2106

Early onset ataxia – an international database

Steinlin M, Baxter P, Boltshauser E, Brankovic V, Catsman-Berrevoets CE, Bertini E, Kennedy C, Mancini F, Nemeth A, Schöls L, Sival D, Synofzik M. *Department of Neuropaediatrics, Development and Rehabilitation, University Children's Hospital, Berne, Switzerland – maja.steinlin@insel.ch*

Background: Problems of ataxia are of increasing interest over the last decade. There are indefinite variable etiologies of congenital and early onset ataxias (EOA)- only very few clearly defined by genetics and/or pathophysiology. We aim to improve knowledge in this field by creating a large-scale database that will allow (i) to identify the frequency of different EOAs, (ii) to assess their natural history, and (iii) to establish a large cohort of unexplained EOA cases that will be accessible for next generation sequencing technologies to identify both known and novel genes presenting with EOA. **Methods:** By a pseudoanonymised, webbased registry we will collect data on children/young adults with congenital or early onset (start <40years of age) ataxias. The following data will be registered: demographics; clinical course including SARA scale, INAS (information on non ataxia symptoms) and quality of life; laboratory and electrophysiological work up; neuroimaging and genetic results. DNA should be collected for each patient locally. Application for collaboration: Accepted for collaboration are people interested in the field of ataxia who are either experienced in management/counseling of ataxic patients or have made other important contribution to the field of ataxia. Each collaborator has access to his own register data. By submission and acceptance of a more comprehensive research project to the steering committee of the EOA group, the necessary data from the registry for this project will given free to the individual researcher. Application to become a collaborator will have to be submitted to the steering group EOA. Summary: By an international approach we aim to collect data on children and young adults with congenital or early onset ataxia – to improve understanding, form phenomological groups, to solve underlying pathophysiology, to assess the frequency of established genes and identify novel EOA genes.

PP3.7 - 2011

Acute and subacute chorea in a French series of 37 children

Doummar D, Grisel C, Roubertie A, Héron B, Gras D, Laroche C, Sabouraud P, Motte J, Maincent K, Isapof A, Rodriguez D, Billette de Villemeur T. *Neuropédiatrie, Centre de référence mouvements anormaux de l'enfant, Hôpital Trousseau, Paris, France – diane.doummar@trs.aphp.fr*

Chorea is characterized by brief, abrupt, irregular, non stereotyped movements. The recognition of this movement disorder is mandatory as it would facilitate proper management. We report 37 children with acute/subacute chorea followed by multiple french neuropediatrics departments. The aim of this retrospective study work is to determine the clinical, etiological characteristics, treatment, and outcome. In our study, we found that chorea was unilateral (15/37), which had no localizing value. It was isolated (12), or associated with behaviour changes or altered consciousness, and proceeded by infectious episodes (16). The inflammatory causes were the most common (20/37, 54%), including 7 Sydenham's chorea, 5 post infectious basal ganglia encephalitis, 2 anti NMDAR encephalitis, 3 systemic lupus erythematosus, and 1 paraneoplastic syndrome. The other etiologies were vascular (8/37, 22%), metabolic or degenerative (n=3), and due to vitamine B12 deficiency (n=1). Repeated explorations before diagnosis were needed in some cases. Despite this, 5 cases remained with unspecific etiology. The evolution of chorea was favourable (n=15) with or without symptomatic treatment, especially in vascular origin. Nevertheless, 3 status choreic

dystonicus required emergency pallidal deep brain stimulation. Furthermore, treatment was specific of the underlying etiology. One prospective case series of acute chorea (n=20) is reported in the literature. As in our study, autoimmune and inflammatory causes are the most frequent. On the other hand, drugs or toxic induced- chorea are reported, as hyperthyroidism. No psychogenic movement disorder is found. Children with Huntington disease rarely present with chorea. Brain MRI with angiography is mandatory to search for basal ganglia abnormalities, (especially in vascular, or metabolic disorders). However it can be normal (autoimmune or post pump chorea). This study highlights the various causes of acute chorea in children, which guides the treatment. Noteworthy, the diagnosis may be difficult and need a long term follow up.

PP3.8 - 1704

Ataxia with vitamin E deficiency in Norway

Elkamil AI, Johansen KK, Aasly JO. *Department of Paediatrics, St. Olav's University Hospital, Trondheim, Norway – areej.elkamil@ntnu.no*

Ataxia with vitamin E deficiency (AVED) is a rare neurological disorder which usually starts in childhood. If not recognized and treated it usually leads to severe neurological impairment. The phenotype is variable but most patients have progressive gait ataxia, dysarthria and polyneuropathy. AVED is a very rare disorder in northern Europe with unknown prevalence. We performed a search in all health regions in Norway to get some estimate of the prevalence in a northern Scandinavian country. The prevalence of ataxias in the southern and eastern regions had been published in 2012. We had one case diagnosed in our department located in Central Norway and one additional was found in the northern part of the country. This was achieved by studying official reports. In all 3 cases the age of onset was in early childhood, around the age of 4 - 6 years. They all experienced gait ataxia and dysarthria. Sadly, none was diagnosed and treated before they had developed severe neurological deficits. The genetic testing showed that all three had pathogenic mutations in the TTPA gene. All were carriers of the non-sense c.400C>T mutation, one was homozygous for that mutation the 2 others were compound heterozygous, either with c.358G>A or c.513_514insTT. The homozygous carrier was by far the most severely affected patient. In conclusion: We postulate that the prevalence of AVED in Norway is around 1 per million inhabitants and if not diagnosed and treated in early childhood it will progress to severe neurological deficits.

PP3.9 - 1603

Alternating hemiplegia in childhood – a clinical and genetic study

Nevsimalova S, Krepelova A, Kemlink D. *Department of Neurology, Charles University, 1st Faculty of Medicine and General Teaching Hospital, Prague, Czech Republic – snevsi@LF1.cuni.cz*

Objective: Alternating hemiplegia in childhood (AHC) is a rare neurological disorder characterized by early-onset episodes of hemiplegia, various paroxysmal symptoms including dystonic features and developmental impairment. Recently, de-novo mutations in ATP1A3 gene were found in patients with AHC2 resembling allelic early rapid-onset dystonia parkinsonism, classified as DYT12. **Patients and methods:** Five AHC patients (3 boys, 2 girls) underwent a longitudinal (5- 20 years) neurological follow-up including neurophysiological examinations (EEG, evoked potentials, video-polysomnography), and neuroimaging, particularly a SPECT study. For Sanger sequencing of the ATP1A3 gene, DNA from peripheral blood samples was extracted and primers for DNA amplification and sequencing were used

to cover all coding regions of the gene. **Results:** Paroxysmal dystonic features increased with age like other movement disorder symptoms including choreiform movements. Similarly to DYT12, dystonic features developed some signs of a rostrocaudal gradient (orofacial dystonia with dysphagia, dyspnoea). The mystery of AHC symptoms completely disappearing during sleep and reappearing again a few minutes after awakening, supports also movement disorder aetiology. ATP1A3 analysis revealed a pathogenic mutation c.2401G>A p. (Asp801Asn) in two patients, c.2839G>A p. (Gly947Arg) in one and 2839G>C p. (Gly947Arg) in another one. No mutation or deletion was detected in the last patient with atypical late onset of the disease. **Conclusions:** Our study suggests that AHC2 and DYT12 may represent a phenotypic continuum of one clinical entity, however, further genotype-phenotype studies are desirable to prove this hypothesis. AHC patients may represent the most severe type of ATP1A3-associated dystonic movement disorder, while DYT12 patients would present only a mild variety of the same disease.

PP4. Neurometabolic disorders

Chair: Rudy Van Coster

PP4.0 - 1506

Longitudinal outcomes from the international disease registry for Niemann-Pick disease type C (NP-C)

Pineda M, Mengel E, Wijburg FA, Vanier MT, Schwierin B, Müller A, Drevon H, Patterson MC. *Fundació Hospital Sant Joan de Déu, CIBERER, Barcelona, Spain – pineda@hsjdbcn.org*

Objective: This disease registry was initiated to evaluate the long-term disease course of NP-C in clinical practice. The current analysis focuses on patients who received miglustat continuously between enrolment and last follow up visit, based on data collected from September 2009 to August 2012. **Methods:** All patients diagnosed with NP-C, irrespective of treatment, were eligible for inclusion in this multicentre, prospective, observational cohort study. Patient demographics, disease characteristics, disability status and treatment data were collected. Disability status was evaluated using a disease-specific disability scale that rated four domains: ambulation, manipulation, language and swallowing from 0 (normal) to 1 (worst). Patients were categorised as “improved/stable” if ≥ 3 out of these 4 domain scores were lower or unchanged between enrolment and last follow-up visit, or as “worsened” if < 3 domain scores were lower or unchanged. **Results:** Eighty out of the 190 enrolled patients (mean [SD] age at enrolment 17.8 [11.5] years; 52.5% female) received miglustat continuously throughout the observation period; mean (SD) exposure 1.19 (0.69) years. Among 74/80 patients with available data, the mean (SD) age at neurological onset was 9.9 (9.3) years. Ten (14%) patients had early-infantile onset (aged < 2 years), 24 (32%) had late-infantile onset (2 to < 6 years), 24 (32%) had juvenile onset (6 to < 15 years), and 16 (22%) had adolescent/adult (≥ 15 years) onset of neurological manifestations. Mean (95%CI) composite disability scores at enrolment and last follow-up visit were 0.39 (0.34, 0.45; N=75) and 0.45 (0.39, 0.51; N=76), respectively. Overall, 52/72 (72%) patients were categorised as ‘improved/stable’; 20/72 (28%) were categorised as “worsened”. Safety and tolerability findings were in line with previous published data. A low proportion of patients had chronic diarrhoea during follow up (7.6%). **Conclusion:** NP-C disease characteristics were in line with previous publications. Disability status was improved or stable in the majority of miglustat-treated patients.

PP4.1 - 1595

X-linked adrenoleukodystrophy in childhood

Kim EY, Park JH, Kook H, Woo YJ. *Department of Pediatrics, Kwangju Christian Hospital, Chonnam National University Medical School, Gwangju, Korea – eykim_kook@yahoo.com*

Purpose: X-linked adrenoleukodystrophy (ALD) is a rare disorder that shows a great deal of phenotypic variability. We subdivided childhood X-linked ALD patients into several phenotypes by the age at onset, the sites of most severe clinical involvement and the rate of progression of neurologic symptoms. **Methods:** Fourteen patients who had been diagnosed as X-linked ALD and followed up for at least one year were enrolled from 1996 to 2010. **Results:** 1. Eleven had childhood cerebral ALD, who showed first neurologic symptoms at 7.29 years and progressed rapidly: interval between first symptoms and vegetative state was 1.48 years, and interval from initial symptoms to death was 3.44 years. Treatment with Lorenzo's oil did not prevent neurologic progression. Two patients who underwent umbilical cord blood transplantation died. 2. Two had adolescent cerebral ALD. They had first symptoms at 11.5 years, and showed tendency to progress less rapidly than childhood cerebral form patients. 3. One “Addison only” patient who had adrenal insufficiency without nervous system involvement remained asymptomatic during Lorenzo's oil treatment. 4. Most cerebral form patients except two showed the lesions in both parieto-occipital white matter in brain magnetic resonance imaging. **Conclusion:** The cerebral ALD was the most common form in childhood and was associated with a grave prognosis.

PP4.2 - 1916

The clinical, biochemical and molecular characterisation of a UK patient with Salla disease. A case report

Venkata NKP, Fry AE, van der Knaap MS, Scully R, Neal JW, Gibbon FM. *Department of Paediatric Neurology, University Hospital of Wales, Cardiff, United Kingdom – Frances.Gibbon@wales.nhs.uk*

Salla disease is a rare autosomal recessive neurodegenerative disorder caused by mutations in the SLC17A5 gene. Salla disease (referring to the area of northeast of Finland where it was first described) has rarely been reported outside of Finland, where the p.R39C founder mutation leads to increased incidence. We report a UK patient with confirmed Salla disease. This male patient was the first child of non-consanguineous white British parents. He presented in infancy with speech and motor delay (sitting 1 year, walking 4 years). The patient subsequently developed ataxia, spastic paraparesis and generalised dystonia. At the age of 12 years he developed severe startle seizures and absences. The patient's EEG was particularly abnormal with high amplitude spike wave discharges. He is now 14 years-old and can speak in simple sentences, finger feeds and dress with assistance. Repeated MRI brain scans showed almost complete absence of myelination of the cerebral white matter, reduced width of the cerebral mantle, thin corpus callosum and atrophic cerebellum. Cerebrospinal fluid analysis revealed an elevated level of N-acetylaspartylglutamate but sequencing of the PLP1 gene was normal. Thin layer chromatography of the patient's urine demonstrated increased sialic acid excretion. Electron microscopy of a skin biopsy from the patient revealed Schwann cells containing intracytoplasmic inclusions. Cultured skin fibroblasts generated a 6 fold increase in free sialic acid. Sequencing of the SLC17A5 gene showed the patient was a compound heterozygote for two mutations: a previously-reported 5 amino-acid deletion (c.802_816del15; p.Ser268_Asn272del) and a novel missense mutation (c.116G>A, p.R39H). Analysis of maternal DNA confirmed that the changes were on different chromosomes. This case highlights Salla disease as a rare cause of leukodystrophy, which needs considered even in patients without a Finnish heritage.

PP4.3 - 1921

Outcome of modified Atkins diet in GLUT-1 patients in western Sweden

Michael E, Darin N. Sweden – eva.michael@vgregion.se

Objective: Glucose transporter protein-1 deficiency (GLUT-1) is a neurological disorder caused by mutations in SLC2A1-gene leading to a transport defect of glucose over the blood-brain barrier. Our aim with this study is to report the broad spectrum of signs and symptoms associated with the disease in childhood and report the effects of treatment with a Modified Atkins diet (MAD). **Methods and material:** There are 7 childhood patients with genetically confirmed GLUT-1 deficiency syndrome in Western Sweden. All are treated with MAD. We have retrospectively studied their medical journals. The effect of MAD was followed using a Clinical Research Form with clinical follow-up after 1, 3, and 6 months as well as after 1 and 2 years. **Results:** Two patients are recently diagnosed, one of which has been on MAD for 1 month and the other is due in May 2013. The remaining patients have been treated for at least 2 years. All patients presented with epileptic seizures, most had motor deficits (4/7), developmental delay (5/7) and attention deficits (4/7). Two had microcephaly, one had exercise-induced dyskinesia and four experienced worsening on fasting. Age of onset was below 2 years of age in the majority. The median CSF-glucose level was 1.9 mmol/L (Range: 1.5–2.2) and the median blood/CSF glucose-ratio was 0.3 (range: 0.28–0.43). Modes of inheritance were sporadic (3/7), autosomal-dominant (1/7) and gonadal-mociasm in 3 siblings. Effects of MAD were a complete disappearance of epileptic seizures and discontinuation of medication (5/5), considerable improvement of the motor deficits (3/5) and improvement of the psychomotor development (5/5). Side-effects were generally mild. **Conclusion:** GLUT-1 deficiency syndrome has a broad clinical phenotype. Due to lack of awareness, the median of doctor's delay before diagnosis is 2.3 years (range 0.1–14.5 years). MAD is an effective treatment with few side-effects, irrespective of age or combination of symptoms.

PP4.4 - 1584

The neuronal ceroid lipofuscinoses in Flanders, Belgium

Keppens K, Peirens G, Standaert L, Mattheeuws S. De Kade, Spermalie Bruges, Belgium – katrien.keppens@mpi-spermalie.be

The neuronal ceroid lipofuscinoses (NCL) are a group of extremely rare inherited neurodegenerative lysosomal storage diseases who can be defined as: "... progressive diseases of the brain and, in most cases, the retina in association with intracellular storage material that is morphologically characterized as ceroid lipofuscin ...". The new classification is based on genetic findings (CLN1-CLN14). In Belgium we lack epidemiological information and a standardized approach. **Objectives:** Starting from the available individual and demographic data, we aim to evolve towards a standardized multidisciplinary approach. This can facilitate early diagnosis and better support for all concerned. **Material and methods:** In this retrospective study, data from the medical files of patients who resided in Ganspoel or Spermalie are included. These are the 2 specialized institutes for the education of the visually impaired in Flanders. "Contactpunt NCL", a patient support group, provided some extra info. Seen its predominance, we focused especially on the juvenile form. **Results:** The data of 21 patients with NCL, born between 1964 and 2004, were revised. Early visual failure due to retinal dystrophy was the presenting symptom in all patients. Interval between symptoms and diagnosis was longer than 1 year in 13 cases. Before 1990 diagnosis consisted on the detection of vacuolised lymphocytes and electron microscopic investigation. After this date DNA-analysis was performed. Other parameters were checked: epilepsy, geographical spread, survival rates, death causes. **Conclusions:** Early visual

failure is a specific presenting symptom. Although diagnosis is facilitated through genetic testing, the delay between onset of symptoms and final diagnosis is still (too) long. We are convinced that increased awareness, structural measures (register, reference centre, multidisciplinary cooperation) and a standardized approach can lead to less delay in diagnosis, offer better support and service for the patients and next of kin and eventually can be a stimulus for research initiatives.

PP4.5 - 1813

Nonclinical development of rhTPP1 enzyme replacement therapy for NCL2

Vuilleminot BR, Kennedy D, Katz ML, Coates JR, Lobel P, Tsuruda LS, Henshaw J, Musson D, Keve S, Cahayag R, Tiger P, O'Neill CA. BioMarin Pharmaceutical Inc., California, USA – bvuilleminot@bmrn.com

Neuronal Ceroid Lipofuscinosis, type 2 (NCL2) is caused by lack of tripeptidyl-peptidase I (TPP1) enzyme activity. Patients accumulate CNS lysosomal storage materials and exhibit progressive neurodegeneration and resulting loss of cognitive, motor, and visual functions, typically beginning by age 4. Death typically occurs by early adolescence. BioMarin is developing recombinant human (rh) TPP1 enzyme replacement therapy. To bypass the blood-brain barrier and facilitate CNS distribution, the enzyme will be administered by intracerebroventricular (ICV) infusion to the cerebrospinal fluid (CSF). The nonclinical assessment of rhTPP1 evaluated the pharmacology, pharmacokinetics, and safety in disease and normal animal models after CNS delivery. The pharmacodynamic profile was assessed in two NCL2 disease models, the Tpp1-knockout mouse and TPP1-null Dachshund, which recapitulate many aspects of the human disease. In these disease models, administration of rhTPP1 resulted in a reduction of lysosomal storage, attenuation of clinical decline, improvement of cognitive and motor function, and lifespan extension compared with vehicle treated controls. CSF and plasma pharmacokinetics, as well as CNS distribution, were assessed after administration to cynomolgus monkeys and Dachshunds. Peak CSF exposure after ICV infusion was 100- to 1000-fold higher than that in plasma and remained above the lysosomal Kuptake for 2–3 days post-dose. The administered rhTPP1 distributed widely in the brain resulting in concentrations 2- to 10-fold greater than the endogenous wild-type level in many sites. ICV administration resulted in an expected delivery device related inflammation along the catheter track in all animals, including vehicle treated controls. Mild to moderate anaphylactoid reactions observed after repeat dosing in Dachshunds were mitigated by increasing the duration of the infusions and administration of diphenhydramine. The positive nonclinical pharmacology and safety profiles of rhTPP1 offer promise for the planned first in human clinical trial of ICV administered rhTPP1 in NCL2 patients.

PP4.6 - 1784

S-adenosylmethionine and S-adenosylhomocysteine in plasma and cerebrospinal fluid in Rett syndrome and the effect of folinic acid supplementation

Hagebeuk E, Duran M, Abeling NG, Vyth A, Poll-The BT. Department of Pediatric Neurology, Academic Medical Center, The Netherlands – e.e.hagebeuk@amc.uva.nl

Objective: Rett syndrome is a neurodevelopmental disorder characterized by cognitive and locomotor regression and stereotypic hand movements. The disorder is caused by mutations in the X chromosomal MECP2 a gene encoding methyl CpG-binding protein. It has been associated with disturbances of cerebral folate homeostasis, as well as with speculations on a compromised DNA-methylation. Folinic acid is the stable form of

folate. Its derived intermediate 5-MTHF supports the conversion of homocysteine to methionine, the precursor of S-adenosylmethionine (SAM). This in turn donates its methyl group to various acceptors, including DNA, thereby being converted to S-adenosylhomocysteine (SAH). The SAM/SAH ratio reflects the methylation potential. The goal of our study was to influence DNA methylation processes and ameliorate the clinical symptoms in Rett syndrome. **Methods:** We examined the hypothesis that folinic acid supplementation, besides increasing cerebrospinal fluid (CSF) 5-MTHF ($p=0.003$), influences SAM and SAH and their ratio. In our randomized, double-blind crossover study on folinic acid supplementation, ten female Rett patients received both folinic acid and placebo for 1 year each. **Results:** It was shown that both SAM and SAH levels in the CSF remained unchanged following folinic acid administration ($p=0.202$ and $p=0.097$, respectively) in spite of a rise of plasma SAM and SAH ($p=0.007$; $p=0.009$). There was no significant change in the SAM/SAH ratio either in plasma or CSF. **Conclusion:** The apparent inability of Rett patients to upregulate SAM and SAH levels in the CSF may contribute to the biochemical anomalies of the Rett syndrome. Our studies warrant further attempts to promote DNA methylation in the true region of interest, i.e. the brain.

PP4.7 - 1709

Aspartylglucosaminuria in a non-finnish patient: a case report

García Puig M, Delgadillo Chilavert V, Roche Martínez A, Fernández Zurita C, Escofet Soteras C, Lorente Hurtado I. *Department of pediatric neurology. Hospital Parc Taulí Hospital, Sabadell (Barcelona) Spain – mgarciap@tauli.cat*

Introduction: Aspartylglucosaminuria (AGU) is an autosomal recessive lysosomal storage disease due to a defect in the AGA gene, which abolishes the activity of the aspartylglucosaminidase (AGA) enzyme. The most characteristic feature is progressive mental retardation. AGU is estimated to affect 1 in 18,500 people in Finland, this condition is much less common outside of Finland. **Clinic case:** A 6-year old boy, was visited because of learning difficulties, delay speech and clumsiness. His parents were not consanguineous. He was the product of a full-term pregnancy with normal delivery. Though apparently normal at birth, their development milestones were slow. Physical examination showed language difficulty and clumsiness. Neuropsychological testing revealed IQ scores in the lower limit of the normality. Complementary test included: Karyotype, X-fragile: normal; Brain MRI: cerebellar atrophy. Blood Metabolic screening (lactate, pyruvate, ammonia, amino acids, congenital disorder of glycosylation) and Urinary metabolic screening (amino acid, organic acid, mucopolysaccharides, creatine deficiency study, purines): normal; MLPA Subtelomeric analysis: normal In childhood the patient learned new skills abnormally slowly. Mean IQ on WISC-IV scale (10y): 73. From 14 years old he showed slight deterioration of both cognitive and motor skills, and behavioral changes. IQ on WISC-IV scale (14y): 55. Complementary test to rule out neurological progressive disease were performed; brain MRI remained stable; electromyoneurographic, ophthalmological and cardiac examination, abdominal ultrasound were normal. Urinary oligosaccharide analysis detected an abnormal excretion of aspartylglucosamine. Assay for AGA enzyme in fibroblasts reveal a very low activity, establishing a definitive diagnosis of AGU. **Conclusions:** Clinical diagnosis of AGU is difficult; the initial presentation may be subtle and signs may be variable, resulting in frequent delays in diagnosis. The main signs and symptoms are progressive mental retardation, facial dysmorphism, connective-tissue involvement and psychiatric problems. Biochemical detection is easy by urine chromatography. No specific therapy is available.

PP4.8 - 1602

Neonatal onset of a Canavan disease in a Lybian non jewish ashkenazi patient

Lakhthar I, Nagi S, Miladi N. *National Institute Mongi Ben Hamida of Neurology La Rabta 1007, Tunis, Tunisia – najoua.miladi@rns.tn*

Neonatal onset of a Canavan disease in a lybian non-jewish ashkenazi patient Canavan disease is a genetic neurodegenerative disease caused by mutations in the ASPA gene. Important clinical features are macrocephaly, hypotonia, head lag and developmental delay. Patients show elevated urinary concentrations of NAA. We reported here a case of an eight month and a half year old girl, born to related Lybian non-Jewish parents, from complicated pregnancy (eclampsia) and without perinatal risks, brought to our department for the etiologic diagnosis of severe developmental delay. The neurological exam shows total absence of psychomotor development with central hypotonic syndrome and slight spasticity of the lower extremities with bilateral Rossolimo sign and important macrocephaly. Epileptic seizures were not yet expressed in the infant. MRI findings shows a hyperintense T2 signal interesting bilaterally and symmetrical all subcortical white matter, and periventricular regions with U fibres involvement and a bilateral signal abnormalities in thalamus and pallidum. Proton magnetic resonance spectroscopy of the brain shows an increase in the concentration of N-acetylaspartic acid (NAA). Although it is a panethnic disease, information on affected individuals in populations of Non-Ashkenazi Jewish origin is rather limited. Ongoing research aims at a better understanding of Canavan disease and underlying mechanisms as a basis for new therapeutic approaches.

PP4.9 - 1616

Tay-Sachs disease in a Turkish patient due to c.78G>A HEXA mutation: a case report

Arsilan M, Ünay B, Vurucu S, Gül D, Akın R. *Department of Pediatric Neurology, Gülhane Military Medical School, Ankara, Turkey – mutluayarsilan@yahoo.com*

Tay-Sachs disease (TSD) is an autosomal recessive, neurodegenerative disorder caused by intralysosomal storage of the GM2 ganglioside, resulting from deficient β -hexosaminidase A activity due to β -hexosaminidase α -subunit (HEXA) mutations. TSD has been reported in children of virtually all ethnic, racial, and religious groups. Tay-Sachs disease used to be prevalent (1 in 3900 live births) among Ashkenazi Jews but heterozygote screening and counseling programs led to a 90% reduction of the disease in this high-risk population. At least seven different mutations were identified in Turkish Tay-Sachs patients to date. This report describes the first Turkish Tay-Sachs patient with c.78G>A (p.W26X) HEXA mutation.

Friday 27 September 2013

PP5. Varia (sleep, oncology, trauma)

Chair: Richard Newton

PP5.0 - 1888

Retinal hemorrhages in a university hospital: not always abusive head injury

Mattheij M, Venstermans C, de Veuster I, Peerenboom K, Kenis S, Vanderstraete I, Ceulemans B. *University Hospital Antwerp, Belgium – m.a.c.mattheij@gmail.com*

Objectives: Studies have shown that retinal hemorrhages (RH) and subdural hematomas (SDH) are frequently seen in the pres-

ence of shaken baby syndrome (SBS). Many authors state that presence of RH is a pathognomic finding to diagnose SBS. According to our experience, this assumption is incorrect. We performed a retrospective study on children admitted to our university hospital with RH. **Material and methods:** Our study included 29 children with RH, aged 1–18 months old, admitted to our hospital from the year 2000 to 2013. Story and physical examination during presentation, medical course, coagulation tests, metabolic investigations, skeletal survey and head circumference of the infant and his parents were collected. Retinal findings as well as central imaging (CT and MRI) were reassessed to obtain a standardized description. Evaluation reports by social services or civil/criminal courts were collected. **(Preliminary) results:** Of the 29 children, 23 were found suspect of SBS by the medical team and/or social services. In 5 of the 23 cases shaking was admitted. Three cases showed intraparenchymal hematomas, 4 interhemispheric blood, 4 cerebral edema, 6 compression of a ventricle, and 3 papilledema. In 15 of the 23 cases diffusion-weighted MRI was performed: 6 showed diffuse lesions, 4 showed bilateral lesions. In 2 of the 6 non-suspect cases a clear etiology was found (accidental trauma or cerebral aneurysm). None of the 4 remaining cases showed intraparenchymal or interhemispheric blood, cerebral edema, compression of a ventricle, diffuse lesions on diffusion-weighted MRI or papilledema. Three of the 4 cases showed an accelerated growth of the head circumference months before presentation. **Conclusion:** According to our study infants can present RH and/or SDH without SBS. Infants with a large head circumference could be predisposed to retinal or subdural hemorrhages with or without a minor trauma.

PP5.1 - 1846

Pediatric TBI: acute and 1-year MRs/DTI findings

Holshouser BA, Ghosh N, Tong KA, Pivonka-Jones J, Rundquist M, Ashwal S. *Departments of Radiology and Pediatrics, Loma Linda University School of Medicine, USA – sashwal@llu.edu*

Objective: We present longitudinal MR spectroscopic and DTI findings in children with complicated mild/severe TBI. **Methods:** Studies were done (7–15 days & 1 year) with MRI (3D-T1W, 3D-T2W, FLAIR, SWI, DTI-mean FA, ADC, AD, RD) and with 3D MRSI (10 mm slabs-corpus callosum–brain stem). MRSI voxel data were overlaid onto DTI white matter (WM) data to compare DTI parameters to metabolite ratios (NAA/Cr, NAA/Cho, Cho/Cr) for each voxel and region. Neuropsychological evaluations were done (3, 12 months). **Results:** We studied 17 TBI (13.2yrs; GCS: 3–15) and 15 controls (11.5 yrs). Initial MRI found decreased NAA/Cr and NAA/Cho ratios in all regions in TBI patients compared to controls. Mean FA values were decreased in corpus callosum (CC), basal ganglia (BG), parieto-occipital and temporal white matter. The mixed model analysis which accounts for age effects, showed a significant recovery of NAA/Cr only in 3 regions - BG ($p=0.01$), temporal gray ($p=0.03$) and thalami ($p=0.01$) and showed no significant longitudinal recovery of DTI metrics compared to controls. The initial NAA ratios and mean FA measurements correlated significantly with IQ and memory deficits evaluated at 12 months after injury. **Conclusions:** Early decreases in NAA represent neuronal loss or dysfunction and early FA reductions represent structural white matter injury. At 12 months, MRS showed significant recovery of metabolite ratios only in 3 regions, whereas, no regional DTI metrics recovered. This suggests incomplete metabolic and axonal recovery as the source of cognitive impairment.

PP5.2 - 1844

Advanced MR and spectroscopic imaging in adolescents with chronic post-concussive symptoms following sports-related concussion

Bartnik-Olson BL, Grube M, Wang H, Wong V, Holshouser BA, Ashwal S. *Departments of Radiology and Pediatrics, Loma Linda University Medical Center, USA – sashwal@llu.edu*

Objective: There is growing interest in using advanced MRI techniques (diffusion tensor imaging, DTI; perfusion weighted imaging, PWI) to identify and quantify microstructural axonal injury and perfusion abnormalities in adolescents with sports related concussion (SRC). We investigated these changes in a group of post-concussive symptomatic adolescents. **Methods:** We studied 13 adolescents (16 ± 4 years) who sustained a SRC (1–24 months before imaging) and 14 controls (15 ± 4 years). Symptoms included headache (persistent or intermittent, $n=13$), dizziness ($n=3$), and cognitive ($n=6$) or behavioral changes (including depression, $n=4$). DTI and PWI data were acquired on a Siemens Tim Trio 3T scanner. Region of interest DTI (FA, MD, RD) and PWI (CBF, CBV, MTT) analysis was performed. **Results:** FA and RD were reduced in the genu of the corpus callosum in SRC subjects compared to controls ($p=0.05$ and $p=0.04$). SRC subjects also showed reduced rCBF ($p=0.03$) and rCBV ($p=0.05$) in the right thalamus and a trend ($p=0.06$) towards reduced rCBF and rCBV in the left thalamus. **Conclusions:** Lower callosal FA values have been reported after mild TBI and indicate axonal injury. Elevated RD in this region suggests the presence of myelin damage along with axonal injury. rCBF and rCBV also were reduced in the thalami of SRC subjects and may be due to post-injury vascular disruption or impairment of microvascular responsiveness. Our findings suggest that DTI and PWI reflect different components of the complex injury that occurs after SRC and that both are sensitive indicators of lasting injury in chronically symptomatic athletes.

PP5.3 - 1676

The risk factors of severe brain injury by head trauma under 6 years old children

Na YH, Cha BH. *Wonju Severance Christian Hospital, Korea – cha12bho@yonsei.ac.kr*

Objectives: The head trauma is common type of injury coming to emergency room during childhood period, especially under 6 years old children. We would like to evaluate the risk factors of severe brain injuries associated with the head trauma occurring under 6 years old children. **Material and methods:** We retrospectively reviewed the medical records of 392 children, who came to emergency room of Wonju Severance Christian Hospital from March, 2011 to February, 2012 due to head trauma. We evaluated the clinical characteristics of these children for risk factors of severe brain injuries. **Results:** The 1981 children under 15 years old came to emergency room due to traumatic injuries. Among them, 554 children (28.0%) had head trauma and 392 children (70.8%) were under 6 years old; under 3 years old, 244 (62.2%) and between 3 and 6 years old, 148 (37.8%). the male and female ratio was 1.65:1. The causes of head trauma were falling down (77.6%), strucken by objects (8.2%), car accident (7.9%) and unknown (6.3%). The most of children (77.1%) were no neurologic symptoms and signs, but there were noted that intracranial hemorrhage was 24 (6.1%); male 58%, skull fracture, 10 (2.6%); male 80%, seizure, 8 (2.0%); male 75%, intracranial hemorrhage with skull fracture, 14 (3.6%); male 71%, and soft neurologic symptoms, 10 (2.6%); male 67%. The younger aged and male children were more prone to severe brain injuries. **Conclusions:** The head trauma is common during childhood period, especially under 6 years old children. The most of head trauma children are no severe neurological damages but the severe brain injuries such as intracranial hemorrhage are more common to younger and

male children. So we should have more close attention to male and younger aged children preventing severe brain injuries by head trauma.

PP5.4 - 1971

Cognitive and neural characteristics of mathematical difficulties in children with mild traumatic brain injury (TBI)

Van Beek L, Ghesquière P, Lagae L, De Smedt B. *Parenting and Special Education, Faculty of Psychology and Educational Sciences, University of Leuven, Belgium – Leen.VanBeek@ppw.kuleuven.be*

Acute and long-term impairments in academic skills have been reported following TBI in children (Johnson et al., 2009). It turns out that mathematics rather than reading or spelling is the most compromised in these children (Ewing-Cobbs et al., 2004). However, a precise characterization of the mathematical difficulties in pediatric TBI is currently unavailable. Extending the existing body of data, the current study aimed to provide a detailed characterization of the mathematical difficulties in TBI at both behavioral and neural levels. Fifteen semi-acute pediatric mild TBI patients were investigated and compared with 15 matched controls. Behavioral data, including measures of numerical processing, arithmetic and working memory as well as neuro-imaging data were collected. Because diffuse axonal injury is common in TBI and might account for the persistent cognitive problems after TBI (Niogi & Mukherjee, 2010), we used Diffusion Tensor Imaging (DTI) to examine microstructure white matter abnormalities in TBI and related these measures to behavioral performance in children with mild TBI and controls. Against the background of the existence of a fronto-parietal network that is consistently active during calculation tasks (Arsalidou & Taylor, 2011), we investigated fronto-parietal white matter connections and their association with performance on the administered behavioral measures. More specifically, we used DTI tractography to delineate the left Arcuate Fasciculus (AF) that connects frontal and temporo-parietal regions that are active during arithmetic. Preliminary data confirm the specific association between arithmetical competence and fractional anisotropy in the left AF. Data are currently being analysed and we will be able to make conclusions on whether a fronto-parietal white matter deficit can be found in children with mild TBI who have arithmetical difficulties.

PP5.5 - 1845

Acute and 1 year susceptibility-weighted MRI of hemorrhagic shearing injury after pediatric TBI

Tong K, Al-Ramadhani R, Rundquist M, Pivonka-Jones J, Holshouser BA, Ashwal S. *Departments of Radiology and Pediatrics, Loma Linda University School of Medicine, USA – sashwal@llu.edu*

Objective: MRI susceptibility-weighted imaging (SWI) accentuates paramagnetic properties of blood products and depicts more hemorrhagic brain lesions after traumatic brain injury (TBI) than conventional MRI. We present initial/1 year SWI data in 17 pediatric TBI patients. **Methods:** Hospitalized pediatric patients with moderate/severe TBI (GCS score <13 or intracranial injury on CT scan) underwent MRI acutely (7–17d post TBI) and at 1 year. SWI was analyzed using an off-line post-processing program, “SPIN”, to semi-automatically count and measure the volume of lesions. The number/volume of lesions between the initial and one year study were compared and correlated with initial injury and gender. **Results:** We studied 17 patients (6–17 yrs; 12 males; 13-motor vehicle, motorcycle, ATV or pedestrian accidents; 4 falls). The number of SWI lesions/patient on the initial MRI ranged from 0 to 299. The number/volume of hemorrhages on the acute MRI did not correlate with the initial GCS score. By 1 year, the number (up to 81.3%) and volume (up to 84.5%) of hemorrhages

decreased. Surprisingly, 9/17 patients retained more than 50% of the original hemorrhagic volume. We did not observe gender differences in resolution of the number/volume of hemorrhages. **CONCLUSIONS:** About 50% of moderate/severe TBI patients have persistent SWI hemorrhagic lesions 1 year after injury. There was no association in degree of hemorrhage resolution with gender or initial GCS. Further analysis will determine if there are regional differences in the resolution or persistence of hemorrhages, correlation with other clinical and imaging variables, associations with lesion location or specific neurological/neuropsychological outcomes.

PP5.6 - 2044

Methylphenidate in children with narcolepsy/cataplexy

Pons van Dijk G, Jansen K, Lagae L, Buyse G. *University Hospitals Leuven, Belgium – g.ponsvandijk@gmail.com*

Introduction: Narcolepsy-cataplexy is an uncommon sleep disorder that can present in childhood. There is little experience with modafinil in pediatric narcolepsy due to limited efficacy/safety data. **Methods:** We retrospectively evaluated efficacy and safety of methylphenidate therapy in all pediatric narcolepsy (with or without cataplexy) patients followed at our institution between 2003 and 2013. **Results:** We identified 13 children with narcolepsy (age of presentation 6–15 years), of whom 3 had secondary narcolepsy. Three patients were excluded because of medical follow-up elsewhere. In the group of primary narcolepsy (age of presentation 6–11 years), 4/7 responded favorable on methylphenidate. Three of them had cataplexy. Excessive daytime sleepiness (EDS) improved in all, cataplexy improved in 2/3, and in 1 additional medication was needed for night terrors. Total follow-up duration was 3 to 10 years. From the three who used modafinil, one switched to modafinil because EDS did not respond enough to methylphenidate, one switched because he reached the age of 18 and from that age modafinil is reimbursed in Belgium. The third never tried methylphenidate because parental refusal. Two of them also had cataplexy and they had a total follow-up of 4 to 7 years. In one EDS improved only partially, cataplexy improved in both partially and 1/4 needed additional medication for night terrors. The 3 children with secondary narcolepsy (age of presentation 10–15 years) responded well on methylphenidate. The causes were craniopharyngioma (1) and pilocytic astrocytomas (2), with a follow-up duration of 2 to 3 years. Two of them also showed cataplexy. All aspects of narcolepsy improved with methylphenidate. Overall, 7/10 responded well on methylphenidate without any significant side-effects. **Conclusion:** Whereas modafinil is the first choice drug option in adults with narcolepsy with or without cataplexy, our findings suggest that methylphenidate is an effective and well tolerated treatment in pediatric patients.

PP5.7 - 1954

Long-term outcome in children with lowgrade tectal tumors and acquired obstructive hydrocephalus

Aarsen FK, Arts WFM, Van Veelen-Vincent ML, Lequin MH, Catsman-Berrevoets CE. *Erasmus University Hospital-Sophia Children's Hospital, The Netherlands – f.aarsen@erasmusmc.nl*

Objective: To study long-term neurologic, cognitive and behavioral deficits in children with a low grade tectal tumor and acquired obstructive hydrocephalus. **Method:** In a consecutive series of 12 children with low-grade tectal tumor diagnosed in our hospital neurologic, neuropsychologic, and radiologic data were prospectively collected. Intelligence, memory, attention, language, visual-spatial, and executive functions were assessed. Follow-up ranged from 1 year to 10 years. **Results:** At follow-up, most frequent neurologic disability was fatigue in children with

a low-grade tectal tumor. They scored lower on sustained attention, long-term memory and had more behavioral problems. Factors influencing cognition were duration of symptoms of raised intracranial pressure and persisting severe hydrocephalus. The cognitive problems resulted in 60% of children needing assistances of special services at school. **Conclusion:** At long-term, children with a low-grade tectal tumor display invalidating neuropsychologic impairments due to compression of supratentorial structures in the cerebello-cortical circuitry by the obstructive hydrocephalus resulting in educational problems. Adequate and timely treatment of hydrocephalus may result in better cognitive functioning. Neuropsychological findings in children with tectal glioma and obstructive hydrocephalus are very similar to findings in children with the cerebellar cognitive affective syndrome after cerebellar tumor surgery. This suggests that at least part of this syndrome in children after cerebellar tumor surgery is caused by the effects of obstructive hydrocephalus.

PP5.8 - 1542

Vincristine induced neuropathy in children with acute lymphoblastic leukemia – prevalence and electrophysiological characteristics

Jain P, Gulati S, Seth R, Bakhshi S, Toteja GS, Pandey RM. Division of Pediatric Neurology, AIIMS, Delhi, India – puneet_mpa@yahoo.com

Objectives: With better survival rates in childhood acute lymphoblastic leukemia (ALL), the focus is increasing on the late effects of treatment and ways to monitor and prevent them. The prevalence of vincristine induced neuropathy have been poorly documented in childhood ALL survivors. The aim of the current study was to assess the prevalence of neuropathy (clinical and electrophysiological) in a cohort of childhood ALL patients >5 years of age who had completed their chemotherapy regimen. **Methods:** This cross-sectional study was carried out in the Departments of Pediatrics and Medical oncology at a tertiary care centre in North India from October 2011 to June 2012. After obtaining the ethical clearance, 80 consecutive children, meeting the inclusion and exclusion criteria, were enrolled. Informed written consent was taken. Detailed nerve conduction studies were performed and Reduced version of Total Neuropathy Score (TNSr) was calculated. **Results:** 80 consecutive children were enrolled. The mean age at the time of evaluation was 11.2 ± 3.2 years. The children on average were 20.5 ± 11.8 months post-chemotherapy. The mean interval between the VCR injection and evaluation was 20.6 ± 11.8 months (3–39 months). The mean cumulative VCR dose during the treatment was 25.8 ± 9.3 mg. Around 13.8% children had clinical evidence of peripheral neuropathy. Twenty-seven children (33.75%; 95% CI: 23.6–45.2%) had peripheral neuropathy electrophysiologically. Symmetric motor axonal polyneuropathy was the most common pattern of involvement with common peroneal nerve most commonly involved. Twenty-seven children (33.75%) had TNSr score ≥ 1 . **Conclusions:** Neuropathy may be a long term adverse effect of VCR rather than being limited to acute neurotoxicity during therapy. Neuropathy may persist despite stopping VCR therapy. Thus, early detection of neuropathy and dose alteration of VCR is important during chemotherapy.

PP5.9 - 1991

Effect of hypothyreosis on the developing chick cerebellum

Larsen SM, Aden P, Paulsen RE, Goverud IL. Oslo University Hospital, Department of Clinical Neurosciences for Children and University of Oslo, Norway – s.m.larsen@medisin.uio.no

Objectives: Brain development in humans is a complex process needing optimal environment in utero, good health and nutritional level of the mother so that processes such as cell

proliferation, programmed cell death, and migration are timed correctly. Thyroid hormones play a pivotal role in these processes but detailed mechanisms are still unknown. **Material and methods:** We have used a chicken embryo model to test hypothyreosis in the developing cerebellum, by injecting the thyreostatic drug methimazole into eggs on embryonic day 14 (E14), and then sacrificing the embryos on E17 and E19. Investigation of cell proliferation was done by BrdU labeling, injected 3 h before sacrifice. Morphological cell death was quantified in HE microscopy. Western blot has been used to investigate migration of granule neurons measuring the level of PAX6 protein as marker. **Results:** Our results showed that cell proliferation was physiologically reduced during this period. Similar tendencies were seen in mild and severe hypothyreosis (BrdU). Programmed cell death or apoptosis is physiologically reduced in this period. Our study shows that mild hypothyreosis delayed this process in this period, and severe hypothyreosis probably even more. Western blot showed a tendency to physiological reduction in expression of PAX6 protein in this period. Expression of PAX 6 in severe hypothyreosis increased rather than decreased. **Conclusions:** Lack of thyroid hormone delays cell death, and results in changes in migration marker PAX6, suggesting that cerebellum may be a target for hypothyreotic neurotoxicity.

PP6. Neurogenetic and mitochondrial disorders

Chair: Haiki Rantala

PP6.0 - 1815

Everolimus for subependymal giant cell astrocytomas (SEGAs) associated with tuberous sclerosis complex (TSC): results from the EXIST-1 trial by age category

Jozwiak S, Brechenmacher T, Segal S, Franz DN. The Children's Memorial Health Institute of Warsaw, Poland – sergiusz.jozwiak@gmail.com

Objective: To examine the impact of age on the efficacy and safety of everolimus treatment for SEGAs associated with TSC for patients in the EXIST-1 trial (NCT00789828). This trial previously demonstrated that everolimus was superior to placebo for reducing SEGA volume ($P < 0.0001$) with a safety profile consistent with previous reports in the TSC population. **Material and methods:** Patients of any age with ≥ 1 SEGA lesion (≥ 1 cm in longest diameter) were randomized (2:1) to receive 4.5 mg/m²/day everolimus (titrated to blood trough levels of 5–15 ng/mL) or placebo. The primary endpoint was SEGA response rate (proportion of patients with $\geq 50\%$ reduction in sum of volumes of all target SEGAs [≥ 1 cm in longest diameter] compared with baseline). Skin lesion response rate was one of the key secondary endpoints and was assessed in patients with ≥ 1 skin lesion at baseline. Adverse events (AEs) were monitored at every visit. The data for everolimus patients aged <3 (n=13), ≥ 3 to 18 (n=55), and ≥ 18 years (n=10) and placebo patients aged <3 (n=7), ≥ 3 to 18 (n=26), and ≥ 18 years (n=6) are reported herein. **Results:** The SEGA response rate for patients aged <3 , ≥ 3 –18, and ≥ 18 years was 23% (95% CI, 5%–54%), 40% (95% CI, 27%–54%), and 50% (95% CI, 19%–81%) for everolimus, compared with 0% (95% CI, 0%–41%), 0% (95% CI, 0%–13%), and 0% (95% CI, 0%–46%) for placebo. All skin lesion responses were partial (improvement $\geq 50\%$ – $<100\%$). For everolimus and placebo, respectively, skin lesion responses were seen in 2/12, 31/51, and 5/9 patients and 0/7, 4/25, and 0/6 patients aged <3 , ≥ 3 to 18, and ≥ 18 years, respectively. **Conclusions:** SEGA and skin lesion responses were observed in all everolimus age categories. The small sample size in some age categories may have limited the results.

PP6.1 - 2162

Hamartin and tuberin expression studies: further insights into TSC1 and TSC2 genes in a cohort of patients with well defined phenotype

Lannoy N, Durant J-F, Corbisier T, Ambroise J, Nellist M, Jansen A, Pelc K, Nassogne M-C, Gala J-L, Lederer D, Vikkula M, Sznajder Y. *Centre de Génétique Humaine UCL, Cliniques Universitaires Saint-Luc, Brussels, Belgium – nathalie.lannoy@uclouvain.be*

Tuberous sclerosis complex (TSC) represents one autosomal dominant genodermatosis with multisystemic involvement. In 20% of patients with definite TSC diagnosis, point mutation or deletion/duplication either in TSC1/TSC2 genes can't be identified. Neither other mechanisms nor gene anomalies contribute so far to the cause of TSC. To further evaluate on TSC1 or TSC2 genes involvement in TSC patients, we conduct a distinct expression study. In a cohort of 132 index patients referred with definite, possible or probable TSC diagnosis, 25 (19, 5, 1 respectively) were not found with a deletion or mutation. In two familial presentations segregation was completed as RT-PCR quantification of 24 TSC1/TSC2 mRNA (DNA and RNA from blood samples and from 5 normal and/or abnormal fibroblast cultures). Gene expression modulation was carried out after normalization with β -actin housekeeping gene and with DU145 cell line as qPCR calibrator using the $2^{-\Delta\Delta Ct}$ method. Sequencing of TSC1/TSC2 promoters and flanking 5'/3'UTR regions were studied from DNA of 8 definite TSC patients. In one familial presentation, haplotype segregation identified an association to TSC2 locus. Among the 24 TSC patients - after validation with healthy controls - expression studies identify normal, elevated or decreased hamartin or tuberin levels (in one only or both TSC alleles) in 50% patients of all classified. In one patient, expression studies from pigmented skin revealed abnormal values compared with the normal skin. Decreased TSC2 mRNA value was observed in patient with familial association to TSC2 locus. Any sequence distortion was found in both promoters as in 5'/3'UTR regions of TSC1/TSC2 genes in 4 definite TSC patients presenting expression anomalies. The present results postulate on additional genetic heterogeneity or epigenetic mechanism to possibly explain occurrence for TSC when expression studies were abnormal. In case of normal levels, one or more other genes could be associated with TSC phenotype.

PP6.2 - 1668

Early EEG monitoring following prenatal diagnosis predicts epileptogenesis in tuberous sclerosis

Moavero R, Cusmai R, Vigeveno F, Toscano A, Caforio L, Bernardi B. *Child neurology and psychiatry unit, Tor Vergata University Hospital, Rome, Italy – rominamoavero@hotmail.com*

Objectives: To describe the role and the usefulness of a close EEG monitoring in children with tuberous sclerosis complex (TSC), following a prenatal diagnosis. **Material and methods:** We present 3 patients with negative familial history, in which the routine fetal ultrasound revealed the presence of multiple cardiac rhabdomyomas. Between 30 and 32 weeks of gestation we performed a fetal MRI, which was able to detect the presence of subependymal nodules or tubers, allowing a definite prenatal diagnosis of TSC. Due to large rhabdomyomas and to the risk of cardiac symptoms, we planned delivery by cesarean section in tertiary centres with experienced neonatal cardiologists. Soon after birth, all these children began a close EEG monitoring, with awake/sleep EEG performed every 3–4 weeks. All the families have been informed of the high risk of epilepsy of TSC infants in the first year of life, and have been educated to recognize focal subtle seizures and epileptic spasms. **Results:** EEG monitoring allowed us to identify focal epileptiform abnormalities early and to observe their evolution towards multifocal abnormalities. In

the child who developed epileptic spasms we observed a further evolution toward secondary bilateral synchronization and a tendency toward a pre-hypsarrhythmic pattern the day before the appearance of spasms. The immediate treatment with vigabatrin early reversed this EEG pattern, and we never observed again abnormalities suggestive of an epileptic encephalopathy. **Conclusions:** Our data suggests that epileptogenesis is a slow process, taking several weeks or months from the first EEG epileptiform abnormalities to the first seizure. The close EEG monitoring allows us to detect subtle changes in the EEG pattern which might indicate an evolution towards epilepsy. The immediate detection and treatment of seizures is crucial to minimize the possible long-term neurodevelopmental sequelae of early life seizures.

PP6.3 - 1724

X-linked sideroblastic anemia and ataxia: a fourth family with identification of a novel ABCB7 gene mutation

D'Hooghe M, Selleslag D, Mortier G, Van Coster R, Vermeersch P, Billiet J, Bekri S. *Department of Neurology and Child Neurology, Hospital Sint-Jan, Bruges, Belgium – marc.dhooghe@azsintjan.be*

X-linked sideroblastic anemia and ataxia (XLSA-A) is a rare cause of early onset ataxia, which may be overlooked due to the usually mild asymptomatic anemia. The genetic defect has been identified as a mutation in the ABCB7 gene at Xq12-q13. The gene encodes a mitochondrial ATP-binding cassette (ABC) transporter protein involved in iron homeostasis. Previously only three families have been reported, each with a distinct missense mutation in this gene. We describe a fourth family with XLSA-A and a novel mutation in the ABCB7 gene. Mutations in this gene should be considered in any unexplained X-linked ataxia, even in the absence of clear hematological changes. The whole blood total erythrocyte protoporphyrin measurement may be used as a screening tool. The precise diagnosis of XLSA-A gives important information about the management, the prognosis and the genetic implications. For many references, see: D'Hooghe M, Selleslag D, Mortier G, Van Coster R, Vermeersch P, Billiet J, Bekri S. X-linked sideroblastic anemia and ataxia: A new family with identification of a fourth ABCB7 gene mutation. *Eur J Paediatr Neurol.* 2012 Nov;16(6):730–5. doi: 10.1016/j.ejpn.2012.02.003. Epub 2012 Mar 6.

PP6.4 - 1601

Aicardi-Goutieres syndrome in a Lybian family

Lakhthar I, Turki I, Miladi N. *National Institute Mongi Ben Hamida of Neurology La Rabta 1007, Tunis, Tunisia – najoua.miladi@rns.tn*

Aicardi-Goutieres syndrome in a Lybian Family Ines Lakhthar, Ilhem Turki, Najoua Miladi National Institute Mongi Ben Hamida of Neurology La Rabta 1007 Tunis Tunisia Aicardi-Goutières syndrome (AGS) is a progressive encephalopathy, possibly with a recessive autosomal pattern of inheritance, which has onset in the first year of life and is characterized by acquired microcephaly, basal ganglia calcifications, white matter abnormalities, chronic lymphocytosis in the cerebrospinal fluid (CSF) and raised interferon-alpha (INF-alpha) in the CSF. We report here a case of a seven year old boy, born to healthy, related parents (distant consanguinity), from non-complicated pregnancy and without perinatal risks, presenting at the age of one month and a half a severe psychomotor regression. The parent's history revealed similar clinical features on two sisters aged respectively five and one year and a half, and three cousins born to related parents. The neurological exam showed tetraplegia, upper limb dystonic movements, oral-facial dyskinesias, nystagmus and absence of eye contact. Cerebral CT scan showed bilateral and symmetrical calcifications in the cerebellum, the dentate nucleus, basal ganglia and periventricular regions. MRI demonstrated a

leukoencephalopathy aspect, calcifications and severe atrophy. Laboratory results (blood and urinary phosphorus and calcium, serum total parathormone, lactate, pyruvate, amino and organic acid chromatography) permitted to exclude common and rare causes of basal ganglia calcifications. TORCH serology was negative. Analysis of the CSF was performed searching increased levels of INF- α . AGS is a genetic disease with a severe clinical picture. It can be misdiagnosed as a congenital infection or, unless a brain CT scan is performed, as a leukoencephalopathy of unknown origin. Current studies aiming to clarify the molecular mechanisms underlying the pathogenesis of AGS could lead to the development of new therapeutic strategies.

PP6.5 - 1922

Incidental findings in array CGH

Keymolen K, De Rademaeker M, Van Den Bogaert A. Center for Medical Genetics, UZ Brussel, VUB, Belgium – Kathelijn.Keymolen@uzbrussel.be

Array Comparative Genomic Hybridization (array CGH) is nowadays widely used in the diagnostic work-up of intellectual disability, congenital anomalies and psychiatric disorders. In contrast with the standard karyotype, it allows us to pick up microdeletions - and duplications, thus increasing the number of patients for which the etiology of their problem can be demonstrated. In few cases, the array CGH result also uncovers susceptibility to serious late(r)-onset disorders, such as hereditary cancer syndromes. Although the risk for such an incidental finding is low, the physician who prescribes the analysis should be aware of this possibility and should inform the patient and/or the parents before the test is undertaken. In case of a parentally inherited aberration, the carrier parent is equally at risk for the concerned disorder and pretesting counseling should address this item too. We will illustrate the possibility of incidental findings on array CGH with two cases. The first patient is an infant with congenital anomalies and severe hypotonia. Array CGH analysis reveals a 23Mb deletion of 5q22.1q23.1. This region includes the APC gene, responsible for Familial Adenomatous Polyposis. This child will thus require close gastrointestinal follow-up from the age of 10 years on. Since the deletion is de novo, the parents are not at increased risk. The second patient is a girl with bilateral aniridia. She has a 15 Mb deletion on 11p14.1p11.2, encompassing the PAX 6 gene, which explains the ocular phenotype. However, the deletion also includes the WT1 gene, involved in renal neoplasia. Close monitoring allowed the early detection and treatment of a kidney tumor in the child. **Conclusion:** we want to draw the attention of the prescriber of array CGH to the small but existing risk of incidental findings with important consequences for the patient. Pretest information is therefore mandatory.

PP6.6 - 1797

Isolated complex I deficiency and atypical clinical courses in three patients due to novel mutations in NDUFS1 and NDUFV1

Björkman K, Sofou K, Darin N, Kollberg G, Holme E, Tulinius M, Oldfors A, Moslemi AR. The Queen Silvia Children's Hospital, Sahlgrenska University Hospital, Göteborg, Sweden – kristoffer.bjorkman@vgregion.se

Objectives: To report three patients with atypical clinical course, to add to our understanding of genotype-phenotype correlations in genes encoding complex I electron input module subunits. **Material and methods:** Three patients with isolated complex I deficiency. One girl, patient 1, who presented at birth with hypotonia and feeding difficulties, and died at 5 weeks of age. Two sisters, patients 2 and 3, who presented at 6–7 months of age with progressive muscle weakness and delayed motor development, and have since showed a mild clinical course with long life

span and normal mental development. **Results:** Metabolic findings indicated isolated complex I deficiency. Molecular genetic analysis showed compound heterozygosity for two novel point mutations in NDUFS1 for patient 1 and compound heterozygosity for two novel point mutations in NDUFV1 for patients 2 and 3. A literature review of all reported cases of mutations in the affected genes (NDUFS1, 12 patients; NDUFV1, 14 patients) showed that the clinical course of these three patients was atypical with regard to other patients described with mutations in corresponding genes. **Conclusions:** Genotype-phenotype correlations in patients with mutations affecting the genes that encode the electron input module of complex I vary, but patients with NDUFS1 mutation tend to have a shorter life span than patients with NDUFV1 mutation. Even considering this, the reported patients show that atypical clinical courses occur. Identifying the mutations is of importance for accurate genetic counseling. Compound heterozygosity due to the combination of a null mutation and a milder missense mutation may predict a more severe phenotype compared to the combination of two milder missense mutations.

PP6.7 - 1623

Acute liver failure in patients with POLG1 mutations after valproate exposure and their prognosis after liver transplantation

Hynynen J, Komulainen T, Tukiainen E, Nordin A, Arola J, Kälviäinen R, Jutila L, Røytä M, Hiltala R, Suomalainen A, Majamaa K, Mäkitalo H, Uusimaa J. University of Oulu, Oulu University Hospital, Finland – johanna.uusimaa@oulu.fi

Objectives: Patients with mutations in POLG1 gene encoding the catalytic subunit of mitochondrial DNA polymerase gamma have an increased risk for valproate-induced liver failure. The role of liver transplantation for patients with mitochondrial diseases has been controversial. We studied the development of valproate-induced liver failure in patients with POLG1 mutations and the prognosis after possible liver transplantation. **Methods:** Patients with severe valproate-induced liver failure were retrospectively identified from the register at the Department of Transplantation and Liver Surgery, Helsinki University Hospital, Finland (880 liver transplantations since 1988). Liver transplantation and clinical follow-up had been conducted according to routine procedure. POLG1 was analyzed in blood DNA and the mtDNA content in patient and control liver samples was quantified by using real-time quantitative PCR. **Results:** Five out of six patients with valproate-induced liver failure (at 13–34 years) were identified (one patient with reversible liver failure was not studied). Four patients had mtDNA depletion in liver associated with homozygous POLG1 p. W748S and p. E1143G mutations; one being also heterozygous for p. Q497H mutation. One patient had died due to intractable status epilepticus and liver failure without transplantation. Three patients with liver transplant are alive and have survived 4–19 years. One patient has chronic pancreatic insufficiency. Neurological manifestations include ataxia, peripheral neuropathy and occasional epileptic seizures; one patient has been seizure free for 11 years. Furthermore, one patient with a heterozygous POLG1 p. Q1236H mutation without mtDNA depletion in liver died suddenly two years after the liver transplantation. **Conclusions:** Consistent with the recent finding a heterozygous POLG1 p. Q1236H mutation was related to valproate-induced liver failure without mtDNA depletion whereas patients homozygous for POLG1 p. W748S and p. E1143G mutations have mtDNA depletion. We emphasize that POLG1 gene analysis should be performed for all patients with acute liver failure following valproate treatment.

PP6.8 - 1911

A complex V ATP5A1 defect causes fatal neonatal mitochondrial encephalopathy

Jonckheere AI, Renkema GH, Bras M, van den Heuvel LP, Hoischen A, Gilissen C, Huynen MA, de Vries MC, Smeitink JAM, Rodenburg RJT. *University Hospital Brussels, Belgium – an.jonckheere@uzbrussel.be*

Objective: Whole exome sequencing is a powerful tool to detect novel pathogenic mutations in patients with suspected mitochondrial disease. However, the interpretation of novel genetic variants is not always straightforward. Here, we present two siblings with a severe neonatal encephalopathy caused by complex V deficiency. The aim of this study was to uncover the underlying genetic defect using the combination of enzymatic testing and whole exome sequence analysis, and to provide evidence for causality by functional follow-up. **Material and methods:** Measurement of the oxygen consumption rate and enzyme analysis in fibroblasts were performed. Immunoblotting techniques were applied to study complex V assembly. The coding regions of the genome were analysed. Three-dimensional modelling was applied. **Results:** Exome sequencing of the two siblings with complex V deficiency revealed a heterozygous mutation in the ATP5A1 gene, coding for complex V subunit α . The father carried the variant heterozygously. At the messenger RNA level, only the mutated allele was expressed in the patients, while father expressed both the wild type and the mutant allele. Gene expression data indicate that the maternal allele is not expressed, which is supported by the observation that the ATP5A1 expression levels in the patients and their mother are reduced to approximately 50%. Complementation with wild type ATP5A1 restored complex V in the patient fibroblasts, confirming pathogenicity of the defect. At the protein level, the mutation results in a disturbed interaction of the α -subunit with the β -subunit of complex V, which interferes with the stability of the complex. **Conclusions:** This study demonstrates the important value of functional studies in the diagnostic work-up of mitochondrial patients, in order to guide genetic variant prioritization, and to validate gene defects.

PP6.9 - 1900

Early fatal outcome in two patients with defect in NFU1

Van Coster R, Smet J, De Paepe B, Vanlander A, De Lattre E, De Meirleir L, Lissens W, Seneca S. *Department of Pediatrics, Division of Pediatric Neurology and Metabolism, Ghent University Hospital, Gent, Belgium – rudy.vancoster@ugent.be*

Background: Recently, mutations have been detected in NFU1 and BOLA3, two genes involved in iron-sulfur biogenesis. In affected patients, defects in the OXPHOS complexes I and II, in 2-oxoacid dehydrogenase and in lipoate synthesis were found. **Objective:** The objective was to screen our database of patients to find patients with similar clinical and biochemical findings and to sequence the two genes in suspected patients. **Patients and methods:** Patients with encephalopathy, failure to thrive, hyperlactacidemia, increased glycine in cerebrospinal fluid and decreased activities of the complexes I and II were selected. BN-PAGE, western blotting and Sanger sequencing was performed. **Results:** A decreased protein amount in the complexes I and II was visualized using BN-PAGE. A decrease of structural subunits in complexes I and II and low signals of protein-bound lipoic acid were detected by western blotting. Mutations were detected in NFU1 in both patients. One patient carried the 'hotspot' mutation p.Gly208Cys and the other was a compound heterozygote for this mutation and for p.Arg21Pro. **Conclusion:** Only three papers were reported earlier in the literature describing patients with NFU1 deficiency. Our results are concordant with the assumed role of NFU1 in ISC biosynthesis and a novel compound heterozygous mutation is presented here.

PP7. Epilepsy 2

Chair: John Stephenson

PP7.0 - 2029

Morphological ECG changes in seizures: implications for seizure detection

Jansen K, Varon C, Van Huffel S, Lagae L. *Pediatric neurology, University Hospitals Leuven, Belgium – katrien.jansen@uzleuven.be*

Objectives: Epileptic seizures can influence cardiac function in epilepsy patients. This can change the morphology of the ECG signal during seizures. Seizure detection could reduce morbidity and mortality in epilepsy patients. This study aims to develop a method for seizure detection based on morphological ECG changes during seizures in childhood epilepsy. **Material and methods:** ECG segments were selected from recordings of 35 patients admitted to the epilepsy clinic of the University Hospital Leuven. From these recordings, 80 segments of 5 minutes were selected, starting 3 minutes before the onset of 40 partial and 40 generalized seizures. For each segment, a moving window equivalent to 5 heartbeats was shifted with an overlap of 4 heartbeats throughout the whole segment. For each window, a matrix containing the 5 QRS complexes was analyzed using principal component analysis (PCA). The 4th and 5th components were selected as features. These two features, together with the mean RR interval per window, were used to discriminate seizures. **Results:** The positive predictive value (PPV) of the proposed methodology was 79.17% for partial seizures, which were identified in a 7.4 ± 14.3 seconds range. For generalized seizures, the obtained PPV equals 57.38%, and the time difference was 9.6 ± 20.5 seconds. For both types of seizures, about 75% of the changes in the ECG were lagging the onset in the EEG. **Conclusions:** Morphological ECG changes can be used to improve seizure detection in partial and generalized seizures in childhood.

PP7.1 - 1956

Effectiveness and tolerability of perampanel in children and adolescents with refractory epilepsy – first European experience

Biro A, Stephani U, Tarallo T, Bast T, Kurlmann G, Leiz S, Nikanorova M, Wolff M, Haberlandt E, Selch C, Fiedler A, Staudt M, Kluger G. *Clinic for Neuropediatrics and Neurorehabilitation, Epilepsy Center for Children and Adolescents, Schön Klinik Vogtareuth, Vogtareuth, Germany – anna.b.rosen@gmail.com*

Objectives: Aim of this survey was to explore the effectiveness and tolerability of perampanel (PER) in a heterogeneous group of patients under 18 years of age with refractory epilepsies. **Methods:** This observational survey was conducted as a collection of retrospective data from multiple centers in Germany, Austria and Denmark. Clinical course of the first patients treated in these centers with PER was documented. Initial dosage and titration schedule of PER were at the discretion of the treating physician according to medical need. Effectiveness was evaluated by comparing the frequency of seizures between baseline and the last 4-week period of observation. Observation is continuous and planned until an 18-month follow-up. **Results:** The study population consisted of 50 children (mean age: 10.3 years, range: 2–17, male: 22), with various refractory epilepsies classified as focal epilepsy (n=28), generalized epilepsy (n=14), LGS (n=4), Dravet Syndrome (n=2), and others (n=2). The response rate (50% seizure reduction) in the first 3 months of therapy was 26% (13 of 50 patients) in total. Of all patients, 12% (n=6) experienced a 50–75% reduction and 12% (n=6) experienced a more than 75% reduction in seizure frequency. Complete seizure control was achieved in 2% (n=1). Adverse events were reported in 24 cases, mostly mild-

moderate, with remission spontaneously or with decreasing the PER dosage. The most frequently occurring adverse events were fatigue (n=11), agitation or aggressivity (n=9), dizziness (n=5), and changes in appetite (n=5). Severe adverse events (severe behavioral changes, dizziness, fatigue, headache, diarrhea-vomiting) occurred in 6 cases. **Conclusions:** These preliminary data suggest that PER may be effective in the treatment of children and adolescents with refractory epilepsies of different etiologies. There is a lack of pharmacokinetic data in young patients, low titration rates may reduce side effects. Longer follow-up of our patients and further investigations are needed.

PP7.2 - 1886

Do adolescents with epilepsy have adequate knowledge regarding antiepileptic drug treatment?

Prpic I, Bezak B. Rijeka, Croatia – igor.prpic@medri.uniri.hr

Objective: Knowledge and education process regarding drug therapy of epilepsy is very challenging process. So, we investigated general knowledge and sources of information about antiepileptic drug (AED) treatment among adolescents with epilepsy. **Methods:** Written survey containing 29 questions was administrated among 60 randomly selected adolescents with epilepsy (mean age=14.6 years, mean duration of AED treatment 3.7 years) who attended their ordinary check-ups on Paediatric Neurology department in University Hospital Rijeka, Croatia. Questions were formed to investigate adolescent's knowledge towards their illness, their general awareness of drugs and correct usage of AEDs, treatment compliance, and adolescent's main source of education towards their illness and drugs they're using. Parental informed consent was obtained at the beginning of the survey. **Results:** AED was taken without parental control in 70% of respondents, mostly in those adolescents older than 15 years. 78% of respondents named exact dose of drug that they are using. Questions regarding general drug knowledge were correctly answered in 58%. Additional factors relevant for successful treatment and control of epilepsy were correctly recognized only in 28% of respondents. Child neurologist, parents, and internet were major source of information regarding epilepsy and AEDs treatment. **Conclusion:** Results regarding knowledge towards AEDs among adolescents with epilepsy are encouraging. However, great majority of adolescents are not aware of additional factors important in decreasing the risk of harm due to seizure and seizure treatment (regular sleep, alcohol use, appropriate sport activities). Furthermore, in process of reducing and avoiding harm due to epilepsy and AED treatment among children with epilepsy education should be extended to younger children. Nurses, family physicians and psychologist should be more active members in that process.

PP7.3 - 1883

Language area organization in children with non-lesional frontal epilepsy

Tarta-Arsene O, Preoteasa F, Agavriloaei M, Tarta-Arsene E. Pediatric Neurology Department, Clinica Hospital 'Al. Obregia', Bucharest, Romania – otartaarsene@yahoo.com

Purpose: It was described that language areas in children with epileptic seizures is different due to neuroplasticity of a developing brain. In this study, it was analyzed through fMRI the features of Broca's area in children with frontal non-dominant, non-lesional epilepsy and compared with normal children at the same age, in order to find significant differences. **Methods:** 26 children diagnosed with focal frontal non-lesional epilepsy were analyzed and compared with 25 normal children at the same age. The clinical features related to epileptic seizures were analyzed. All subjects had morphological cerebral MRI in order

to exclude a structural lesion in the language area and then they have performed fMRI with specific tasks for activation of Broca area. The results were statistically analyzed and compared with published data. **Results:** The two groups of subjects were statically comparative considering general data: age, sex, social environment, verbal intelligence coefficient and clinical laterality. The epilepsy's analysis showed a median period between the onset of epilepsy and fMRI of almost 4 years and median number of seizures 10 (a sufficient period of time and number of seizures for reorganization of cerebral brain area). The EEGs show an active frontal dominant epileptiform discharges in 60% of cases. All children had succeed to follow efficient the tasks for language activation for Broca's area, and the comparative analyzes showed an abnormal lateralization in epileptic patients, more on the right hemisphere than in normal group (p=0.0327). This aberrant organization was proven to be correlated with onset of seizures below the age of 1 (p=0.0467), presence of status epilepticus (p=0.0424) and treatment with two antiepileptic drugs (p=0.0424). **Conclusions:** This study could be considering as a starting point for the futures studies in evaluation of abnormal language organization of epileptic children.

PP7.4 - 1876

Contribution of magnetic source imaging to the presurgical evaluation of refractory focal epilepsy in children

Badin F, De Tiège X, Op De Beeck M, Van Bogaert P. Department of Pediatric Neurology, Hôpital Erasme, Université Libre de Bruxelles, Brussels, Belgium – fanny.badin@ulb.ac.be

Magnetic source imaging (MSI) combines magnetoencephalography (MEG) and structural cerebral MRI to estimate non-invasively the source location at the origin of magnetic fields recorded by MEG. To evaluate the contribution of MSI in the presurgical evaluation of refractory focal epilepsy in children, we retrospectively selected 24 consecutive patients aged from 2 to 17 years who benefited from MSI in their presurgical work-up. MEG sources location of epileptic events was determined by conventional equivalent current dipole modeling. We first studied the concordance between MEG sources and the presumed location of the epileptogenic zone (PLEZ) as determined by scalp video-EEG, MRI, and FDG-PET data. In a second step, we correlated the extent of MEG sources resection with post-surgical outcome in patients who underwent respective surgery. This was performed by coregistering MEG sources on postsurgical MRI to assess whether they were located inside or outside the resected cerebral tissue. We found MEG epileptic events in 19 children (79%), and good concordance between the PLEZ and the MEG sources in all of them. Seven children had MEG sources outside the PLEZ. In the subgroup of 9 children who were operated on, the seizure-free patients (n=8) had 41% of their MEG sources inside the resection, 77% of their sources in the 1-cm extended area, and 96% in the 2-cm extended area. For the only patient who was not seizure-free, these numbers were 5%, 57% and 87%, respectively. In conclusion, MSI added new information to identify the PLEZ in the presurgical evaluation of this pediatric cohort of refractory epileptic patients. On the other hand, we found that the whole MEG sources resection was not necessary to make the patient seizure-free. The relationship between the extent of resection of tissue containing MEG sources and the post-surgical outcome needs to be prospectively analyzed on a larger population.

PP7.5 - 1768

Efficacy of long-term adjunctive zonisamide therapy in paediatric patients with partial epilepsy: results of an open-label extension study of a Phase III, randomised, double-blind, placebo-controlled trial

Rosati A, Giorgi L, Bradshaw K, Guerrini R. *Neuroscience Department, Children's Hospital Anna Meyer-University of Florence, Florence, Italy – mandrews@mxmcommunications.com*

Objectives: To assess the long-term efficacy of once-daily adjunctive zonisamide therapy in paediatric patients with partial epilepsy. **Material and methods:** An open-label extension study of a Phase III, double-blind, randomised, placebo-controlled, multicentre trial was conducted in patients (age 6–18 years) with partial epilepsy receiving one or two antiepileptic drugs (AEDs). Study began with a double-blind transition period (duration 2–11 weeks), during which patients already receiving zonisamide continued at same dose, while those previously receiving placebo switched to zonisamide, initiated at 1 mg/kg/day and up-titrated to a target of 8 mg/kg/day (maximum 500 mg/day). This was followed by an open-label period (duration 45–57 weeks), during which zonisamide dosing could be adjusted according to tolerability/response. Primary efficacy assessment was responder rate during open-label period (response defined as $\geq 50\%$ seizure frequency reduction from baseline of initial trial). Secondary assessments included seizure freedom rate and reduction in 28-day seizure frequency (from baseline of original trial) during open-label period. **Results:** In total, 144 patients entered the extension study, of whom 72 had received placebo and 72 had received zonisamide during the initial trial; 99/144 (68.8%) patients completed the study. During open-label period, 81/144 (56.3%) patients were responders (95% confidence interval [CI], 47.7%, 64.5%). Results were similar for patients who initially received placebo (40/72; 55.6%; 95% CI, 43.4%, 67.3%) and zonisamide (41/72; 56.9%; 95% CI, 44.7%, 68.6%). Overall, 16/144 (11.1%) patients achieved seizure freedom during open-label period (95% CI, 6.5%, 17.4%); results being identical for patients initially receiving placebo and zonisamide (for both populations: 8/72; 11.1%; 95% CI, 4.9%, 20.7%). Seizure frequency reduction was maintained throughout the study; the median percentage decrease in seizure frequency being 65.9% during open-label period. **Conclusions:** The efficacy of adjunctive zonisamide in paediatric patients with partial epilepsy was maintained over a treatment period of >1 year.

PP7.6 - 687

Does vigabatrin treatment for infantile spasms cause visual field defects? An international multicenter study

Riikonen R, Carmant L, Dorofeeva M, Hollody K, Krajnc B, Renner Primec Z, Szabo I, Wohlrab G, Sorri I. *Kuopio, Finland – raii.riikonen@kolumbus.fi*

There exists little information how often the vigabatrin (VGB) treatment for infantile spasms (IS) causes irreversible visual field defects (VFDs). The aim of this study was to examine IS patients at school age for visual fields to see whether the VGB treatment in infancy had caused defects. Patients and **Methods:** This study included 34 children aged 11 (range 8 to 22 years). Six centers were involved in the study. Nine children had tuberous sclerosis (TS), two other symptomatic (mild brain malformations) and the remaining 23 cryptogenic aetiology for their spasms. Visual fields were examined by the Goldmann kinetic perimetry, by the static Humphrey or Octopus perimetry by experienced perimetrist. Visual fields were re-evaluated by the ophthalmologist (I.S.). **Results:** We found typical VGB-attributed visual field defects altogether in 12/34 (35%) patients. The defects were mild in 5, moderate in 4 and severe in 3 cases. One child out of 12 children who used VGB less than one year (Group 1) had a mild VFD. Four of 9

patients (44%) using VGB up to 22–24 months and 7/13 patients (53%) using VGB more than 2 years (Group 3) had VFDs. Defects were mild (2), moderate (1) and severe (1) in the Group 2, and mild (2), moderate (3) and severe (2) in the Group 3. The mean cumulative doses were 155 g (Group 1), 808 g (Group 2) and 2547 g (Group 3), respectively. The patients with TS had more VFDs (6/9 patients) but their VGB treatment was also longer. The frequency of VFDs varied in different centers. **Conclusions:** The VFDs were found in the same frequency as reported in adults. The plasticity of an infant retina seems not to prevent from the damage. The risk/benefit ratio should always be carefully considered when using VGB. Treatment should be as short as possible.

PP7.7 - 1583

The effectiveness of a low-dose oral diazepam treatment to prevent recurrence of febrile seizures

Park HJ, Kim SY, Choi SH. *MBL Children's Hospital, Eulji Medical University, Korea – phojin71@hanmail.net*

Purpose: Diazepam suppositories or oral diazepam have been used to prevent recurrence of febrile seizures (FS). But this strategy cause many side effects such as sleepiness, lethargy, irritability, and ataxia. This study aimed to investigate the optimum dose of diazepam to reduce the recurrence of FS and side effects in children who have had a febrile seizure attack. **Methods:** The subjects of this study included 528 children with FS who were admitted to Eulji University Hospital from 2008 to 2011. The children divided into four groups according to the dose of diazepam: Group I, 121 patients, received no diazepam therapy, Group II, 129 patients, received oral diazepam in a single dose of 0.1 mg/kg after the febrile seizure, Group III, 127 patients, 0.2 mg/kg, and Group IV, 151 patients, 0.3 mg/kg, respectively. **Results:** Seizures recurred in 6 of 129 children (4.7%) in Group II, 1 of 127 (0.8%) in Group III, and none of 151 children in Group IV. For the 121 untreated patients, FS recurred in 20 children (16.5%). This study revealed a significant difference in the rate of recurrence of FS between children treated with diazepam and those who were not. And the recurrence rate was decreased by the increment of the dosage of diazepam. The adverse effects were observed in 19.9% of children with diazepam, 3.9% in Group II, 12.6% in Group III, and 39.7% in Group IV. The rate of adverse effects was also increased with the increment of dosage. **Conclusion:** An oral diazepam therapy will reduce the recurrence of FS during the same febrile illnesses. We think the optimum dose of diazepam is 0.1 mg/kg or 0.2 mg/kg rather than 0.3 mg/kg. However, the use of oral diazepam after a FS should be carefully considered with weighing the benefits and potential adverse effects.

PP7.8 - 1576

Successful desensitization of oxcarbazepine and ethosuximide after cutaneous adverse drug reactions and HLA genotype in Korea

Lee BL, Yu H, Lee M, Lee J. *Department of Pediatrics, Pusan Paik Hospital, Inje University College of Medicine, Korea – bototii@hanmail.net*

Objective: Allergic reaction to specific antiepileptic drugs (AEDs) can occur in some patients and require a change of therapy. An alternative strategy is to desensitize the patients to the offending drug. This study aimed to investigate the usefulness and safety of desensitization to oxcarbazepine (OXC) and ethosuximide (ETX) in patients who had cutaneous adverse drug reactions. **Methods:** We enrolled 20 patients who had good initial response to OXC (n=19) or ETX (n=1), but who discontinued due to cutaneous adverse drug reactions. Although alternative AEDs were tried on our patients, their seizures were refractory. Therefore, desensitization to OXC was tried in 18 children with partial seizures

and one child with paroxysmal kinesigenic dyskinesia (PKD), and to ETX was attempted in one child with atypical absence seizures. High-resolution human leukocyte antigen (HLA)-A, and -B genotyping was performed to investigate the association between specific HLA allele and OXC-induced cutaneous adverse drug reactions. **Results:** The median age at desensitization was 11.3 ± 3.5 years (range 4.8–16.2 years) and the mean duration of follow-up was 16.2 ± 8.7 months (range 5–37 months). Nineteen patients completed the desensitization protocol to a target dosage over 2–5 months. Five children developed mild itching and erythema during desensitization, but the symptoms disappeared after the next dose increment was withheld for a short period. We did not find specific HLA genotypes associated with OXC-induced cutaneous adverse drug reactions. The frequency of seizure or dyskinesia was reduced to less than baseline in 18 patients. At last follow-up, eight patients were seizure-free, five patients showed >90% reduction and the other four patients had >50% reduction. **Conclusions:** The desensitization protocol was well tolerated and safe without serious allergic reactions. When allergic reactions occur with OXC or ETX and there are no effective drugs, desensitization can be a useful alternative.

PP7.9 - 2061

Haematological parameters in children with epilepsy treated with levetiracetam monotherapy

Dinopoulos A, Paschalidou M, Tsirouda M, Garoufi A, Zafropoulou F, Attilakos A. 3rd department of Pediatrics, University of Athens, "Attikon" University Hospital, Greece – pamar2009@hotmail.com

Objectives: Levetiracetam (LEV), a newer broad spectrum antiepileptic agent, is used successfully as monotherapy for partial onset seizures, rolandic epilepsy and myoclonic epilepsy and appears to be well tolerated with mild adverse effects. However, in contrast with the older antiepileptic drugs which are well known to cause hematological changes, the effect of LEV is not yet sufficiently investigated. The aim of this study was to investigate prospectively the hematological effects of LEV in children with epilepsy. **Material and methods:** The study population consisted of 20 children (8 males, 12 females, aged 2 to 15 years old, mean age 6.5 ± 4.16 years) with epilepsy treated with LEV monotherapy. None of the children were receiving any form of AED medication prior to LEV initiation. Complete blood count (CBC) was performed in all children, before and at 2 and 6 months of LEV monotherapy. **Results:** Lymphocyte absolute count was significantly decreased at 6 months ($p=0.021$) of LEV monotherapy. The rest of the white blood cells count as well as the red blood cells parameters and the platelets were not altered. **Conclusions:** LEV monotherapy may significantly decrease lymphocyte count at six months of treatment in children with epilepsy. This might indicate the need to monitor lymphocyte count and infection tendency in children receiving LEV. The depletion of lymphocytes, which is a primary component of the immune system could be associated with the higher incidence of infections reported in children receiving LEV. Further prospective studies are needed to investigate the effect of LEV in lymphocyte numbers and the possible association with the infection frequency reported in LEV patients.

PP8. Learning disorders/Immunology

Chair: Günter Bernert

PP8.0 - 1978

Rising prevalence of CVI in main stream education calls for a different approach

Depourcq M, Vandamme AL, Bonamie E, Keppens K. De Kade, Spermalie, Bruges, Belgium – katrien.keppens@mpi-spermalie.be

Prevalence data indicate that CVI (Cerebral Visual Impairment) now is the leading cause of vision impairment in children. Better ability of the school support teams in dealing with CVI-related problems ensure that more children remain in main stream education. Whereas better general awareness for (presumption of) visual dysfunction leads to more referrals to CVI-clinics. Therefore we notice an increasing population of children with CVI in main stream education over the last five years. The presence of students with CVI nearing or in secondary education calls for a customized, specific, often multidisciplinary approach. **Objectives:** Better support of CVI students in main stream secondary education. **Material and methods:** Prevalence data of the home intervention team Accent, De Kade, Spermalie Bruges. For better understanding of the needs of CVI students, they are referred to our multidisciplinary team. The data of these investigations are collected in a retrospective study. **Results:** Between 2004 and 2008 only 2 students with CVI attended main stream secondary education and were supported by home intervention team Accent and/or the school support team Spermalie. Between 2009 and 2012 this amount increased to 12 students with CVI. We will give a detailed overview of their needs and concerns and of the typical problems they are confronted with. We will also provide information about the current approach and support. **Conclusions:** Students with CVI in main stream secondary schools demand a different approach and/or support package than children with CVI in primary schools.

PP8.1 - 1634

G.CVI.Tods, a novel diagnostic tool in the assessment of cerebral visual impairment in the young child

Van Parijs K¹, Vandeput A¹, Peirens G^{1,2}, Ortibus E^{1,2}. ¹Centrum Ganspoel, Belgium, ²University Hospitals Leuven, Department of Pediatric Neurology, Leuven, Belgium – els.ortibus@uzleuven.be

Objectives: Cerebral Visual Impairment (CVI), a neurological condition characterized by an impaired visual perception, has a large negative impact on global development. Early detection and early intervention leads to an improved quality of life. In children under 3 years and in those with a multiple handicap, diagnosis of CVI is largely based on observational and subjective methods, due to language or motor disabilities. Moreover, normative data for visual field size are lacking. **Material and methods:** Ganspoel, an institution for the care for visually impaired people, set out to construct a standardized battery for the assessment of visual perceptual skills in this age group. Flemish children of 18, 24 and 30 months with a normal global development and a normal refraction, performed the G.CVI.Tods. The battery consists of a different constellation of subtests depending on age: Visual recognition of o 3D situations (all) o 2D situations (line drawings (30m), colored images & photos (all)) of single objects (photos (18m), line drawings (24, 30m), black & white images & photos unconventional viewpoint (30m), colored images (all)) o simple objects (18m) Motion pursuit (all) Visual field assessment (all) Daily visual functioning (18m). **Results:** Sixty-four children were examined at 18 months, 67 at 24m and 77 at 30m. Sum scores of the visual recognition tasks and of the pursuit of motion task, the highest scores for every quadrant of the visual field

and the questionnaire of daily visual functioning were plotted in frequency distributions per age. Split-half reliability, Cronbach alpha and correlations between the different subtests of the visual recognition tasks showed valid and reliable results. **Conclusion:** Normative data have been gathered for a standardized battery for the assessment of visual perceptual skills in children of 18, 24 and 30 months. In a next project, validity will be evaluated.

PP8.2 - 1914

Functional MRI-guided probabilistic tractography of cortico-cortical and cortico-subcortical language networks in children

Broser P, Groeschel S, Hauser T, Lidzba K, Wilke M. *Pediatric Neurology & Developmental Medicine, University of Tübingen, Germany* – philip.broser@med.uni-tuebingen.de

In this study, we analyzed the structural connectivity of cortico-cortical and cortico-subcortical language networks in healthy children, using probabilistic tractography based on high angular resolution diffusion imaging. In addition to anatomically defining seed and target regions for tractography, we used fMRI to target inferior frontal and superior temporal cortical language areas on an individual basis. Further, connectivity between these cortical and subcortical (thalamus, caudate nucleus) language regions was assessed. Overall, data from 15 children (8f) aged 8–17 years (mean age 12.1 ± 3 years) could be included. A slight but non-significant trend towards leftward lateralization was found in the arcuate fasciculus/superior longitudinal fasciculus (AF/SLF) using anatomically defined masks ($p > 0.05$, Wilcoxon rank test), while the functionally guided tractography showed a significant lateralization to the left (pb.01). Connectivity of the thalamus with language regions was strong but not lateralized. Connectivity of the caudate nucleus with inferior-frontal language regions was also symmetrical, while connectivity with superior-temporal language regions was strongly lateralized to the left (pb.01). To conclude, we could show that tracking the arcuate fasciculus/superior longitudinal fasciculus is possible using both anatomically and functionally defined seed and target regions. With the latter approach, we could confirm the presence of structurally-lateralized cortico-cortical language networks already in children, and finally, we could demonstrate a strongly asymmetrical connectivity of the caudate nucleus with superior temporal language regions. Further research is necessary in order to assess the usability of such an approach to assess language dominance in children unable to participate in an active fMRI study

PP8.3 - 1910

Academic achievement of 7 year old children in Wales born to mothers taking anticonvulsants in pregnancy

Lacey AS, White CP, Pickrell WO, Rees MI, Thomas RH. *Health Informatics Research Unit, Institute of Life Science, Swansea University, Swansea, UK* – Cathy.White@swales.nhs.uk

Objective: Prospective studies suggest that education attainment of children exposed to anticonvulsants in utero is poorer than expected and drug dependent. To avoid accusations of selection bias we used routinely collected education data on a population basis to compare academic achievement of children exposed to anticonvulsants in utero with those who were not. **Methods:** Using the Secure Anonymised Information Linkage (SAIL) database of primary care records in Wales we identified children of women with a diagnosis of epilepsy and recorded the mother's anticonvulsant prescription history. Using national standardised testing the percentage of children of a mother with epilepsy achieving the expected level or above in English or Welsh (first language), mathematics and science were compared to all those without a mother with epilepsy. **Results:** 481 children were identified and

291 mothers took no drugs during the pregnancy. 165 children were exposed to a single anticonvulsant and 25 to polytherapy (11 including Valproate). 81 children were exposed to Valproate in utero, 57 to Carbamazepine, 12 to Phenytoin and 15 to Lamotrigine. 68% of children whose mothers were taking any single anticonvulsant achieved the standard compared with 80% of all children ($p = 0.0003$). For children exposed to Valproate the figure was 65% ($p = 0.002$) and 47% for Lamotrigine ($p = 0.004$). There was no difference for those whose mothers took Carbamazepine ($p = 0.49$) or Phenytoin ($p = 1.0$) in pregnancy. Similar results were found in the individual assessments for language, mathematics and science. Only 52% of children whose mothers took more than one drug in pregnancy achieved the standard ($p = 0.008$). **Conclusions:** Academic achievement is significantly reduced for children exposed to Valproate, Lamotrigine or combinations of anticonvulsants in utero. This study supports the increasing concern that foetal exposure to certain anticonvulsants is deleterious to later cognitive development.

PP8.4 - 1626

Long-term neuropsychiatric follow-up in hyperprolinemia type 1

Di Rosa G, Nicotera N, Lenzo P, Spanò M, Tortorella G. *Dept. of Pediatric, Gynecological, Microbiological and Biomedical Sciences, Unit of Infantile Neuropsychiatry, Univ. of Messina, Italy* – gdirosa@unime.it

Objectives: Although a growing number of patients has been reported, the neuropsychiatric phenotype associated to hyperprolinemia type 1 (HPI) is still under debate. We previously described a small sample of patients with HPI. Now we report an expanded sample with HPI, long-term followed-up at our Unit for a mean duration of 11 years. **Patients and methods:** Neuropsychiatric features and course of 10 patients (3 M), actual age range 9–21 yrs (median 15.3 years) diagnosed with HPI were analyzed. **Results:** Clinical course was characterized by epileptic manifestations and/or cognitive impairment at onset, and subsequently replaced by prevalent psychiatric disorders such as behavioral disturbances and aggressiveness. Social behavior and relational skills were the most markedly impaired in the majority of cases. Learning disorder was present in one patient. Behavioral and psychiatric symptoms were explored in all patients by Child Behavioral Checklist (CBCL) parents' interview. No relationship arose between CBCL scale scores and plasma proline levels, by Pearson's correlational analysis. All tests were 1-tailed, we used an alpha level of 0.05 to assert statistical significance. Any correlation among the eight syndrome CBCL subscale scores, the plasma proline levels and IQs of the 10 patients was significant. As it could be expected, the patients' IQs were inversely related with the total CBCL scores ($r = -0.573$; $p < 0.05$). **Conclusions:** HPI appeared to be a neurodevelopmental disorder with a complex clinical course. In our sample psychiatric and behavioral features were the most prevalent at the long term follow-up. Two unusual findings arose from this series: two patients with West syndrome and one with a complex learning disorder. Further series of HPI patients will help to define the neuropsychiatric phenotype of this disorder, meanwhile, HPI may be included in the diagnostic assessment of neurological and psychiatric patients.

PP8.5 - 2096

Genetic intellectual disability; the Romanian experience based on clinical, cytogenetic and array-CGH techniques

Barca D, Arghir A, Tutulan-Cunita AC, Papuc SM, Iliescu C, Burloiu C, Tarta-Arsene O, Minciu I, Motoescu C, Craiu D, Budisteanu B, Budisteanu M. *Pediatric Neurology Department, Prof. Dr. Alexandru Obregia Psychiatry Hospital, Bucharest, Romania* – diana_barca@yahoo.com

Objective: Global developmental delay (GDD) in younger children

and intellectual disability (ID) are common reasons for referral in pediatric neurology, mental retardation (MR) affecting 2–3% of the general population and being the most common developmental disability. The advances of genetic testing increased the diagnostic yield of unexplained GDD/ID and subsequently the recognition of certain syndromes. The aim of this paper is to present the experience of our team in the investigation of children with GDD/MR using classical and molecular genetic techniques. **Material and methods:** A large number of children – 450 aged between 3 months and 17 years were included in a study regarding the identification of genetic causes of intellectual disabilities. Personal and familial history, clinical (including neurological, dysmorphological, psychological) and paraclinical examinations (brain imaging, EEG, ultrasounds, X-rays) were performed for all the children. Children with MR, autistic spectrum disorder, dysmorphic features and/or malformations were selected for genetic testing, GTG-banded karyotype, FISH, arrayCGH being performed. **Results:** A specific cause for ID was identified in 72 children (16%): a chromosomal abnormality was identified in 54 cases (12%), microdeletion syndromes in 52 children (11.5%), recognizable syndromes in 50 cases (11%). Array-CGH was performed in 45 patients with normal karyotype, but severe phenotype and 8 cases with cytogenetic abnormalities. Rare disorders were identified: 3p interstitial deletion (1 case), 4p interstitial deletion (1), 12p duplication (1), 15q deletion (1), 8p deletion (1 case), 18q deletion (1 case), unbalanced translocations, 4 cases – between 3q and 20q (1 case), 4p and 10q (2 siblings), 4p and 8p (1 case) and MECP2 duplication syndrome (1), Xp duplication (1). **Conclusions:** While clinical diagnosis and conventional techniques form the mainstay of investigation of children with ID, array CGH proved important diagnostic tool.

PP8.6 - 2051

Optic neuritis – etiology and results of treatment

Dunin-Wąsowicz D, Tomaszek K, Borkowska J, Kanigowska K, Hautz W, Jozwiak S. *Neurology and Epileptology Department, Warsaw, Poland – ddwasowicz@wp.pl*

Objectives: Optic neuritis is one of the very severe ophthalmological and neurological problems. Primary cause of optic neuritis is often unknown. The proper early diagnosis and introduction of treatment is important. Optic neuritis cases in children and teenagers are presented. **Material and methods:** Five patients (4 boys, 1 girl) at the age of 9 to 13 years with bilateral optic neuritis were treated and followed-up. The magnetic resonance imaging, as well as cerebrospinal fluid (CSF) analysis and different bacteriological, virusological, parasitological, metabolic and genetic test were performed. **Results:** Pathological changes were present in ophthalmological examinations and also in MR scans and CSF analysis. In one case optic neuritis was associated with meningoencephalitis. Etiological factor of the optic nerves inflammation involvement was confirmed only in one patient. In this case, infection with human cytomegalovirus (HCMV) based on polymerase chain reaction method (PCR) was diagnosed. Lyme disease, tuberculosis, syphilis, herpes zoster, toxoplasmosis, toxocarosis, lupus, vasculitis and diabetes were excluded during diagnostic process. All but one patient recovered completely after treatment with methylprednisolone and intravenous immunoglobulins. Patient with HCMV infection was successfully treated with intravenous ganciclovir (GCV). One male adolescent suffered from severe, progressive optic neuritis and neuropathy. In this patient Leber's hereditary optic neuropathy was not confirmed. There were no multiple sclerosis cases. **Conclusions:** Difficulties with establishing the cause of the optic nerve inflammation involvement are presented frequently. Genetic tests should also be performed. Antiviral treatment seems to be important in some optic neuritis cases.

PP8.7 - 2132

Acute necrotizing Encephalopathy (ANE) caused by mutation in RANBP2: three episodes in two affected family members

Amsallem D, Pâris C, Mougey C, Bévalot J, Rodriguez D, Burglen L. *Department of Paediatric Neurology, University Hospital Jean Minjoz, Besançon, France – damsallam@chu-besancon.fr*

We report a new family in which two children are affected with an autosomal dominant, incompletely penetrant, ANE. A previously healthy 5-year-old French girl presented in 02/2002, with dysarthria, unsteady gait, impaired consciousness, 3 days after fever, cough, vomiting. Laboratory tests were unrevealing, excluding meningitis, encephalitis, inborn errors of metabolism and toxin exposure. Brain T2-weighted MRI showed bilateral signal intensity in thalamus, brainstem, external capsule and cerebellum. With high-dose steroids, she recovered with mild gait disturbance and slowness. MRI brain 10 months later showed only residual lesions in brainstem and cerebellum. Recurrence occurred seven years later. Clinical and radiological signs were more severe. Deterioration led to quadriplegia. CSF protein level was 111 mg/dL. Methylprednisolone pulse therapy had not the same good impact. Leigh syndrome was ruled out before diagnosis of ANE was confirmed. The patient and her mother are heterozygous for a missense mutation (c.1880C→T, p.Thr585Met) in the gene encoding the nuclear pore protein Ran Binding Protein 2 (RANBP2). The outcome was poor: coma for 14 days, more one year in rehabilitation center and she recovered from hypotonia, gait abnormality, tremor, poor swallowing and speech impairment. Four years after hospitalization, she has no cognitive impairment, learns about horticulture, can walk. Mood disorder still remains. A 7-year-old boy presented this year with coma and vomiting, three days after the onset of a febrile illness. His parents were awareness because the girl and he were second cousins. MRI imaging showed multifocal symmetric lesions involving the thalamus, brainstem, external capsule, claustrum and medial temporal lobes. He has the same missense mutation. He was treated with early and repeated high-dose steroids, gammaglobulin, plasmapheresis. Its outcome is better and faster but other case studies are required. The mothers of the two children are carriers of the RANBP2 mutation and had never had any neurologic pathology.

PP8.8 - 2095

Anti-NMDAR encephalitis; presentation of 3 pediatric cases with full recovery

Mastroianni S, Voudris K, Mavrikou M, Triantafyllidou A, Maggina P, Katsarou E. *Department of Neurology, "P and A Kyriakou" Children's Hospital of Athens, Greece – smastr@otenet.gr*

Anti-N-methyl-D-Aspartate receptor (anti-NMDAR) encephalitis is an autoimmune and often paraneoplastic, neuropsychiatric syndrome affecting children and young adults. Currently, the diagnosis is straightforward with the detection of auto-antibodies against NMDA-receptor in serum and/or CSF and outcome is usually favorable with prompt treatment. However recovery period is long, sometimes with relapses, and therefore uncertainties regarding the type and length of immunotherapy remain. We report 3 cases of anti-NMDAR encephalitis presented over the period February 2010 to April 2011. The patients were girls aged at presentation; patient-1: 11 y, patient-2: 6 y, patient-3: 10 y. All had developed after a viral-like illness, a deteriorating condition which progressed from psychiatric symptoms with seizures and dyskinesias into a state of unresponsiveness, with catatonic features and autonomic instability. Patients-1 and -2 presented as "acute psychosis" with prominent dyskinetic features and normal brain MRI, EEG and CSF findings. Patient-3 was presented as "limbic encephalitis" (CSF pleocytosis, seizures responding to conventional antiepileptics and abnormal brain MRI). The diag-

nosis of anti-NMDAr encephalitis was confirmed in our three cases, 4 wks, 7 wks and 1 wk after the symptom presentation. None of the patients had associated tumor. All patients received 1st line immunotherapy with IVIg and pulse methylprednisolone followed by oral steroids with slow tapering (8 mo, 3 mo and 2 mo respectively). Cyclophosphamide was added to the treatment of patients-1 and -3, after 2 weeks, because of the severity of neuropsychiatric symptoms (5 and 4 monthly cycles respectively). Patient -2 had improved considerably before the onset of treatment and after 2 months of 1st line immunotherapy she had minimal behavioral deficits. Treatment discontinued after substantial clinical and cognitive improvement (total treatment duration 9mo, 3mo and 5mo respectively). We present the clinical data of 3 children with anti-NMDAr encephalitis who started immunotherapy at different stage of the disease. All children have eventually returned to school without problems.

PP8.9 - 1902

Tick-borne encephalitis in children – high risk of incomplete recovery

Fowler Å, Forsman L, Eriksson M, Wickström R. *Neuropediatric Unit, Department of Women's and Children's Health, Karolinska Institutet, Sweden – asa.fowler@ki.se*

Tick-borne encephalitis (TBE) is a vector-borne disease that affects both adults and children. In adults, TBE is followed by an

incomplete recovery in up to 40%; the main complaints being headache, fatigue and cognitive impairment. The situation for children with TBE is less well studied and cognitive problems following TBE may be overlooked. **Objective:** To examine long-term outcome after tick-borne encephalitis (TBE) in children. **Material and methods:** In this population-based cohort, 55 children with TBE with CNS involvement infected during 2004–2008 were evaluated 2–7 years later using the Rivermead post-concussion symptoms questionnaire (n=42) and the Behavior Rating Inventory of Executive Functioning (BRIEF) for parents and teachers (n=32, n=22, respectively). General cognitive ability was investigated in a subgroup (n=20) using the Wechsler Intelligence Scales for Children, 4th edition (WISC-IV). **Results:** At long-term follow-up, 2/3 of the children experienced residual problems, the main complaints being cognitive problems, headache, fatigue and irritability. More than one-third of the children were reported by parents or teachers to have problems with executive functioning on the BRIEF, mainly in areas involving initiating, organizing activities and working memory. Children who underwent WISC-IV testing had a significantly lower working memory index compared with reference norms. **Conclusion:** A large proportion of children experience an incomplete recovery following TBE with central nervous system involvement. Cognitive problems in areas of executive function and working memory are the most prevalent. Even if mortality and severe sequelae are low in children following TBE, all children should be followed after TBE to detect cognitive deficits.

POSTERS

Cerebral palsy

P1 - 2109

Assessment of bone mineral density disorders in children with cerebral palsy and epilepsy

Tosun A, Erisen S, Unuvar T, Dursun S. *Adnan Menderes Medical School, Department of Pediatric Neurology, Aydin, Turkey – aysetosun2000@yahoo.com*

Objectives: The aim of this study was to evaluate bone metabolism and mineral density disorders; to determine the effect of possible risk factors including immobilization, mental retardation, calcium and vitamin D deficiency, usage of antiepileptic drugs in children with cerebral palsy-epilepsy. **Material and methods:** Prepubertal 30 patients with diagnosis of cerebral palsy, 54 with epilepsy and 38 with cerebral palsy-epilepsy and 30 healthy children were included into the study. Serum calcium (Ca), phosphorus (P), alkaline phosphatase (ALP), 25 OHD3, parathormone (PTH) levels were evaluated and bone mineral density (BMD) were assessed by DEXA. Presence of malnutrition was assessed with Gomez scores. **Results:** Severe malnutrition was detected in 11% of patients with epilepsy, 36.7% of cerebral palsy, and 44.7% of cerebral palsy-epilepsy. Higher Gross Motor Function Classification System (GMFCS) levels were associated with higher malnutrition rates ($p < 0.05$). Serum Ca levels in cerebral palsy and epilepsy-cerebral palsy groups were detected significantly lower than epilepsy and healthy children groups ($p = 0.001$). The lowest serum 25 OHD3 value was detected in epilepsy-cerebral palsy group (63.2%). Moreover, it was significantly lower in patients receiving more than one anticonvulsant ($p < 0.05$). Serum 25 OHD3 value was significantly related to sunlight, serum Ca, and level of GMFCS ($p < 0.05$). However, there was no relation between serum Ca and BMD and seasons. Abnormal BMD was found in 61 patients (50%). Osteoporosis was detected in 3.7% of patients with epilepsy, 50% of cerebral palsy, and 39.5% of cerebral palsy-epilepsy. Immobility, mental retardation, using of long duration antiepileptic drug were the main reasons for abnormal BMD. **Conclusion:** Cerebral palsy patients who have immobility, mental retardation, nutrition disorders and receiving antiepileptic drug have higher risk for lower BMD. Serum 25 OHD3 levels should be evaluated in such patients and they should be assessed for BMD periodically.

P2 - 1976

Clinical-imaging correlations in cerebral palsy

Minciu I, Barca D, Iliescu C, Tarta-Arsene O, Craiu D. *“Carol Davila” University of Medicine, Department of Neurology, Pediatric Neurology, Neurosurgery, Psychiatry - Pediatric Neurology Clinic No. II, Bucharest, Romania*

Introduction: Neuroimaging is important for identifying cerebral palsy (CP) etiology. **Material and method:** Using the CP registry, the imaging investigations correlated with clinical data of patients with diagnosis - CP admitted in Paediatric Neurology Clinic Bucharest during year 2010 were retrospectively analysed. SPCE CP classification (spastic, ataxic, dyskinetic) was used. The motor impairment severity was assessed with GMFCS. All patients underwent cerebral CT or MRI. Lesions were classified as: malformations, periventricular white matter lesions (PWML), grey matter lesions (GML), white and grey matter lesions (WGML), other, no lesion. Statistical software package and chi square test were used for data processing. **Results:** 379 CP children were analysed. Spastic CP forms prevailed (76.2%). Most children (>87%) with CP had neuroimaging abnormalities. WML were the most

frequent (38.5%), followed by WGML (~30%). PWML were correlated with spastic diparesis ($p < 0.001$). WGML correlated with spastic hemiparesis, and GML with dyskinetic forms ($p < 0.001$). Malformations were significantly associated with ataxic forms and spastic hemiparesis ($p < 0.001$). We found significant correlations between WGML and the presence of epilepsy ($p < 0.001$), severe/profound mental retardation. Microcephaly was correlated with malformations, WGML and “other types of lesions” ($p < 0.001$). Strabismus was present in 92% of the children with PWML ($p < 0.001$). WML were correlated with GMFCS III, IV ($p < 0.000$) in our series. WGML were correlated with GMFCS I, but also V ($p < 0.000$). **Conclusions:** Clinical forms and comorbidities were significantly correlated with the type of imaging lesion. The lesion type was correlated with the severity of functional impairment and, most likely, the degree and extent of the lesion, which could not be measured. Therefore, the same type of lesion in terms of description resulted in slight or severe impairment. The CP registry will serve as a base for further research.

P3 - 1961

Development of a clinical algorithm for children with toe-walking

Wacks M, Sen S, Varghese K, Watson D, Mankad K, O'Driscoll M, Kinali M. *Paediatric Neurology Chelsea and Westminster Hospital NHS Foundation Trust, United Kingdom – michael.wacks@chelwest.nhs.uk*

Background: Toe-walking is a common presentation within Paediatric Neurology and Neurodevelopmental services. Children under 2 years may toe-walk until an independent gait has been established. Although beyond this age, idiopathic toe-walking occurs, it is a diagnosis of exclusion and warrants assessment to exclude conditions such as cerebral palsy, autism, and neuromuscular diseases. **Objectives:** 1. Establish the epidemiology of toe-walkers within a large single centre paediatric cohort. 2. Establish an association between toe-walking and other diagnoses. 3. Establish the diagnostic yield of MRI brain and spine in toe-walkers in those with and without additional neurological signs/symptoms. 4. Develop an appropriate clinical algorithm for screening of children presenting with toe-walking. **Method:** We plan to identify children who toe-walk who were seen within Neurology and Neurodevelopmental services in Chelsea and Westminster Hospital from 2009 to April 2013. A retrospective pilot study was carried out of 60 randomly selected children who attended the Neurodevelopmental Services between 2009 and 2013 using the search criteria “Toe Walking”; reviewing their clinic letters, assessment reports and investigations. **Results of pilot:** Out of 60 case notes reviewed, 12 children had definite histories of toe-walking. Of these, 4 had cerebral palsy, 3 had global developmental delay, 2 had autism, 1 had a specific speech and language disorder, 1 had no underlying diagnosis and 1 only had a single audiology review. Four of the 12, had an MRI brain and spine; 3 had normal imaging and 1 had subtle cerebral changes which were thought to unrelated to the toe-walking. **Conclusion:** The pilot study demonstrated that 12 children (20%) toe-walked. These 12 children showed a significant association with cerebral palsy, autism, speech and language development and global developmental delay. A retrospective study of a larger cohort is currently in progress to produce data allowing the above aims to be met.

P4 - 1946

Quadriplegia following minor trauma in a three year old child with Chiari-I malformation – a management challenge

Nabialek T, Kaliaperumal C, Leonard J, Flanagan M. *Temple Street Children's University Hospital, Dublin, Ireland – tomasz.nabialek@gmail.com*

Introduction: Spinal cord injuries following minor trauma are

rare. Ten cases have been described in children. Four were diagnosed with underlying Chiari-I malformation, among whom one had an associated non-displaced atlas fracture. Among patients with Chiari-I malformation one underwent surgery and three were managed conservatively. **Case description:** We describe a case of a three and a half year old girl with previously undiagnosed Chiari-I malformation who acquired high cervical spinal cord syndrome (C4 level) with quadriplegia, paradoxical breathing, areflexia, loss of sensation, and urinary retention following tumbling on a sofa. Initial MRI revealed extensive hydro-syringomyelia and Chiari-I malformation. She underwent foramen magnum decompression. Spinal cord oedema and syringomyelia improved within 20 days. A ventriculo-peritoneal shunt was inserted for subsequent hydrocephalus. Two months post injury, she remains clinically unchanged. She required mechanical ventilation and is on weaning regime of BiPAP following RSV infection. **Discussion:** Among victims of minor trauma resulting in spinal injury, the symptoms and their sequence can be similar in children with and without underlying Chiari-I malformation. Malformation was present in 45% of known cases; therefore it should be seen as a risk factor. Possibly Chiari-I malformations remained undiagnosed in some of the patients in the era pre-MRI imaging. In the case described above, there was a management dilemma, when Chiari-I malformation and cord oedema were diagnosed. Considered underlying tumour was ruled out with a follow-up MRI. **Conclusion:** Asymptomatic Chiari-I malformation can present in children after minor trauma and this can be debilitating. When a well child is diagnosed with Chiari-I malformation this risk should be discussed with parents. Surgery may be needed in asymptomatic patients with Chiari-I and syringomyelia. We recommend a foramen magnum decompression in case of significant neurological compromise following minor trauma.

P5 - 1927

Strength in antagonist muscles of the lower limbs in ambulatory children with bilateral spastic cerebral palsy, 7–16 years, versus typically developing controls

Darras N, Tziomaki M, Pasparakis D, Papavasiliou A. Elepap Gait Analysis and Motion Analysis Center, Greece – theon@otenet.gr

Objective: We aimed to compare the pattern of strength development of antagonist muscle groups, between ambulatory patients with Bilateral Spastic Cerebral Palsy (BSCP) and Typically Developing Controls (TDC). **Methods:** Eighty-six TDC and 142 ambulatory patients with BSCP were grouped in five age groups from age 7–16 in two-year intervals. The strength of hip adductors and abductors, hip extensors and flexors, knee extensors and flexors and ankle dorsiflexors were measured by the same examiner through a Hoggan Microfet2 digital hand held dynamometer. Force data analysis was performed: A) using Absolute Force (AF) in lbs and B) Normalized Force (NF) to body weight. Descriptive statistical analysis and ANOVAs were used (level of significance = 0.05). **Results:** Force development graphs of the pairs of antagonist muscles measured showed an almost parallel force development in most of the NF diagrams in both BSCP and TDC. Imbalance in the NF values between the hip extensors and flexors was clearly identifiable in patients; this was related to the fact that hip extensors in ambulatory children with BSCP were exhibiting values close to TDC, while hip flexors were exhibiting significantly lower values across all age groups. The same pattern of imbalance was also found in the other antagonist muscle groups. NF values amplified the imbalance differences as compared to the AF. **Conclusion:** This study revealed that muscle strength imbalance in ambulatory patients with BSCP is present from at least age 7 years and does not change significantly up to age of 16 years. In BSCP, a constant pattern of significant muscle strength imbalance between antagonist muscles across all ages

was identified. Hip abductors, hip flexors and knee flexors were found significantly weaker than adductors and extensors.

P6 - 1887

Variation in health care for children and young people with cerebral palsies: a retrospective multi-centre audit

Horridge KA, Balu R, Tennant PWG, Rankin JM. City Hospitals Sunderland, UK – karen.horridge@mac.com

Objectives: To establish whether there is variation in health care for children and young people with cerebral palsies across northern England. **Material and methods:** Retrospective medical record audit of 389 children and young people registered on the North of England Collaborative Cerebral Palsy Survey (NECCPS) living in 15 geographical districts, born 1995–2002, with subsequent data validation by clinicians. Data was collected on cranial magnetic resonance imaging [MRI] (marker of aetiological assessment), hip and spine status, pain and its management, feeding and nutritional status. **Results:** The audit sample was representative of all contemporaneous cases reported to the NECCPS. There was significant variation between reporting districts in access to MRI, orthopaedic surgeons for the least mobile children and young people, recording of state of spine and of weight and height percentiles ($p < 0.001$). 67% had a discussion about pain recorded, of which 87% had a management plan. Those from the most deprived population quintile were significantly less likely to have had a discussion about pain recorded in their notes than those in the least deprived quintile ($p = 0.045$). **Conclusion:** There is variation in important aspects of health care, between districts in the north of England. This data will assist with working towards more equitable health care and thus provide more equal opportunities for the best health outcomes for all.

P7 - 1841

Longterm development of VLBW-infants with cerebral palsy. Results of a population-based study

Veelken N, Just K. Asklepios Clinic North, Hamburg, Germany – N.Veelken@asklepios.com

During a 3 years period 91% of preterm infants with birthweight under 1501 g who were born in Hamburg, Germany, were involved in a longitudinal study. Cross-sectional examinations were performed at the age of 2, 6 and 9 years of age. In 42 of the 371 children (11.3%) cerebral palsy (CP) was definitely found at the age of 6 years. CP was classified as spastic diplegia in 29 (69%) children. In 3 (7%) spastic hemiplegia, in 5 (12%) spastic tetraplegia and in 5 (12%) other forms of CP were found according to the definition of Hagberg. 22 (52%) of these patients were examined again in adulthood at the age of 21–24 years. They were representative in terms of severity of handicap and type of CP. At that age 15 patients suffered from spastic diplegia, 3 from spastic hemiplegia and 4 from spastic tetraplegia. All hemiplegic patients as well as four diplegic patients were able to walk independently. All tetraplegic patients could not move around anyhow. 4 patients showed a motor disability level I according to GMFCS-classification, 3 patients level II, 6 patients level III and IV and 3 patients level V. 12 patients were living independently or with minor help, 10 patients needed major support or were dependent on continuous help in daily life. Only 6 patients (27%) did not achieve any school graduation, 14 finished with secondary school graduation (7 with “Hauptschulabschluss”, 7 with “Realschulabschluss”) and 2 with high school graduation (Abitur). 12 patients (55%) showed a Body Mass Index (BMI) below ($5 = 23\%$) or above ($7 = 32\%$) normal range. A major percentage of former VLBW-patients with cerebral palsy is able to achieve normal school education and to live independently despite of a definite motor disability. Only a minor percentage remains dependent on major support.

P8 - 1769

Treatment methods of mild spastic CP from 8 to 15 years of age: a population based study

Rackauskaite G, Bech BH, Uldall P, Østergaard JR. *Dep. of Pediatrics, Aarhus University Hospital, Denmark – gjirac@rm.dk*

Objectives: To describe the use of splints, physiotherapy, occupational therapy and intramuscular Botulinum toxin injections (BTA) in preteens (8–12y) and teens (13–15y) with mild cerebral palsy (CP). **Material and methods:** A national wide parent questionnaire to 8–15 years old children with cerebral palsy was sent by mail in 2012. A total of 216 participants had mild spastic CP (Gross Motor Function Classification System (GMFCS) level I and II). Proportions of children getting physiotherapy (during the last 12 months), occupational therapy (during the last 12 months), Botulinum toxin injections (during the last 12 months) and use of splints (during the last 3 months) were calculated with a 95% confidence interval (CI). Odds ratio (OR) for teens compared to preteens were calculated. **Results:** More preteens used physiotherapy: 82% (CI 76–89%) compared to teens 72% (CI 62–81%). No difference was found for use of occupational therapy: 38% (CI 30–47%) of preteens and 34% (CI 24–44%) of teens. A large difference was found for BTA: 17% (CI 10–23%) of preteens and 7% (CI 2–13%) of teens. We only found a small difference in the use of splints, 29% (CI 20–36%) of preteens and 22% (CI 13–31%) of teens. The OR differed statistically significantly for BTA ($p=0.043$), but not significantly for other treatment modalities. **Conclusions:** We demonstrated a tendency of getting less physiotherapy and occupational therapy, minor use of splints, and a significantly less administration of Botulinum Toxin in teens as compared to preteens in a population based sample of mild CP. Minor use of Botulinum toxin injections can be explained by diminishing dynamic spasticity in older children. The differences in other treatment modalities could not be explained by that, neither by differences in GMFCS levels. Longitudinal studies are needed in order to examine the tendency of declining use of physiotherapy.

P9 - 1573

Long term response following the treatment of hip adductor spasticity in children with cerebral palsy using intra-muscular botulinum toxin A – a single centre experience from Singapore

Ong H-T, Lin JBY, Lim KJL, Hui JHP. *Kho Teck Puat-University Children's Medical Institute, National University Health System, Singapore – Hian_Tat_Ong@nuhs.edu.sg*

Objectives: To assess the magnitude of the effects of intra-muscular injection of botulinum toxin A (BTX-A) on hip adductor muscles in children with cerebral palsy, and the need for subsequent repeat injections. **Methods:** Children below 8 years with dynamic spasticity of the hip adductor muscles were prospectively evaluated in a 6-year period from year 2000 to 2005. Range of motion of the hip was assessed using the Modified Tardieu Scale and recorded as R1 and R2. Muscle tone was assessed using the Modified Ashworth Scale (MAS). Repeat evaluations were performed at intervals of between 4 to 6 weeks, and 3 months post-injection. Physical therapy was intensified in the 3 months following the injection. The children had subsequent half yearly reviews till December 2012 to assess the need for repeat injections. **Results:** There were 14 children (11 boys, 3 girls) with a total of 43 hip adductor muscle injections administered in the study period. Five of these children subsequently had repeat injections for the same adductor muscles. Twelve data sets were excluded due to default visits or patient uncooperativeness, leaving a total of 31 data sets analysed. After 4 to 6 weeks, there was an average improvement of 6.7° in R1 and 7.1° for R2. For muscle tone, there was an average improvement of 0.5 on the MAS. Three months post-injection, there was an average improvement of 5.3° in R1 and 6.5° for R2. Average improvement for muscle tone was

0.4. **Conclusion:** The beneficial effects of intra-muscular BTX-A injection are evident and maximal by 4 to 6 weeks and for most patients, these benefits continued 3 months post-injection. This provided an important therapeutic window for intensive physical therapy to take place so as to achieve permanent functional gains, as less than half the patients required re-injection to the same muscles.

P10 - 2161

The biomechanical evaluation of gait in monitoring of treatment in children with cerebral palsy – preliminary data

Kopyta I, Jochymczyk-WoŹniak K, Michnik R, Jurkojae J, Chuchnowska I. *Department of Neuropediatrics, Medical University of Silesia, Katowice, Poland – ilonakopyta@autograf.pl*

Introduction: Recently the fast progress in the development of systems attending the three-dimensional gait evaluation is being observed. The methods enable the objective gait evaluation of the gait in children with cerebral palsy (CP). One of the indexes used to the analysis is Gillette Gait Index (GGI), complying 16 clinically meaningful kinematic and three-dimensional parameters. **Material and method:** The study was conducted with application of the three-dimensional system of gait analysis BTS Smart and carried by the team of pediatric neurologists, physiotherapists and engineers. Spatial-time parameters of gait and courses of angles of joint of lower limbs were determined on the basis of conducted research. Those parameters were used in estimation of Gillette Gait Index. The analyzed group consisted of five CP patients treated with botulin toxin (three children with hemiparesis, one with diparesis and one with quadriplegia), intensively rehabilitated after the botulin treatment. The data were compared to two patients put on rehabilitation without the botulin treatment. The patients treated with botulin were evaluated three times: before the botulin administration, then three and six months after it. In the other patients' group the evaluation was conducted three months after rehabilitation start. The results of gait evaluation were compared to the gait pattern of the healthy children; the normal values were worked out by the authors. **Results:** After the botulin treatment and rehabilitation the increase of the gait speed and frequency of steps were observed; the GGI decreased both after three and six months of observation. **Conclusion:** The authors regard the results presented above as the pilot-study; the evaluation of the larger groups of children with cerebral palsy is conducted. In the authors' opinion the objective method of CP children gait evaluation may be the helpful tool for clinicians to optimize the way of CP children treatment.

P11 - 1780

Dystonic cerebral palsy in monozygotic twins with 10p15.3 microdeletion syndrome

Vargiami E, Ververi A, Kyriazi M, Papathanasiou E, Gioula G, Gerou S, Al-Mutawa H, Kambouris M, Zafeiriou DI. *1st Department of Pediatrics, Aristotle University of Thessaloniki, Greece – athenaververis@yahoo.com*

Submicroscopic deletion of 10p15.3 is a rare genetic disorder, currently reported in 21 unrelated patients. It is mainly associated with cognitive/developmental deviations, speech delay/language disorder, motor delay, craniofacial dysmorphism, hypotonia, brain anomalies and seizures. The size of the deleted region ranges between 0.15 and 4 Mb and does not generally correlate with patients' phenotype. A monozygotic female twin pair with a de novo 2.7 Mb deletion of 10p15.3 is herein reported. The girls presented at the age of 8 months with severe developmental delay and failure to thrive since the first month of life. Their perinatal and family history was unremarkable. On admission they both exhibited generalized dystonia with increased

muscle tone and excessive deep tendon reflexes, microcephaly, progressive swallowing dysfunction, laryngomalacia, small omphalocele, mild dysmorphic features and complete absence of head control, voluntary movements and visual/auditory responsiveness. Both patients' brain MRIs demonstrated dilatation of ventricles, subarachnoid spaces, anterior interhemispheric fissure and sylvian fissures bilaterally. Cranial radiography revealed partial fusion of both coronal sutures. Visual and brainstem auditory evoked potentials were markedly abnormal, indicating severe visual and sensorineural hearing impairment. The electroencephalogram, as well as a screening for inborn errors of metabolism, were unremarkable. Both patients required gastrostomy and tracheostomy before the age of 1 year. They were, additionally, managed with physical therapy, as well as baclofen and low-dose haloperidol. Their current state at the age of 2 years is relatively stable. The index patients' phenotype includes features, such as dystonic cerebral palsy, visual and sensorineural hearing impairment, laryngomalacia, craniosynostosis and omphalocele, which have not been previously reported in individuals with 10p15.3 deletion. It is necessary to consider these novel clinical features and investigate their possible relationship with the recently recognized 10p15.3 microdeletion syndrome.

P12 - 2084

Foramen magnum decompression as emergency surgery for acute upper cervical spinal cord compression in a 3 years old girl with tetraplegia

Aziz M, Kaliaperumal C, Sattar M. *Children University Hospital, Temple Street, Ireland – mohdazli@me.com*

Background: Spinal cord injuries (SCI) are relatively uncommon in paediatric age group. Incidence varies from 1 to 10% of all spinal injuries. In United States, about 12000 people a year sustain a spinal cord injury. Main causes in paediatric age group are birth injuries, falls, motor vehicle accidents, sports injuries, diving and trampoline accidents and violence (gun shots or stab wounds). Chiari malformation as a cause of acute SCI is rare, and has been reported in four cases previously. **Case description:** A 3 years old girl previously healthy child presented with acute tetraplegia after a minor fall. She was playing on top of a sofa and landed on the cushion seats. Sudden loss of bilateral upper limb power was noted and child was brought to local emergency department and transferred to national paediatric hospital as spinal injury. **Results of investigations:** Initial assessment showed horizontal movement of both feet but not against gravity, power 2/5 bilaterally. Due to trivial nature of injury, an emergent magnetic radiological imaging (MRI) was not obtained. MRI of cervical spine carried out 8 hours after admission and 18 hours after event showed cerebellar tonsillar herniation by 7 mm and Chiari Malformation Type I with severe oedema of cervical spinal cord. **Treatment:** She underwent emergency Foramen Magnum decompression. Surgical findings are hypertrophied posterior atlanto-occipital membrane and hard and tough occipital and posterior foramen magnum skull bones. Post decompression, free cerebrospinal fluid (CSF) flow and cerebellar tonsils pulsations was noted. Post-operatively, child remained tetraplegic and currently undergoing intensive rehabilitation. **Discussion:** Trivial nature of trauma should never be underestimated, with development of acute and rapidly deteriorating paralysis.

Epilepsy

P13 - 2112

Mutations in PLCB1 in early infantile epileptic encephalopathy: expansion of the phenotypic and genotypic disease spectrum

McTague A, Wentzensen I, Meyer E, Ngho A, Applegate C, Batista D, Kossof E, Wang T, Kurian MA. *Neurosciences Unit, UCL-Institute of Child Health, London, United Kingdom – a.mctague@ucl.ac.uk*

Introduction: Phospholipase C beta 1 (PLCB1) is a post-synaptic receptor-activated G protein-coupled phosphodiesterase, which plays a key role in diverse developmental and functional aspects of the central nervous system. Homozygous deletions of chromosome 20p13 disrupting the promoter region and first 3 coding exons of PLCB1 have been described in two reports of early infantile epileptic encephalopathy (EIEE) occurring within consanguineous families 1, 2. We describe a patient presenting with developmental delay and epilepsy with novel PLCB1 mutations. **Methods:** Case note review and molecular genetic investigations. **Results:** The patient presented at 6 months of age with developmental regression followed by the onset of intractable focal and generalised seizures from 10 months. EEG revealed generalised slowing and multi-focal discharges. MRI brain showed a hypoplastic corpus callosum and generalised decrease in brain volume. Diagnostic microarray studies revealed a heterozygous 476Kb deletion of 20p13 (encompassing part of PLCB1), which was maternally inherited. The deletion breakpoints were between 8,094,442–8,094,510 bp and 8,580,65–8,580,722 bp. Direct Sanger sequencing revealed a novel intron 1 splice site variant, which was paternally inherited (c.99+1G>A). **Conclusion:** Mutations in PLCB1 cause a wide spectrum of early onset epileptic encephalopathies, now including non-specific EIEE. The heterozygous deletion identified in this African-American case appears almost identical to that reported by in a family of Palestinian descent2 suggesting a role for the flanking LINE elements in this recurrent deletion. This novel report of compound heterozygosity expands the PLCB1 phenotype and genotype and provides an excellent example of chromosomal microdeletions unravelling deleterious recessive mutations which cause human disease.

P14 - 1538

Severe neonatal epileptic encephalopathy with burst-suppression pattern with mutation in PIGA gene – a case report

Maier O, Jaeger G, Joset P, Steindl K, Pajarola S, Rauch A. *Children's Hospital of Eastern Switzerland, Department of Child Neurology, Switzerland – oliver.maier@kispiisg.ch*

We report a male neonate, gestational age of 38 weeks, birth weight 4600 grams delivered by cesarean section and presenting with respiratory distress requiring intubation and mechanical ventilation. On day 5 the child developed tonic seizures with ocular deviation and with a burst-suppression pattern in the EEG. The seizures were refractory to conventional antiepileptic drug therapy (Phenobarbitone, Phenytoin, Levetiracetam, Vigabatrin). Brain MRI showed cerebellar and opercular atrophy and white matter immaturity. The child had dysmorphic features with prominent forehead, depressed nasal bridge, high arched palate. The central tone was poor. On echocardiatic evaluation there was mild pulmonary hypertension, but no other pathology. Abdominal ultrasound was normal. In view of uncontrollable seizures and the dismal prognosis associated with the MRI findings, a decision was taken with the parents to limit intensive care measures. The child died on day 15 due to respiratory failure. Genetic analysis (exom sequence analysis, confirmed by Sanger sequence analysis) revealed a mutation (c.532C>T (p.Arg412) in the

PIGA gene (phosphatidylinositol glycan class A (MIM 311770), the mother is heterozygote for this mutation. PIGA mutations show x-linked inheritance. The phenotype was described for the first time in 2012 (Johnston et al. 2012). Mutation in the PIGA gene can cause severe epileptic encephalopathy with burst-suppression pattern in EEG and are associated with brain pathology, dysmorphic feature, muscular hypotonia and poor prognosis. The Inheritance is X-linked.

P15 - 1733

A novel SCN2A missense mutation in a Slovenian girl with early-onset epileptic encephalopathy

Gnidovec Strazisar B, Writzl K, Paro Panjan D, Neubauer D, Nakamura K, Matsumoto N, Saitsu H. *Department of Child, Adolescent and Developmental Neurology, University Children's Hospital, Ljubljana, Slovenia – barbara.gnidovec@mfmf.uni-lj.si*

Objective: Mutations in SCN2A gene are associated with variety of epileptic syndromes. We report a novel SCN2A missense mutation in a girl with severe early-onset epileptic encephalopathy. **Case report:** Soon after birth patient presented with predominant tonic seizures with multifocal spikes in EEG. Seizures were refractory to antiepileptic treatment but showed somehow a good response to i.v. fosphenytoin with several days of seizure freedom after fosphenytoin rescue therapy. Patient had poor eye contact and poor spontaneous movements with generalized hypotonia and brisk tendon reflexes. Extensive neurometabolic evaluation was normal and early MRI showed thinning of the corpus callosum. With time EEG evolved to a pattern of modified hypsarrhythmia without clinical transition to spasms. Patient continued with frequent tonic seizures up until six months of age when seizures were finally controlled by a combination of topiramate, lamotrigine and valproate. From the neonatal period on patient demonstrated a significant developmental delay. At the current age of 24 months she is still seizure free on valproate monotherapy with her EEG showing slowing with rare multifocal epileptic discharges. High resolution melt analysis and direct sequencing revealed a de novo c.787G>A missense mutation in SCN2A predicted to cause p.A263T change in domain I of Nav1.2 channel. **Conclusion:** We have identified a novel SCN2A missense mutation as the etiology for early-onset epileptic encephalopathy further expanding the spectrum of clinical disorders caused by SCN2A mutations.

P16 - 2021

Copy number variation involving ABCB1 gene in a child with epileptic encephalopathy – a role in pathogenesis and/or multidrug resistance?

Quintas S, Moldovan O, Serafim S, Ávila M. *Pediatric Neurology Unit and Department of Genetics, Centro Hospitalar Lisboa Norte -Hospital de Santa Maria, Lisbon, Portugal – sofiamendesquintas@gmail.com*

Introduction: Rare copy number variations (CNVs) have recently been established as important risk factors for epileptic encephalopathies, although the establishment of a clear pathogenic role for the CNVs identified in individual patients might be conflicting. **Clinical case:** We report a three years old boy with an epileptic encephalopathy, beginning at 1.5 month with infantile spasms, developmental retardation and an EEG showing multifocal epileptiform abnormalities. Since then he has been treated with several anti-epileptics (valproate, topiramate, fenobarbital, vigabatrin, zonisamide, levetiracetam, lamotrigine, clobazam, rufinamide, clonazepam, phenytoin, carbamazepine and eslicarbazepine), in different associations, as well as pyridoxine, oral prednisolone and ketogenic diet, without seizure control. Nowadays he has daily head drops and tonic seizures, multifocal epileptiform activity and no focalizing ictal activity on EEG and

since 30 months of age is under vagal nerve stimulation (plus zonisamide and phenobarbital), with a 50% reduction in seizure frequency. He has a global developmental delay and no other abnormalities on physical examination. An extensive etiologic workup was carried out, the following exams showing no alterations: cerebral MRI (twice, last one at 29 months age, 3 Tesla); metabolic evaluation, karyotype and CDKL5 gene mutations search. CGH array done at three years of age showed a CNV with probable clinical significance: a 4.14 Mb duplication of 7q21.11q21.13, involving the ABCB1 gene. **Discussion:** Various data support the hypothesis that the overexpression of antiepileptic drug transporters may play a pivotal role in drug resistance in epilepsy. P-glycoprotein, encoded by the ABCB1 gene might mediate at least part of the resistance, although some conflicting evidences exist for the role of known ABCB1 polymorphisms in antiepileptic drug resistance. The authors discuss the etiologic role of the large CNV found in the epileptic encephalopathy of this patient and/or in his refractoriness to antiepileptic drugs, since it involves the ABCB1 gene.

P17 - 2103

Early epileptic encephalopathies associated with STXBP1 mutations: three new patients with different electroclinical profile evolving to infantile spasms

Barcia G, Chemaly N, Van Bogaert P, Gobin S, Barnerias C, Kaminska A, Munnich A, Desguerre I, Dulac O, Nabbout R. *Department of Neuropediatrics, Centre de Référence des Epilepsies Rares, Inserm U663, Hôpital Necker Enfants Malades, Paris Descartes University, Paris, France – giulia.barcia@inserm.fr*

Mutations in STXBP1 (MUNC18.1), encoding syntaxin binding protein 1, have first been reported in early onset epileptic encephalopathy with suppression-bursts (Saitsu, 2008), then in infantile spasms (Otsuka, 2010) and in patients with non syndromic mental retardation without epilepsy (Hamdan, 2010). We report the electroclinical profile of three patients with three novel de novo STXBP1 mutations presenting with infantile spasms after three different evolutions. Patient 1, born premature at 26 weeks of gestational age, presented infantile spasms with hypsarrhythmia at age of 4 months not preceded by other seizure types. She presented normal EEG background before epilepsy (performed for premature follow-up) onset with no spikes neither suppression burst pattern. IS were pharmacoresistant till the age of two years when seizures progressively stopped. The child, actually aged of three years, is seizure-free and presents a profound mental delay. Patient 2 presented focal motor seizures since the age of 2 months associated to focal abnormality on EEG with normal background activity. At 3 months spasms in series appeared and EEG showed hypsarrhythmia. At two years, the child has ongoing seizures (spasms) despite many AEDs trials. He presents with a severe psychomotor delay. Patient 3 presented infantile spasms at age of 1 month associated to suppression burst pattern with evolution to hypsarrhythmia. Seizure responded to treatment and since the age of two years the patient is seizure-free. Actually, at the age of 13 years, she presents a profound mental delay with autistic traits. Two of our patients did not presented with suppression burst pattern and in one case, EEG was normal before the onset of spasms. These cases emphasize the place of STXBP1 analysis in infantile spasms.

P18 - 2040

A series of epileptic encephalopathies: an array-based genotype-phenotype correlation in a Turkish cohort of children

Topcu M, Konuşkan B, Alikasifoglu M, Aktas D. *Unit of Pediatric Neurology, Hacettepe University Faculty of Medicine, Ankara, Turkey*

Background: Epileptic encephalopathies are characterized by an

epilepsy with the first week of life, severe developmental delay and usually a poor prognosis. Determining the underlying etiology responsible for infantile epileptic encephalopathy is a clinical challenge worth undertaking to facilitate advice on the recurrence risk and to allow the option of prenatal testing. **Methods:** To determine molecular pathology in 15 patients with epileptic encephalopathy, array-based comparative genomic hybridization (array-CGH) were performed on DNA's from the patients. **Results:** Deletion of ARFGAP1, CHRNA4 and KCNQ2 genes on 20q13.3; deletion of GRINA and PLEC genes on 8q24.3; deletion of the SCN gene cluster on 2q24.4; deletion of DTNB gene on 2p23.3–24.3; duplication of EHMT1 on 9q34.2–34.3; duplication of DCX gene on 6p22.3–22.3; duplication of GRIK5 on 19q13.2–13.31; duplication of BRD2 gene on 6p22.1–22.3; duplication of KCNQ1 on 11p15.4; duplication of DOC2A, QRT and SEZGL2 on 16p11.2, duplication of NTAN1 on 16p13.1 were observed in our patients. **Conclusion:** We performed an array-CGH study to the patients with epileptic encephalopathy, found the genomic rearrangements affecting disease-causing and genes involve pathways. The success of our preliminary array-CGH study allows us to expand the cohort. According to the available literature, this is the first comprehensive array-CGH evaluation of a Turkish cohort children with epileptic encephalopathy.

P19 - 1501

Long term accidental overdose of levetiracetam in an infant

Ozkale Y, Ozkale M, Saygi S, Erol I. *Baskent University Faculty of Medicine, Department of Pediatrics, Adana, Turkey – semra_saygi@yahoo.com*

Introduction: Levetiracetam is one of the new anticonvulsant drug which has a high therapeutic index and potential antiepileptogenic effects. Herein, we report a patient with multidrug refractory epilepsy and Ohtahara syndrome who was accidentally administered 300 mg/kg/day for 35 days by her mother. **Case report:** A 10-month-old female was admitted to the Baskent University Hospital, Adana, Turkey due to an overdose of levetiracetam. She had been followed by our child neurology department from the newborn period as she suffered from Ohtahara syndrome. She was treated with vigabatrin, topiramate, calcium folinate, vitamin B6 and levetiracetam. She was accidentally administered 10 times the recommended dosage of levetiracetam by her mother and remained on this dosage for 35 days. At physical examination, the infant's vital signs were normal. Neurological examination revealed apathy and profound hypotonia with brisk deep tendon reflexes. Laboratory testing revealed the following: leukocyte count, 13700/mm³, hemoglobin, 11.8 g/dl; platelet count, 359,000/mm³. Liver and kidney function tests and serum electrolyte levels were normal. She was hospitalized for observation of levetiracetam adverse effects. Treatment with vigabatrin, topiramate, calcium folinate, and vitamin B6 were continued. Her apathy resolved within 2 days and we did not observe any other side effects. Her laboratory analyses showed no abnormalities in blood chemistry or complete blood count. The girl was discharged after 7 days with her usual dose of levetiracetam. **Conclusion:** To our knowledge, the present case is the youngest child to have received a long-term levetiracetam overdose. Accidental levetiracetam overdose in children and even in infants requires discontinuation of the drug, without any changes in safety or efficacy. In addition, re-administration of the drug at the correct dosage in our patient resulted in no adverse effects.

P20 - 2138

Use of perampanel in 2 children with refractory focal epilepsy

Mewasingh LD, Varadkar S, Buonaiuto K. *Imperial College Healthcare NHS Trust, London, United Kingdom – leena.mewasingh@imperial.nhs.uk*

Case 1: A 15 yr old girl developed childhood onset Herpes Simplex encephalitis with extensive bitemporal involvement resulting in refractory epilepsy, learning difficulties and frontal executive problems. Her daily focal seizures have proven drug-resistant with multifocal discharges on EEGs. She was awaiting VNS placement (not a candidate for epilepsy surgery). Perampanel was added to her AEDs (keppra and zonisamide), with significant improvement in seizure control at 4 mg. For the first time the patient was having 2 weeks seizure interval. At doses of Perampanel 6 mg, worsening of seizures was noted. Currently she is maintained on 4 mg nocte, her VNS is being deferred and zonisamide being weaned off. Both parents and the young person are pleased with the above outcome. **Case 2:** This 14 yr old girl has multiple cavitating brain lesions in keeping with latent CNS TB. She has a single lesion in her R mesial temporal lobe, which is the focus of her focal seizures. Given drug interaction with her anti TB medications her antiepileptic drug regime was modified, consisting of Lamotrigine with perampanel recently added at 2 mg. Her seizures remain frequent and on a daily basis with plans to increase Perampanel to 4 mg and eventually 6 mg nocte if tolerated. She is within the epilepsy surgery work-up programme. Neither patient has had dizziness on perampanel. **Discussion:** Perampanel is a new antiepileptic medication licensed for children >12 years old, with a novel mechanism of action as a non-competitive AMPA receptor antagonist on the glutamate receptor of post-synaptic neurons. In the first case its efficacy resulted in VNS being deferred; whilst in the second case a clear response is yet to be demonstrated. As further experience in its use is obtained, the role of Perampanel in drug resistant childhood epilepsy will become clearer.

P21 - 2126

The vitamin D deficiency in patients with newly diagnosed idiopathic epilepsy

Sonmez FM, Donmez A, Canbal M, Namuslu M. *Turgut Ozal University, Faculty of Medicine, Department of Child Neurology, Ankara, Turkey – mjgsonmez@yahoo.com*

Objective: Vitamin D is a hormone and there are some roles in calcium and bone homeostasis, cell proliferation. Also, recent studies indicates that vitamin D and its receptors play an important role in the brain. Several studies shown a link between vitamin D deficiency and epilepsy. In this study, we investigated the 25-OH Vitamin-D3 levels together with other bone markers (Calcium, phosphorus, alkaline phosphatase and Parathormon) in patients with idiopathic epilepsy. **Methods:** During the 2011 September–2012 November, This study included 60 patients (34 females and 26 males) with idiopathic epilepsy whose ages change between 5 and 16 years (the mean age was 9.6±3.2 years) and 49 healthy child (25 females and 24 males, aged between 5 and 16 years). We retrospectively analyzed laboratory records of the patients and evaluated the levels of calcium, phosphorus, alkaline phosphatase, PTH and 25-OH Vitamin-D3. Exclusion criteria included mental retardation, previous history of status epilepticus, previous history of AED use, skin, liver, gastrointestinal, bone or kidney disease. The levels under 20 ng/ml were described as vitamin D deficiency. **Results:** There was no significant difference in the age, gender distribution and levels of Calcium, Phosphor, alkaline phosphatase and PTH. The levels of 25-OH Vitamin-D3 showed a statistically significant decrease compared to the control group. **Conclusion:** The results of this study demonstrated that vitamin D may play important role in

epileptic patients. The next step would be to investigate the relation of the low vitamin D levels and supplementation therapy to the outcome of epilepsy.

P22 - 2098

Sleep EEG recordings in childhood absence epilepsy spectrum

Tsirouda AM, Dinopoulos A, Mponakis A, Pons R, Paschalidou M, Pavlopoulou I, Tsoumakas C. 3rd Department of Pediatrics University of Athens, "Attikon" University Hospital, Greece – mtsirouda@yahoo.com

Objectives: Childhood absence epilepsy is a common pediatric epileptic disorder at the age of 2–10 years old. It is characterized of gradually increase of absence seizures in combination with automatisms. Several epileptic syndromes have absences as the only or most predominant seizure type and their EEG-patterns are quite similar. The EEG-patterns conclude generalized 2.5–4 Hz spike and slow-wave discharges. The episodes always occur during hyperventilation and some syndromes demonstrate photosensitivity. The purpose of the research is studying the interaction between sleep architecture and epileptic discharges in patients with absences. **Material and methods:** Twenty children between the age of 3.5–14 (mean=611/12) years old (70%female) with typical or atypical absences were studied. Routine-EEG including hyperventilation (5min), photic stimulation and sleep polysomnography were performed before the onset of drug treatment. **Results:** Fourteen children (70%) were diagnosed with CAE, 3 with JME, 2 with MAE and 1 with EMA. Eight children (40%) were treated with valproic acid. Ethosuximide, lamotrigine or combination was used for the rest. All children showed 3–4 Hz generalized SWD with bifrontal locate during hyperventilation (mean time of absence occurrence = 103.5 seconds) and 4 had photosensitivity. The discharges were recorded in all children's sleep mostly in stages I, II of NREM. Activation of the discharges is observed during stages II and SWS, thus there is a fragmentation of the epileptic complexes and attenuation of epileptic activity during REM-sleep. Partial discharges were recorded in 50% of children with different localization. The mean of discharges (either generalized or partial) per hour during the sleep study was approximately 35 epileptic discharges per hour (less = 20.92, most = 82.16). **Conclusions:** There is a qualitative and quantitative change of electrographic activity during sleep in children with childhood absence epilepsies. Further longterm and comparative research should be conducted 6 months and 1 year after treatment onset in order to estimate possible changes in sleep.

P23 - 2094

Increasingly focal loss of regeneration in a patient with BECTS developing a CSWS with partial subsequent recovery under steroids; a longitudinal case study with fMRI, night-EEGs and neuropsychology

Bölsterli Heinze BK, Oser N, Critelli H, Nageleisen-Weiss A, Schmitt B, Schneider JF, Huber R, Datta AN. Pediatric Neurology Department, University Children's Hospital Zürich, Switzerland – alexandre.datta@ukbb.ch

Objectives: We demonstrate the course of regression with loss of nocturnal regeneration due to epilepsy in a child with BECTS evolving to CSWS with partial recovery. **Methods:** Sleep deprivation EEG at 8.5 years; 4 night EEGs at 9.0, 9.5, 9.75 and 10 years with sleep slow wave slopes (from first to last hour of sleep) as a marker of nocturnal regeneration; Language fMRI at 9.5 years; neuropsychological testings at the age of 8.7, 9.0 and 9.75 years. **Results:** Initially right hemispheric centro-temporal sharp waves at 8.5 years became bilateral at 9 years. Slow wave slope analysis showed a reduced slope change in both left and

right hemispheric foci (-2.6%) and a normal one in the rest of the brain (-28.0%). Language functions decreased with no clearly visible negative impact in school performance. Regression signs came up at 9.5 years. CSWS was confirmed; slow wave slope analysis revealed a loss of regeneration with an increasing slope (+5.6%) in both foci and a reduced regeneration in the rest of the brain (-6.8%). Steroids were initiated. 3 months later, the patient regained normal school performance and neuropsychological testing improved. Despite seizure freedom slow wave slope change even got worse in both foci (+11.4%) and in the rest of the brain (+2.4%). Steroid treatment was continued for other 3 months. After that, EEG showed a clear decrease of nocturnal epileptic activity with an improvement of the slow wave slope change. **Conclusion:** A girl with BECTS developed a CSWS with a complete loss of regeneration in both foci and decreased regeneration in the rest of the brain. Neuropsychological testing anticipated left hemispheric dysfunctions 5 months prior to regression. Steroid treatment improved school performance, led to seizure freedom. Nocturnal regeneration only improved after 6 months of steroids indicating most probably the delay of neuronal recovery.

P24 - 2085

Experience and clinical utility of prolonged video-EEG monitoring in pediatric patients of a tertiary center

Sampaio M, Rocha R, Castro A, Pires I, Leão M, Augusto-Ribeiro J. Neuropediatrics Unit, Hospital Pediátrico Integrado, Centro Hospitalar S. João, Porto, Portugal – mafaldansampaio@gmail.com

Introduction: Prolonged video-EEG (vEEG) monitoring is a valuable tool in the evaluation of paroxysmal events and it is usually done in epilepsy monitoring units. However, in the context of limited financial resources, prolonged vEEG monitoring performed in the pediatric ward may also be effective and useful to characterize paroxysmal events and epilepsy. **Objectives:** To evaluate the clinical utility of prolonged vEEG monitoring in patients with paroxysmal events, performed in the pediatric ward of a tertiary center. **Material and methods:** Retrospective study of clinical and vEEG reports of patients submitted to prolonged vEEG monitoring from September 2011 to March 2013. EEG NicoletOne LTM® equipment was used. Analysed data included demographic and clinical characteristics and utility of monitoring (success in the registration of typical events, diagnosis of events and impact in subsequent management). **Results:** A total of 58 sessions were performed for a sample of 53 patients, with a median age of 5 years (1 month to 17 years) and 29 (55%) were male. The median length of stay was 2 days (12 hours to 5 days). Forty-six sessions (79%) were clinically useful, 25 for paroxysmal disorders/events, and 21 for epilepsy. The majority of events was registered with good video and EEG quality. The range of events per session was 4 to 28, with a mean of 20 events per patient. Following monitoring, antiepileptic therapy was discontinued in 3 patients. **Conclusions:** Prolonged vEEG monitoring is a useful method in the evaluation of patients with paroxysmal events, differentiating epileptic versus nonepileptic phenomena, with consequent clinical decisions. Our results confirm its utility in the daily clinical practice of a neuropediatrics unit.

P25 - 2072

Diagnostic clues and difficulties in Dravet syndrome starting from 34 Dravet patients analysis within Romanian Research Group for Rare Genetic Epilepsies

Craiu D, Barca D, Burloiu C, Butoianu N, Deconinck T, Gos M, Hoffman-Zacharska D, Iancu D, Minciu I, Motoescu C, Sandu C, Tarta-Arsene O, Weckhuysen S, Iliescu C. "Carol Davila" University of Medicine, Department of Neurology, Pediatric Neurology, Neurosurgery, Psychiatry - Pediatric Neurology Clinic No. II, Bucharest; Pediatric Neurology Department, Al. Obregia Hospital, Bucharest, Romania – dcraiu@yahoo.com

Objectives: Although clinical and genetic spectrum of Dravet Syndrome are currently intensively studied, there are still undiagnosed or delayed diagnosed cases. We present pitfalls and diagnostic clues starting from cases studied by the Romanian Epilepsy Network and Romanian Research Group for Rare Genetic Epilepsies within RES Consortium EuroEpinomics. **Material and methods:** 34 Dravet phenotype patients selected from Romanian databases in the project 6EUROC, partner of RES EuroEpinomics Consortium were studied concerning age and modality of onset, clinical, EEG, imaging and genetic aspect. **Results:** One case with slight facial hypoplasia and cheiloschisis associating cortical malformation and nodular periventricular heterotopia had delayed diagnosis of Dravet syndrome despite typical early onset prolonged focal seizures with fever on both sides. Vaccination associated short seizure at onset was diagnostic clue in a prematurely born child with global developmental delay, with subsequently resistant epilepsy. SCN1A mutations were demonstrated. Ethical issues were raised by cases with single focal febrile status epilepticus in normally developed infants. Diagnosis delay varied from 0 to 3 years after the first seizures. Afebrile seizures were present at onset in 3 cases. Patients with newly identified mutations did not associate a particular phenotype. **Conclusions:** Association of structural pathology (migration disorders or post-hypoxic-ischaemic lesions) does not exclude Dravet syndrome diagnosis (with SCN1A mutation). Vaccination associated seizures and/or prolonged unilateral seizures in infants should raise suspicion for Dravet phenotype. Testing for SCN1A mutation in an infant with normal development after the first focal febrile status epilepticus is debatable from the ethical point of view.

P26 - 2068

Epilepsy and learning disorders

Charollais A, Rolland A, Lemarchand M, Marret S. *Neuropediatrie Medecine neonatale*, Rouen, France – aude.charollais@chu-rouen.fr

Benign idiopathic epilepsies are frequent in children. Recently, specific neurocognitive disorders have been reported as being associated with type of benign epilepsy and localization. We report the case of a young boy who consulted for global learning disorders. Examination revealed low activity benign focal epilepsy with centrottemporal spikes, associated with very slight activation during sleep. Following 10 month of treatment with a 20mg per kg dose of valproate, neurocognitive assessment revealed a 22 point and 5 point rise in non verbal and verbal skills respectively. The young patient received concomitant speech therapy, but there was already a clear overall improvement in his visual attention. His Eeg measurement improved however there was persistence of spike and wave rushes with some night-spikes without activation. He is currently a pupil at a mainstream secondary school, whereas 4 years previously he had been under consideration for referral to a special school. There is little evidence in the literature that treatment of electroencephalographic abnormalities impacts on learning and in particular on oral language. Nevertheless, case by case analysis confirms the need to record sleep patterns to identify the neurocognitive disorder in question and even for older children. The prognosis for benign

epilepsy remains positive. Nevertheless, benign epilepsy can result in serious neurocognitive disorders, which must be taken into consideration during the basic learning phase. Individualized treatment is therefore mandatory for children with benign epilepsies.

P27 - 2058

Effect of levetiracetam monotherapy on lipid profile in children with epilepsy: a prospective study

Paschalidou M, Attilakos A, Garoufi A, Tsirouda M, Papadopoulos I, Dinopoulos A. 3rd Department of Pediatrics, University of Athens, "Attikon" University Hospital, Greece – pamar2009@hotmail.com

Objectives: Antiepileptic drugs, such as carbamazepine, often increase the serum concentrations of serum lipids. Studies evaluating the effect of levetiracetam (LEV), a newer broad spectrum antiepileptic agent, on serum lipid levels are very limited. The aim of this study was to investigate prospectively the effect of LEV monotherapy on serum lipid profile in children with epilepsy. **Material and methods:** The study population consisted of 20 children (8 males, 12 females, aged 2 to 15 years old, mean age 6.5 ± 4.16 years) with epilepsy treated with LEV monotherapy. None of the children were receiving any form of AED medication prior to LEV initiation. Serum total cholesterol (TC), low-density lipoprotein cholesterol (LDL-C), triglycerides (TGs), high-density lipoprotein cholesterol (HDL-C), apolipoprotein A-I (apo A-I), apolipoprotein B (apo B) and lipoprotein (a) [Lp(a)] were evaluated in all children, before and at 2 and 6 months of LEV monotherapy. **Results:** TC and HDL-C were significantly increased at 6 ($p=0.011$ and $p=0.012$, respectively) months of LEV treatment. There were no significant alterations in LDL-C, TGs, apo A-I, apo B and Lp(a) levels during the study. **Conclusions:** LEV monotherapy may cause significant alterations in TC, and HDL-C levels in children with epilepsy, occurring early in the course of treatment. Long-term, large, prospective studies are required to clarify the possible effect of LEV on serum lipid profile, the underlying mechanisms involved and its clinical significance.

P28 - 2016

Cognitive and behavioural study of 24 consecutive patients with a Dravet syndrome

Villeneuve N, Laguiton V, Viellard M, Lepine A, Chabrol B, Dravet C, Milh M. *Pediatric Neurology Unit, Timone children Hospital and Henri Gastaut Hospital*, Marseille, France – mathieu.milh@ap-hm.fr

Aim: To describe cognitive and behavioural profile of 24 patients with Dravet syndrome (DS). **Methods:** We administrated Weschler intelligence scale and Vineland scale between the age of six and ten, in 24 patients with DS followed in our institution. Statistical analysis (Spearman rank order and Pearson correlation coefficient) were used to correlate epilepsy characteristics with the cognitive state. **Results:** SCN1A was mutated in 22 patients out of 24. After the age of 6 years, none of DS patients had a normal IQ using WISC. When interpretable, their cognitive profile was characterized by an attention deficit, an inability to inhibit impulsive responses, perseverance and deficit in planning function. Adminstrating Vineland scale in 23 patients, we showed that socialisation skills were significantly higher than communication and autonomy skills. We did not find any significant correlation between the developmental quotient assessed between 6 and 10 years of age and the majority of epilepsy characteristics during the first two years in this small group of patients. **Interpretation:** An impairment of executive function may explain most of the behavioural and cognitive phenotype of the DS patients. The severity of the cognitive impairment is mostly due to low com-

munication and autonomy capacities, whereas the socialisations skills are relatively preserved, in contrast to autism.

P29 - 2013

Temporal lobe epilepsy (TLE) in children: etiologies in a cohort of 20 Tunisian patients

Abid I, Ellouz E, Hsair I, Ayedi I, Kammoun F, Triki C. *Child Neurology Department, Sfax, Tunisia – ad.imen@yahoo.fr*

Introduction: The etiology of TLE in different children cohorts have been infrequently studied. The aim of this study is to analyze the data of 20 children diagnosed with TLE in order to describe the etiology of TLE in children. **Methods:** A retrospective clinical, electric and radiological analysis was carried out on children diagnosed with TLE seen in the neuropsychiatric department of Hedi chaker Hospital-Sfax (Tunisia). All patients had neurological examination, cerebral MRI with axial and coronal T1, T2 weighted images, and at least one EEG. **Results:** Our patients were divided into three groups according to likely etiology: Group1 (G1) with 10 patients (50%) with symptomatic TLE due to cortical malformations or non-progressive tumors: 4 children had focal dysplasia, 2 had other located focal malformation, 3 had glial tumors, and one had cavernoma. Group 2 (G2) consisted of 4 children (20%) with mesial temporal sclerosis in MRI, and group 3 (G3) comprised 6 patients (30%) with no abnormality in neuroimaging and no significant antecedents (cryptogenic TLE). Patients including into G2 and G3 had pharmaco-resistant epilepsy and had psychological problems such as mental retardation or learning disabilities. **Conclusions:** Etiology differences between children with TLE may have prognostic implication; in fact in our series, G1 and G2 were statically associated with poor outcome. We found this classification very useful in the assessment of patients with TLE.

P30 - 2008

Treatment of dystonia and epilepsy in 3 patients with ARX mutations

Selch C, Wohlrab G, Hackenberg A, Bast T, Biro A, Hasse A, Berweck S, Staudt M, Kluger G. *Clinic for Neuropediatrics and Neurorehabilitation, Epilepsy Center for Children and Adolescents, Schön Klinik Vogtareuth, Germany – cselch@schoen-kliniken.de*

Objectives: Mutations in the X-chromosomal ARX (Aristaless-Related- Homeobox) gene cause both nonsyndromic and several forms of syndromic mental retardation. The phenotypes are characterized by pleiotropy. Common clinical features include epilepsy, brain malformations, genital abnormalities and dystonia. Dystonia has previously described as a clinical feature in patients with ARX mutations, however, there is hardly any information about antidystonic treatment in affected patients. **Methods:** retrospective evaluation of 3 out of 4 patients (3 male patients, age 4–17, including one pair of brothers) with ARX-mutations presenting with dystonia and epilepsy. 1 patient had epilepsy but no dystonia. **Results:** Gene analysis in the pair of brothers showed identical 21bp GCG repeat expansions in exon 2 of the ARX gene c.333_334ins(GCG)7, leading to an expansion of the first of four alanine tracts. The third patient was found to be hemizygous for a previously not described de-novo mutation with duplications in the alanine repeats c.315_335dup; p.Ala109_Ala115dup. All patients had infantile spasms with onset at 4–6 months and further developed generalized tonic-clonic seizures. Epilepsy was treated with multiple antiepileptic drugs including benzodiazepines, barbiturates, steroids, valproic acid, vigabatrin, levetiracetam and oxcarbazepine. All patients responded to combination therapy including VPA, 2 became seizure free. Dystonia in all patients presented in the first months of life. One patient developed severe status dystonicus at the age of 10 years. Dystonia was

successfully treated with tetrabenazine (1/3), oral baclofen (3/3), intrathecal baclofen (1/3) and L-DOPA (1/3). **Conclusion:** Dystonia is an important clinical feature in some patients with ARX mutations. Dystonic symptoms may present even before the onset of epilepsy in early infancy and may be difficult to differentiate from epileptic seizures. Successful therapeutic options include baclofen, administered orally or even intrathecally. No general conclusions can be drawn from this case evaluation but may give an impulse for collaborated clinical observations and data collections.

P31 - 2001

Refractory epilepsy and retinal involvement in a patient with ring chromosome 14

Deconinck N, Diakogeorgiou A, Pelc K, Monnier A, Deleener A, Sznajder Y. *Department of Neurology, Huderf, ULB, Belgium – nicolas.deconinck@huderf.be*

Background: To date less than 100 patients identified with a Ring chromosome 14 have been published so far [1]. Standard karyotype leads to the identification of ring chromosome 14 whereas different breakpoints and size of deletion have now been confirmed using molecular karyotype technology. Parent of origin effect may modulate phenotype (imprinting). Intellectual disability which is almost always severe is not related to the size of the deletion but rather to the severity of epilepsy [2]. Dysmorphic features are reported to be distinctive with a “long and sometimes asymmetric face”, full cheeks, high forehead, horizontal eyebrows; short and bulbous nose). Characteristically, abnormal eye features (abnormal retinal pigmentation, Drüsen, “abnormal macula”, strabismus) are associated with more proximal deletion 14q11.2 band encompassing NRL and RPGR1P1 genes. Natural History A girl of unrelated healthy parents was admitted to neurologic department for seizure at the age of 11 months. Pregnancy and delivery were unremarkable but for neonatal isolated microcephaly (–2SD). OFC remained along –2SD. Development was noted to be normal. Seizures became progressively refractory to treatment while work-up did not identify brain anatomic malformation as any other anatomic malformation. Ophthalmologic exam identified unspecified retinal pigmentation anomaly with small Drüsen; eye contact was poor. Important intellectual disability, and particularly expressive language delay were recorded. She is very smiling and has a pleasant personality. Standard karyotype identified r(14) in all cells. **Conclusions:** Patients with r(14) develop a distinctive spectrum of phenotype as epileptic history. Long term follow-up with special care to seizure, education and ophthalmologic involvement can be guaranteed. Additional investigation are still required to better understand variable expressivity, gene haplo insufficiency, second allele involvement as for a possible role of imprinting.

P32 - 1982

Clinical impact of long-term nocturnal home monitoring for detection of epileptic seizures in pediatric patients

Van de Vel A, Cuppens K, Bonroy B, Milosevic M, Van Huffel S, Vanrumste B, Lagae L, Ceulemans B. *Antwerp University Hospital – University of Antwerp, Belgium – anouk.van.de.vel@uza.be*

Objective: The gold standard for detecting epileptic seizures is video/EEG, but its discomfort does not allow long-term home measurement and analysis is not yet automated therefore does not allow real-time alerts. Our team has developed a system based on three-axial accelerometers (ACM), radar and video. The aim of this study is evaluating its efficiency, comfort and user friendliness in a long-term home situation. **Material and methods:** The system consists of a camera, IR source and radar attached to a pole that is placed in the corner of the patient's

room, four wireless ACM attached to the patient's wrists and ankles using elastic bracelets, and a laptop receiving (through Bluetooth), processing and storing recordings that contain movement. So far we have monitored four patients for one month and obtained at least 17 nights with complete data for each patient. Before applying the algorithms that our team developed for different seizure types (see EPNS 2011), we started analyzing the data offline for extraction of long and intense movement and used video verification for confirmation of suspected seizures. **Results:** As our data do not contain EEG signals, the control sets of seizures are those recorded by the caregivers who are surveilling the patient on a semi-continuous basis, with or without audio-based detection. For all four patients, more seizures of different types have been found after data analysis than noticed by the caregivers. **Conclusions:** Long-term measurement of epileptic seizures and discussion of results with the patient's physician, caregiver and parents has lead to valuable feedback for improvement of our system towards user friendliness, comfort and utility. The efficiency of the system has been proven by the fact that more than the witnessed seizures have been detected, but needs to be further explored by measuring other patients.

P33 - 1977

Seizure and cognitive outcomes of epilepsy surgery for glioneuronal tumours in childhood: the timing of intervention

Ramantani G, Kadish NE, Anastasopoulos C, Strobl K, Stathi A, Brandt A, Mayer H, Wagner K, Schubert-Bast S, Korinthenberg R, van Velthoven V, Zentner J, Schulze-Bonhage A, Bast T. *Epilepsy Centre, University Hospital Freiburg, Germany – georgia.ramantani@uniklinik-freiburg.de*

Purpose: To investigate the seizure and cognitive outcomes of children and adolescents undergoing resective surgery for glioneuronal tumor-related refractory epilepsy and determine their predictive factors, with an emphasis on time-related variables. **Methods:** We retrospectively analyzed the findings of presurgical evaluation, resection types and outcomes over 1.3–12.3 years (mean 7.3) of 29 consecutive children and adolescents who underwent resection at the Epilepsy Center Freiburg in 2000–2011. The mean age at epilepsy onset was 7.9 years (range 0–15.4), the mean age at surgery was 11.7 years (range 2.6–17.3), and the mean epilepsy duration was 3.8 years (range 0.3–15.3). Aetiology comprised 13 dysembryoplastic neuroepithelial tumors and 16 gangliogliomas, with additional focal cortical dysplasia in 5 cases. **Results:** 86% of children were seizure free 12 months after surgery and 76% remained seizure free at final follow-up; 62% discontinued antiepileptic drugs. Gross-total resection was related to significantly higher rates of seizure-freedom. Higher presurgical cognitive functioning (full scale IQ, verbal IQ) was related to shorter epilepsy duration independent of age at epilepsy onset, thus determining postsurgical functioning. Overall, improvements in verbal IQ, performance IQ and visual memory as well as a trend towards improvement in full scale IQ were established after surgery. No deterioration in any of the cognitive variables was noted on a group level. **Conclusion:** With completeness of resection predisposing to favorable outcomes regarding seizure alleviation, a short latency to surgery appears crucial in preserving cognitive functions, thus supporting early surgical intervention.

P34 - 1967

Developing paediatric EEG in urban and rural settings in Rwanda

Dan J, Pelc K, Muganga N, Van Steirteghem S, Lepage P, Binagwaho A, Cheron G, Dan B. *Ecole Polytechnique, ULB, Brussels, Belgium – bernard.dan@ulb.ac.be*

Paediatric epilepsy has been increasingly recognised as a health

care priority in Africa. High prevalence is related to predisposing factors such as perinatal insult, infectious disease, traumatic brain injury and other brain stressing factors. Availability of antiepileptic drugs may vary widely depending on the place and time. However, supplies of cheaper drugs such as phenobarbitone and phenytoin are often sufficient. In Rwanda, carbamazepine, sodium valproate, benzodiazepine and sometimes other antiepileptic drugs can also be prescribed. Still, there is a high prevalence of complications related to seizure disorder. A major difficulty relates to diagnosis. Access to electroencephalographic equipment, which is regarded as indispensable in high-income countries is at best scarce. We aimed to assess the feasibility of low-cost wireless electroencephalography in urban and rural settings in Rwanda. We adapted a 14-channel recording system originally designed for brain-computer interface primarily used in video gaming. Clinical EEGs were recorded in 30 children aged between 15 months and 15 years with various presentations (including epilepsy, cerebral palsy, developmental delay and absence of neurological disorders) either in city hospital or rural health care centres in Rwanda. Nursing personnel was trained to place the headset according to a standard protocol, verify electrode impedance, perform the recording, and transfer the raw digital data via internet (either locally or transporting a flash disc according to available facilities) to a server. Data was processed using a dedicated software that we developed for medical analysis of EEG traces. We listed caveats and limitations and designed strategies to overcome them. We conclude that EEG can be recorded in children in rural and urban Rwanda by health care personnel using low-cost hardware and internet facility (or transport of compact digital drive), and analysed centrally in a hospital centre with possible remote support.

P35 - 1937

A new variant detected in GRIN2A by whole-exome sequencing in a patient with intellectual disability with intractable epilepsy

Per H, Caglayan AO, Canpolat M, Bilguvar K, Gümüş H, Kumandas S. *Department of Pediatric Neurology, Medical Faculty, Erciyes University, Kayseri, Turkey – huseyinper@yahoo.com*

Objectives: A six year old female patient was submitted to our clinic due to mild intellectual disability, intractable epilepsy and delayed speech. She was born at 37-gestational week with 2950gr birth weight. During the neonatal period, she had feeding difficulties and vomiting. She was hospitalized due to polycythemia, hypoglycemia, congenital hypothyroidism and asphyxia. On her EEG, epileptic encephalopathy was detected and antiepileptic therapy was started with valproate, pyridoxine, lamotrigine, clobazam, clonazepam, clonazepam, phenytoin, sulthiame, lev-tiracetam, vigabatrin, carbamazepine, rifinamide, ethosuximide, primidone, zonisamide, synacthen, IV Ig and ketogenic diet according to the seizure type. An internal shunt was implanted due to symptomatic frontal arachnoid cyst. TANDEM Mass spectroscopy and urine organic acids were normal. **Material and methods:** To assess the underlying genetic defect, we performed whole exome sequencing on the patient. **Results:** We identified heterozygous missense variant mutation (R1285K) in GRIN2A, mutation of which are responsible from epilepsy and neurodevelopmental defect syndrome (OMIM:613971). **Conclusions:** Here we describe the first Turkish patient diagnosed with this rare disorder through whole-exome sequencing.

P36 - 1936

The effects of valproic acid monotherapy on the body's vitamin K status in children

Ayvaz A, Içağasioğlu D. *Şanlıurfa, Turkey – aayvaz@ttmail.com*

Introduction: Our study aims to investigate Vitamin K reserves

in children using valproic acid (VPA), a subject not formerly reported in the literature, and the effects of VPA use for a period of one year on Vitamin K reserves. **Material and method:** The study conducted prospectively at the Cumhuriyet University, Turkey over a period of one year included 25 children (14 male, 11 female) aged between 4 to 17 who received antiepileptic drugs (VPA) for the first time and continued the therapy with this single drug. Patients were divided into two stages as pre-puberty and puberty according to Tanner's criteria, and the ratio of carboxylated osteocalcin and undercarboxylated osteocalcin were measured using the ELISA method both pre-therapy and one year post-therapy. **Findings:** Although carboxylated osteocalcin demonstrated a minimal increase in the pre-puberty group, it was observed to decrease in the puberty group. We noted that, although higher in the pre-puberty group, undercarboxylated osteocalcin was observed to decrease compared with their start values in both groups. **Discussion:** The results of our study demonstrate that the body's Vitamin K reserves tended to decline in our puberty group patients, that there was a weakened capacity to meet the need, and that the bone metabolism was negatively affected.

P37 - 1895

Association of Down syndrome and epilepsy with atypical absences and astatic seizures

Dica A, Acinte I, Tarta-Arsene O, Barca D, Iliescu C. *Department of Pediatric Neurology, Clinical Hospital "Al. Obregia", Bucharest, Romania – iliescu_catrinel@yahoo.com*

Purpose: Down syndrome (DS) it is the most common genetic condition characterized by a supplementary 21 chromosome usually from the mother side. Association with epilepsy was described in 1.4–17% of children with DS. Most frequent types of epilepsy in childhood are infantile spasms. Our aim is to present 2 cases of girls with DS and epilepsy with generalized seizures, with astatic seizures and atypical absences respectively, with an extremely prompt response to levetiracetam. **Methods and results:** Case 1: 3 years old girl with DS, with onset of epileptic spasms at 5 1/2 months old, remitted after synthetic ACTH, at 14 months. Severe developmental delay with autistic traits. Onset of astatic seizures at 1 year 9 months old, daily, frequent, interictal EEG showed generalized spikes and waves and polyspikes waves discharges, no clinical events. Cerebral MRI showed a small right lenticular lacunae. Extremely prompt response to levetiracetam, clinically and on EEG. Case 2: 7 years old girl with DS and moderate developmental delay. One febrile seizure at 1 year old. Onset of seizures at 6 years 3 months old, with features suggesting atypical absences - staring, eyelid blinking, slight chewing, unresponsiveness, hiper/hipotonia, duration - seconds. EEG trace showed bilateral spikes and waves discharges with associated clinical events - as described before, 5 seconds. Levetiracetam was started with a spectacular response - seizure control from the first doses. **Conclusion:** We wanted through this paper to highlight the association of DS and epilepsy with generalized seizures - astatic seizures, atypical absences - and the prompt response of our cases to levetiracetam. Taking into consideration these facts, we consider that levetiracetam could be the first choice for children with such seizures, and maybe even for epileptic spasms associated to Down syndrome

P38 - 1894

The development of a new Children's Epilepsy Surgery Service (CESS) for England

Verity C. *Cambridge, United Kingdom – christopher.verity@addenbrookes.nhs.uk*

Objectives: To report on the development, the structure and

the aims of the new CESS service for England. **Material and methods:** Recognising the need to improve the quality of children's epilepsy surgery throughout England, the NHS National Specialised Commissioning Team invited children's epilepsy centres to apply for a place in a new national Children's Epilepsy Surgery Service. During November 2011 an Evaluation Panel that included international experts visited the centres that had applied to be part of the national network. **Results:** The panel recommended that there should be four centres in England and that the care of children undergoing epilepsy surgery should be concentrated in those centres. A National Clinical Co-ordinating Group has been established, made up of representatives from each of the four centres, to ensure that the network provides a world class service. To facilitate consistent performance an on-line database (based on International League Against Epilepsy criteria) has been developed to standardise the collection of data about clinical management and follow-up. Difficult cases will be discussed between centres, working towards the development of a "national multidisciplinary team". **Conclusions:** The aim is to improve quality by concentrating expertise and to increase the number of children who are assessed and treated. About 110 children a year currently have epilepsy surgery in England. It is estimated that more than double this number would benefit from epilepsy surgery, so there are plans to increase capacity of the service. Advances in technology have enabled detailed non-invasive assessments allowing many more children to be evaluated. The four CESS centres are eventually expected to see 1,050 referrals each year with about 350 selected for surgery. We aim to publicise the new CESS service because ongoing collaboration with centres around Europe will help to improve standards of care for children undergoing this complex surgery.

P39 - 1891

Compare the value of ambulatory EEG (AE) and video telemetry (VT) in diagnosis and classification of seizures

Iqbal M, Prasad M, Mordekar S, Kandler R. *Sheffield Childrens Hospital, Sheffield, UK – drmehtabch@yahoo.com*

Objective: Compare the value of ambulatory EEG (AE) and video telemetry (VT) in diagnosis and classification of seizures. **Method:** The EEG department database was interrogated retrospectively for children having both AE and VT recording during the period March 1998 to August 2011. Only patients referred for purposes of diagnosis of attacks and classification of epilepsy were included. Patients admitted for pre-surgical evaluation of epilepsy were excluded. 48 patients were included in the study; M:F ratio 0.7:1, mean age 11.5 years, range 2 to 21 years. All patients had only 1 telemetry but 9 patients had more than 1 ambulatory recording. For the purposes of the study the result from the ambulatory recording preceding the video telemetry was used. Information regarding reason for referral and result of the long term EEG investigations was obtained. **Results:** The reason for request was for diagnosis of attacks in 77% of AEs and 52% of VTs, classification of epilepsy in 16% of AEs and 43% of VTs. Recording length for AE was: 24 hours (68%) 48 hours (25%) and 72 hours (6%). Recording length for VT was 1–3 days (60%) and 4–5 days (40%). Typical attacks were recorded in 68% of AEs and 56% of VTs. The EEG helped in diagnosis in 66% of AEs and 62% of VTs. The EEG helped in classification in 21% of AEs and 56% of VTs. 62% of patients where AE was inconclusive (21% of the total) went on to have a VT. The combined yield of the investigations was 89%. **Conclusion:** AE is an effective tool for diagnosing seizures in two thirds of children. Where AE is inconclusive, VT improves the diagnosis in a further fifth. VT is superior to AE in classifying seizures.

P40 - 1882**What is the predominant feature of epilepsy in Down syndrome?**

Tarta-Arsene O, Barca D, Iliescu C, Budisteanu M, Motoescu CH, Magureanu SA, Craiu DC. *Pediatric Neurology Department, Clinical Hospital "Al. Obregia", Bucharest, Romania – otartaarsene@yahoo.com*

Purpose: Down syndrome is a genetic disease due to an abnormality of chromosome 21, most frequent as trisomy related to mother's age. In the definition of this disease, it was not describe as a specific trait epilepsy. This study will retrospectively analyze the features of epileptic seizures in children diagnosed with Down syndrome in a tertiary clinic from Romania, from a period of 5 years. **Methods:** retrospectively all files of children admitted for Down syndrome were analyzed and the patients who had epileptic seizures were included in the study. The clinical data (onset, types of seizures, clinical and mental exam, treatment, evolution) was analyzed and compared with lab tests (EEG and cerebral MRI) in order to find characteristic features of this association. The results were compared with published studies. **Results:** 9 patients (67% girls, 33% boys) with Down syndrome had different epileptic syndromes: 5 had infantile spasms, 3 focal seizures and one girl had only absences with eyelid myoclonia. The onset of seizures was below the age of one in 66% percent. The EEGs showed generalized discharges concordant to the epileptic seizures in 6 patients. 5 patients had complete control of seizures: 3 with infantile spasms with short time of corticotherapy, one girl with infantile spasms developed myoclonic atonic seizures and the patient with eyelid myoclonia with levetiracetam. One of the patients with infantile spasms evolved in Lennox-Gastaut syndrome and died at the age of 6 due to a status epilepticus. All patients with focal seizures have a concordant structural lesion related to a vascular abnormality and have partial control with carbamazepine. **Conclusions:** Evolution of seizures in this genetic disease is dependent on existence of structural abnormality because only genetic traits are in general a good prognostic factor.

P41 - 1877**Low-frequency repetitive transcranial magnetic stimulation (r-TMS) treatment in children with refractory focal epilepsy: two case reports**

Thordstein M, Pegenius G, Andreasson A, Hallböök T. *Departments of Clinical Neurophysiology, Gothenburg, Sweden – andreasson@vgregion.se*

Background: Over recent years, neuromodulation, with rTMS has been reported to be valuable for treatment of different conditions where the pathophysiologic background is believed to be a central nervous dysfunction. One such entity is epilepsy where positive effects have been reported in adults. In children, the experience is almost non-existing. Given that the technique is non-invasive and that there is no reason to believe that it could be harmful, it seems reasonable to try it at least in severe cases that do not respond to conventional therapy. **Methods:** Daily one hour sessions of low frequent repetitive TMS (rTMS, 0.5 Hz) were used to treat two children with severe epilepsy. A two year, eight months old boy has Alper's disease and entered an epilepsia partialis continua with rhythmic jerking of the left upper extremity, mainly the hand. The seizures were pharmacoresistant and scalp-EEG could not reveal the seizure focus. The hand area of the primary motor cortex was localised using navigated TMS based on the patients structural MR. This position was used for rTMS treatment. A six year, three months old girl had a CSWS syndrome due to cortical malformations. After tapering of corticosteroids her seizure situation worsened. Scalp EEG revealed a number of seizure foci. While waiting for a planned neurosurgical treatment, rTMS was used directed by the EEG localisations. **Results:** The treatment sessions were mainly

uneventful, in the majority the children slept during the stimulations. (The boy often needed a light procedural sedation though.) During two weeks of treatment, the number and severity of seizures reported by parents and personnel were reduced for both patients. **Conclusions:** rTMS can be performed successfully in small children. The procedure requires a lot of resources. If tried in less severe cases than the ones described, it may be even more efficient.

P42 - 1873**Effect of anti-epileptic therapy on serum homocysteine in children**

Kishore P, Pandey RR, Warsi S. *Holy Family Hospital, New Delhi, India – praveen_kmc@yahoo.com*

Background: Elevated plasma Homocysteine concentration is associated with increased risk for vaso-occlusive disease like cerebrovascular stroke, coronary artery disease, and also the risk of resistance to anti-epileptics and refractory epilepsy. Hyperhomocysteinemia has been frequently associated with the administration of Anti epileptic drugs (AED). This study aims at evaluating the effect of anti-epileptic therapy on serum Homocysteine levels in children. **Methods:** 53 children (Males – 32, Females – 21) with Seizures in age group of 6 months–14 years, were recruited from the Pediatric Outpatient and Inpatient department of Holy Family Hospital, New Delhi were included in the study. Serum Homocysteine (Hcy) levels of Children already on AEDs for >6 months (Group A) were compared with Children before Initiation of Anti epileptic drugs (Group B). These children were followed up after 6 months of Anti epileptic therapy and Serum Homocysteine was compared (Group C). **Results:** Average Hcy levels in subjects who had already received >6 months of antiepileptic drug therapy were $12.58 \pm 2.68 \mu\text{mol/l}$, compared to $8.83 \pm 2.82 \mu\text{mol/l}$, at recruitment ($p=0.001$). Significant increased levels were also observed in children followed up after 6 months of AED – $10.27 \pm 3.06 \mu\text{mol/l}$ compared to $8.63 \pm 2.90 \mu\text{mol/l}$ at initiation of AED. 9 children who received >1 AED had significantly higher levels – $14.15 \pm 2.56 \mu\text{mol/l}$ compared to children on monotherapy – $10.22 \pm 3.06 \mu\text{mol/l}$. Carbamazepine therapy for 6 months caused significant increase in Hcy $10.78 \pm 2.82 \mu\text{mol/l}$ compared to baseline of $9.30 \pm 2.70 \mu\text{mol/l}$ ($p=0.016$). **Conclusions:** AEDs in children, particularly in those receiving multidrug or long duration treatment, cause hyperhomocysteinemia. This holds immense significance in malnourished populations.

P43 - 1869**Effectiveness of corticosteroid therapy of intractable epilepsy in children depending on the initial changes in encephalogram**

Shalkevich L. *Belarussian Medical Academy of Postgraduate Education, Minsk, Belarus – leoshal@yahoo.com*

74 children with pharmacoresistant epilepsy in the age of 6 months to 16 years were examined. In addition to anticonvulsant therapy the following corticosteroids were prescribed: prednisolone (N=31) and dexamethazone (N=43). Average daily dosage of dexamethazone made $0.42 \pm 0.3 \text{ mg/kg}$ per day, that of prednisolone – $2.5 \pm 1.4 \text{ mg/kg}$ per day. Initial EEGs were divided into 3 groups: those with registered epileptiform phenomena on normal background rhythm – 25.7% of patients, EEG with dominating of disorganized activity without epileptiform patterns – 43.2% of patients, with epileptiform activity on changed background – 31.1%. Maximum effectiveness of corticosteroid therapy was seen on EEG with disorganized activity without epileptiform changes. In this group it became possible to fully terminate seizures in 62.2% of patients, in 12.5% of children treatment was ineffective. Number of seizures declined by 25% in 9.3% of patients, by 50% - in 12.5%, by 75% - in 3.5%. Effectiveness of

treatment in two other groups was essentially lower and results were alike: termination of seizures was noted in 31.6% of patients with isolated epileptic activity on EEG and in 34.8% of patients with combination of epileptiform activity and diffused disorganizing of background activity, the amount of seizures declined by 25% accordingly in 21% and 21.7% of patients, by 50% - in 21% and 17.4% of patients, by 75% - in 5.4% and 8.7%. Total absence of influence of CS upon course of disease was noted in 21% and 17.4% of them. **Conclusion:** received results of CS effect indicate at predominance of indirect anticonvulsant effect in their action which determinates the main range of application – epilepsies connected with breach of brain bioelectrical activity maturation, and in lower measure – symptomatic forms of epilepsy with organizing of epileptic activity focus at the background of normally formed neurons.

P44 - 1868

Clinical progress and prognosis of epilepsy in tuberous sclerosis complex

Djuric M, Kravljanc R, Tadic B, Peric M, Radojicic B. *Mother and Child Health Care Institute of Serbia "Dr Vukan Cupic", Belgrade, Serbia – m.djuric@ptt.rs*

Purpose: More than 90% patients suffering from tuberous sclerosis complex (TSC) have epilepsy, and in more than 60% of them it is the first presenting symptom. Seizures are often resistant to antiepileptic drugs and have a negative impact on the neurocognitive development. The aim of this study was to evaluate the clinical features and prognosis of epileptic seizures associated with TSC. **Method:** The medical records of 57 patients who satisfied the diagnostic criteria for TSC and were followed up for at least 2 years at the Neurologic Department of Mother and Child Health Care Institute of Serbia, between January 1988 and december 2012 were reviewed. Age of seizure onset, initial seizure type, clinical progress of seizures, efficacy of different treatment and psychologic development were evaluated. **Results:** From the 52 patients evaluated (5 had no seizures) for seizures onset, it was in the first year of life in 85%. Seizures stopped in 41.6%. Occasional seizures and severe refractory epilepsy were seen in 58.4%. The most frequent type of seizures was partial. In the group with seizure onset in the first year of life, there was a cessation of seizures in 37.5%. and in patients with later onset in 42.8%. The difference was not statistically significant ($p = 0.867$). In the group with partial onset seizure they stopped less frequently than in spasm onset patients (10%: 33.3%) but the difference did not reach statistical significance ($p=0.16$). because of small sample. **Conclusions:** Epilepsy in TSC has a poor prognosis both in terms of chronicity and developmental outcome. In our group of patients type of initial seizure and seizure onset time did not influence the prognosis. New insight in pathophysiology of TSC in recent years has led to clinical recommendations for treatment of epilepsy that may improve the outcome in these patients.

P45 - 1854

Telangiectasias as a neurocutaneous feature

Schieving JH, Willemsen MAAP, Seyger M, Weemaes C, Theelen T. *Radboud University Nijmegen Medical Centre, Nijmegen, The Netherlands – j.schieving@neuro.umcn.nl*

Telangiectasias are prominent small vessels (venules, capillaries or arterioles) that are visible as small red-purple focal lesions in the skin and mucous membranes. They can serve as a cutaneous marker for many different diseases, either primary (mostly hereditary) disorders like Hereditary Haemorrhagic Telangiectasia (HHT) and ataxia telangiectasia or secondary to other diseases like connective tissue disorders and cutaneous mastocytosis. Pa-

tients with telangiectasias are seen by general health practitioners, (pediatric) neurologists, dermatologists or ophthalmologists. In this presentation we give an overview of the different disorders in which telangiectasias are a prominent feature, focusing on neurocutaneous disorders in which they serve as a marker for establishing the right diagnosis. The pattern of distribution of the telangiectasias, their age of onset and associated features are helpful to distinguish between the different disorders.

P46 - 1852

Parental experience and views about use of ketogenic diet in children and its impact on their quality of life

Jayapal SSK, Mandava V, Jayawant S, Chandratre SR. *Children's Hospital, Oxford (CHOX), Oxford University Hospitals NHS Trust, Oxford, UK – dr_sathiya@yahoo.co.in*

Objective: To obtain parents' and carers' views on their experience of ketogenic diet (KGD), impact on quality of life (QOL) of children and their views to improve services. **Method:** Parents of children who were on KGD from January 2008-January 2012 were contacted by a single telephonic administrator for a survey using standard questions. Consistency was maintained in the tone and questions were read out following an introduction and parental consent. The responses were rated from 5 (strongly agree) to 1 (strongly disagree). **Results:** Parents of 11/15 children on KGD during the study period could be contacted and consented for a telephonic survey. 9/11 parents strongly agreed that the information regarding KGD and its side effects were adequately explained by doctors and dieticians and felt adequately supported by dieticians during KGD therapy. 8/11 strongly agreed that KGD was easy to initiate and maintain. 7/11 strongly agreed that KGD improved the QOL of children leading to a positive impact on the whole family. 6/11 strongly agreed (5/11 agreed) that KGD reduced seizure frequency and 9/11 reported reduction in emergency department attendances. Overall the experience with KGD treatment was positive in 10/11 families. Some parental comments regarding KGD were: "we wouldn't survive without it"; "she was out of the wheel chair" and "(KGD) just made our lives happier and easier". Parents' suggestions to improve KGD services include need for offering motivation to families at the start of KGD, improved communication between dieticians and families and easy accessibility to local KGD services. **Conclusion:** Most parents perceived KGD as a positive experience decreasing seizure frequency and emergency department attendances and improving children's quality of life. Adequate motivation prior to KGD commencement, improved dietetic support during KGD therapy and easy accessibility to KGD service may improve compliance with KGD therapy and parent satisfaction.

P47 - 1794

Early predictors of long-term cognitive, emotional and behavioural outcome in children with ESES: a retrospective study

Weijenberg A, Vlaskamp DRM, Elting JW, Veenstra WS, Gutter T, Geerts Y, Brouwer OF, Callenbach PMC. *Department of Neurology, University Medical Centre Groningen, The Netherlands – a.weijenberg@umcg.nl*

Objectives: Long-term outcome of Electrical Status Epilepticus during Sleep (ESES) is generally unfavourable but hard to predict in individual children. Longer duration of ESES and younger age at onset of ESES have been reported to be predictors of poor outcome, whereas any treatment response is associated with a relatively better prognosis. This study aimed at determining possible other early predictors of long-term outcome. **Material and methods:** We retrospectively studied a cohort of 35 children with ESES, treated at the University Medical Centre Groningen (UMCG) and the Epilepsy Clinic of SEIN, Zwolle. We examined

possible early predictors including duration between onset of clinical symptoms and definite diagnosis of ESES (diagnostic delay), and spike-wave-index (SWI). To evaluate long-term outcome, school performance as well as cognitive, emotional and behavioural functioning was assessed with the parent-reported Brain Injury Alert - adapted for children with ESES. **Results:** Mean age at onset of epilepsy was 4.2 years; at onset of symptoms suggestive of ESES 6.5 years; and at diagnosis of ESES 7.6 years. SWI >85% was present in 40.0%, SWI 75–85% in 34.3%, and SWI <75% in 25.7%. Parents of 23 children (response rate 65.7%) completed the questionnaire (66.7% focal seizures, 60.9% symptomatic epilepsy). Median diagnostic delay was significantly longer in children with a negative change of depressive feelings (16.0 vs 2.6 months, $p=0.027$) and in children with learning difficulties (11.8 vs 0.0 months, $p=0.005$). SWI >85% was overall associated with a less favourable outcome: categorized SWI differed significantly between children with and without a negative change in three parameters of the questionnaire: understanding language ($p=0.013$), depressive feelings ($p=0.007$), and indifference ($p=0.049$). **Conclusions:** In this retrospective study, both prolonged diagnostic delay and higher SWI are associated with unfavourable long-term outcome and might therefore be early predictors for cognitive, emotional and behavioural outcome in children with ESES.

P48 - 1793

Treatment of convulsive status epilepticus in the UMCG: a retrospective, observational study

Vlaskamp DRM, Brouwer OF, Callenbach PMC. *Department of Neurology, University Medical Centre Groningen, University of Groningen, The Netherlands – d.r.m.vlaskamp@umcg.nl*

Objectives: Little is known about clinical practice with respect to the application of guidelines in the treatment of Convulsive Status Epilepticus (CSE). This retrospective, observational study evaluated treatment of episodes of CSE in children at the University Medical Centre Groningen (UMCG). **Material and methods:** Episodes of CSE were derived from the UMCG database of children with epilepsy aged <18 years at time of their first (a)febrile seizure. Included for this study were episodes of CSE lasting ≥ 10 minutes, occurring between January 2000 and October 2012, in children aged >1 month. Treatments used in the UMCG were compared with recommendations from two most recent Dutch treatment guidelines for CSE in children aged >1 month. **Results:** 269 episodes of CSE occurring in 69 children (53.6% male, median age 4.3 years; range 0.1–16.3 years) were included; 219 (81.4%) of the episodes started outside the hospital, 118 (43.9%) had remote symptomatic aetiology, 96 (35.7%) were accompanied by fever. Half of the CSE episodes lasted <30 minutes. Rectal diazepam was first treatment choice in first (58.9%; administered in ambulance in 46.6%) and subsequent episodes of CSE (43.3%; administered by parents at home in 55.1%). Intravenous clonazepam (and diazepam in first episodes of CSE) was preferred as second treatment choice; intravenous midazolam (and phenytoin as third choice in subsequent episodes of CSE) as third and fourth treatment choice. Individualized treatment protocols were associated with shorter total categorized duration of CSE episodes ($p=0.002$). In acute symptomatic CSE episodes, the sum of administrations of any therapy and the sum of different administered therapies were significantly higher compared to CSE episodes with other aetiology ($p<0.05$). **Conclusion:** Treatment of CSE episodes in the UMCG was overall in accordance with Dutch protocols and evidence-based, except for the frequent use of intravenous clonazepam. Our study highlights the efficacy of individualized treatment protocols.

P49 - 1792

Infantile spasms in the mother and daughter associated with 15q11.2q13.1 chromosome duplication

Riikonen R, Wallden T, Kokkonen H. *Kuopio, Finland – raili.riikonen@kolumbus.fi*

Objective: It is suggested that chromosomal microarray analysis (CMA) should be included in the diagnostic evaluation of patients with infantile spasms and developmental delay, when an evaluation for structural brain lesions and metabolic disorders reveal no abnormal findings. We add now a new genetic novel disease to the genetic list of infantile spasms. **Material and methods:** We describe here infantile spasms in a mother and daughter. Both showed very similar clinical course: normal-slightly subnormal early development, onset of infantile (flexor) spasms and typical hypsarrhythmia at age of 8–9 months, good response to ACTH, and low normal cognitive development in the mother and but global delay in the child who has been exposed to valproate in utero. The cases were primarily considered to have cryptogenic aetiology. The mother developed epilepsy at age of 23 years with good control with valproate. Both had normal brain MRI. **Results:** Through etiological investigations did not reveal any aetiology. Chromosomal microarray analysis using HumanCytoSNP-12 (v2.1) chip (Illumina) revealed the 6.2 Mb size 15q11.2q13.1 duplication inherited from the mother (arr 15q11.2q13.1 (22,754,322–28,941,318)x3 mat, Hg19). The duplication was found in the daughter and also in the mother as well as in her autistic brother. **Conclusions:** This is the first report of maternal inheritance of 15 chromosome duplication (dup(15)(q11.2q13.1) in infantile spasms. The group of patients with cryptogenic aetiology will decrease when more careful chromosomal studies will be made. Our report is expanding the phenotype of chromosome 15q duplication syndrome.

P50 - 1774

Respiratory and sleep disorders in female CDKL5 patients

Hagebeuk EE, van den Bossche R, de Weerd AL. *SEIN, Zwolle, The Netherlands – ehagebeuk@sein.nl*

Objective: In female children with drug-resistant seizures and developmental delay from birth, atypical Rett syndrome caused by mutations in the CDKL5 gene should be considered. Several clinical features resemble classic Rett syndrome. Respiratory and sleep abnormalities are frequently present in Rett syndrome, whereas little is known in patients with CDKL5 mutations. **Method:** In four genetically confirmed female patients with CDKL5 mutations (age range 2–15y), the presence of breathing and sleep abnormalities was evaluated using the validated Sleep Disturbance Scale for Children and polysomnography (PSG). **Results:** The Sleep Disturbance Scale for Children indicated disorders of initiating and maintaining sleep, daytime somnolence, and sleep breathing disorders. In one patient, PSG showed central apnoeas during sleep: her total apnoea–hypopnoea index (AHI) was 4.9, of which the central AHI was 3.4 / h. When awake, central apnoeas were present in two of the four female children (central AHI 28 / h and 41 / h respectively), all preceded by hyperventilation. PSG showed low rapid eye movement (REM) sleep (9.7–18.3%), frequent awakenings, and low sleep efficiency (range 59–78%). **Conclusion:** Episodic hyperventilation followed by central apnoeas was present while awake in two of four patients. This may indicate failure of brainstem respiratory centres. In addition, low REM sleep, frequent arousals (not caused by apnoeas / seizures), and low sleep efficiency were present. Similar to Rett syndrome, in patients with CDKL5 mutations PSG seems warranted to evaluate breathing and sleep disturbances.

P51 - 1765

Safety and potential impact on growth and developmental skills of long-term adjunctive zonisamide therapy in paediatric patients with partial epilepsy

Guerrini R, Rosati A, Bradshaw K, Giorgi L. *Neuroscience Department, Children's Hospital Anna Meyer-University of Florence, Florence, Italy – mandrews@mxmcommunications.com*

Objectives: To assess long-term safety of once-daily adjunctive zonisamide therapy in paediatric patients with partial epilepsy, and its potential impact on growth and developmental skills. **Material and methods:** Patients (aged 6–18 years) completing a Phase III placebo-controlled trial entered a long-term extension study, comprising a double-blind transition period (patients previously treated with placebo were up-titrated to a target zonisamide dose of 8 mg/kg/day; patients previously treated with zonisamide continued at same dose) followed by flexible, open-label dosing (duration 45–57 weeks). Safety assessments included treatment-emergent adverse events (TEAEs), Tanner stages, skeletal development, Child Behaviour Checklist for Children Aged 6–18 (CBCL 6/18), Physician and Parent/Guardian Global Impression of Change (GIC), and Controlled Oral Word Association Test (COWAT). Growth/development data are presented for changes from baseline of initial trial to Open-Label Visit 5 (V5; Weeks 62–71). **Results:** Of 144 patients entering study, 108 (75.0%) received zonisamide for >1 year. Most TEAEs were of mild or moderate intensity. Treatment-related TEAEs were reported by 39/144 (27.1%) patients; most frequently, decreased weight (6.3%), decreased appetite (4.2%) and headache (2.1%). Rates of serious treatment-related TEAEs and TEAEs leading to discontinuation were low (2.1% and 2.8%, respectively). Median (mean) changes from baseline to V5 were minimal for CBCL 6/18 Total Competence (–1.0 [–0.7]) and Total Problems (–2.0 [–3.0]) scores. Tanner staging and skeletal development were as expected for the study population. Most patients were “Much improved”/“Very much improved” at V5 on both Physician GIC (73.8%) and Parent/Guardian GIC (75.5%). Median (mean) changes from baseline to V5 in COWAT Category Fluency and Letter Fluency scores were 2.0 (2.4) and 0.5 (0.4), respectively. **Conclusions:** Adjunctive zonisamide therapy displayed an acceptable safety profile with no consistent detrimental effects on growth and developmental skills when used to treat paediatric patients with partial epilepsy for >1 year.

P52 - 1759

Clinical and neurologic outcomes of GEFS+ at Cheongju in South Korea

Kim W-S, Sim G-Y. *Chungbuk National University Hospital, Cheongju, Korea – eyunkim@nate.com*

Purpose: Febrile convulsion is the most frequently diagnosed convulsive condition in infancy or childhood, with an incidence of about 2–15%. In this study, we checked clinical feature and neurologic assessment of GEFS+ (Generalized Epilepsy with Febrile Seizure Plus). **Methods:** This study retrospectively examined clinical feature and neurologic assessment of GEFS+. We studied 24 GEFS+ children of Chungbuk National University hospital from January 2012 to December 2012. We formed them into two groups by age of first seizure; Group A (<6 years) and Group B (≥6 years). We analyzed the clinical features, EEG findings and the neurological outcomes of the subjects. **Results:** The mean age of GEFS+ was 5.6 years. 11 subjects had their initial febrile seizures under 6 years of age while 13 subjects after 6 years of age. 5 Subjects had family history of seizure. The types of convulsions were mainly generalized. Eight (33.3%) showed abnormal finding on EEG and eight (33.3%) were treated with anti-epileptic drug. The group with the initial seizures occurred under 6 years of age had more family of seizures, more developmental delay and was treated by antiepileptic drug. **Conclusion:**

This study showed clinical feature and neurologic assessment of GEFS+.

P53 - 1757

Outcome of second-line treatment with valproate or lamotrigine for absence seizure; on the condition that ethosuximide was temporarily unavailable in Korea

Bin JH, Chung SY, Han JY, Eom TH, Kim SJ, Kim YH, Lee IG. *Department of Pediatrics, College of Medicine, Catholic University of Korea, Incheon-si, Korea – sycped@catholic.ac.kr*

Rationale: Ethosuximide (ESX), valproate (VPA) and lamotrigine (LTG) are used as first-line treatment for absence seizure. Since the supply for ESX was discontinued due to its cost problems in 2010, treatment was no more to be extended. ESX monotherapy was replaced by VPA or LMT, and either excluding or switching ESX was done for patients who were originally treated with ESX combined with other anti-epileptic drug. **Methods:** A retrospective study was done for total 36 patients treated with ESX in 4 different hospitals associated with Catholic University of Korea between January of 2010 and December of 2012. **Results:** Among the total number of patients, 24 were treated with ESX monotherapy and 12 with ESX combined with other drug. In monotherapy group, each LTG and VPA was replaced for 12 and 4 patients respectively. Four patients finished treatment schedule, and total 3 patients were lost in the middle of study. Among the 12 patients whose drug was switched to LTG, no seizure occurred in 5 patients, VPA was added to 4 patients and 3 patients switched again to another drug. In 4 patients VPA added, 3 had no problems and 1 had to replace VPA to LTG due to its side effect (weight gain). In combined therapy group, on the other hand, ESX was excluded for 11 patients while 1 switched to other drug. Among the 11 ESX-excluded, 6 patients occurred no problems and 5 patients had to add ESX again. **Conclusions:** We were tried to analyze the treatment outcome for anti-epileptic drug that was changed by external causes. LTG and VPA were chosen for the second-line therapy instead of first. VPA had better outcome comparing to LTG, and LTG-VPA combined therapy was more effective than LTG monotherapy.

P54 - 1752

Prevalence of Idiopathic generalized epilepsy in children and adolescents – population based study

Mazurkiewicz-Beldzinska M, Steinborn B, Pilarska E, Szmuda M, Winczewska-Wiktor A. *Department of Developmental Neurology Medical University of Gdańsk, Poland – mmazur@gumed.edu.pl*

Purpose: Idiopathic generalized epilepsies (IGE) are generally viewed as having favorable outcomes, however the epidemiologic data concerning iIGEs is rather modest due to fact that most studies did not specifically analyze these syndromes. This study addresses the prevalence and clinical outcome in a well-evaluated cohort of patients with IGE. **Material and methods:** All epilepsy patients who entered the Developmental Neurology Departments (In and Outpatients Clinics) during one year period were included in the study and followed prospectively. 1053 children and adolescents with diagnosed and treated epilepsy entered the study. We collected information on seizure freedom, EEG and MRI characteristics, medication use, demographic information and seizure history. Epilepsy syndromes included childhood absence epilepsy (CAE) juvenile myoclonic epilepsy (JME) IGE with only generalized tonic-clonic (GTC) seizure, juvenile absence epilepsy (JAE), epilepsy with myoclonic absences (MAE), and unclassified IGE. **Results:** IGE's among all epilepsy patients counted for 26% of cases. There were majority of patients with CAE (38%), JME (37%), JAE (10%), MAE (6%), IGE with only generalized tonic-clonic (GTC) seizure (4%) and 5% of un-

classified IGE. Most of the patients (68%) were seizure free, 725 on monotherapy. The antiepileptic drugs which were used: valproate followed by lamotrigine, levetiracetam and ethosuximide. **Conclusions:** IGEs constituted 26% of cases in a largely cohort of pediatric epilepsy patients. Childhood Absence Epilepsy and Juvenile Myoclonic Epilepsy represents the majority of IGE cases. 68% of IGE achieved remission with AED therapy, mostly with a single drug.

P55 - 1743

The epilepsy phenotype in septo-optic dysplasia (de Morsier syndrome)

Tarta-Arsene O, Leanca M, Barca DG, Craiu D. *Department of Pediatric Neurology, Clinical Hospital "Al. Obregia", Bucharest, Romania – otartaarsene@yahoo.com*

Purpose: Septo-optic dysplasia, also known as De Morsier syndrome is a rare congenital syndrome involving variable midline brain structures, characterized by visual impairment, pituitary deficiencies, and specific brain abnormalities (absence of the septum pellucidum and corpus callosum). The phenotype is highly variable and the clinical presentation may be mild or extremely severe. Purpose of this paper is to present 2 clinical cases with epilepsy phenotype in Morsier syndrome. **Methods and results:** 2 girls diagnosed with Morsier syndrome have epilepsy syndrome. Clinical examination shows visual disturbances (nystagmus in both patients) and left ptosis in one girl, left hemiparesis in one girl, mild mental retardation in one girl and normal intellect in the other, left hypoacusis in one girl. They have all focal seizures, but one of them (the most affected one) has also generalized traits on EEG with photosensitivity. MRI shows optic nerve hypoplasia and hypoplasia of the corpus callosum and left renal agenesis. Antiepileptic treatment was started, but seizures are partially controlled by treatment with decreased frequency of seizures, but still EEG discharges. **Conclusions:** De Morsier syndrome is a rare syndrome associated with epilepsy and different clinical and EEG traits.

P56 - 1738

Anti-inflammatory treatment can reduce spontaneous recurrent seizure and depressive behavior in rats

You SJ, Pineda E, Shin D, Mazarati A, Sankar R. *Department of Pediatrics, Sanggye Paik Hospital, Inje University College of Medicine, Seoul, Republic of Korea – sjyou@paik.ac.kr*

Objectives: Recent experimental evidence and clinical observations suggest that the inflammatory process involved the pathogenesis of various neurologic diseases including epilepsy and its related morbidity and some kind of anti-inflammatory treatments can prevent inflammatory process in brain and reduce spontaneous recurrent seizures (SRS) and improve symptoms of epilepsy related depression and migraine. However, controversies are still remained. So, we assessed whether epileptic seizures and epilepsy-related depression can be prevented or reduced by 2 weeks of treatment with the anti-inflammatory drugs (AIDs) CAY 10404, a COX-2 inhibitor and recombinant IL-1Ra in 34-day-old male Wistar rats with LiPC-induced SE. **Methods:** The rats were divided into two groups, with one group injected with AIDs and the other control group injected with the same volumes of DMSO and saline, 1 hour before administration of pilocarpine. **Results:** The frequency of SRS was significantly lower in the AIDs treated than in the control group. Immobility time in force swim test was significantly lower in the AIDs treated than in the control animals. Timm staining was rarely observed in AIDs treated rats but was clearly discernible in the inner layer of rats in the control group. The mean gray value difference scores were significantly greater in the control than in the AIDs treated group. **Conclusion:**

we found that the administration of a COX-2 inhibitor and recombinant IL-1Ra, starting before the induction of SE, attenuated the development of SRS and depressive behavior and inhibited mossy fiber sprouting in rats.

P57 - 1731

A case of early onset epilepsy due to duplication of the sodium gene cluster on 2q24 with early seizure remission

Gnidovec Strazisar B, Renner Primec Z, Writzl K. *Department of Child, Adolescent and Developmental Neurology, University Children's Hospital, Ljubljana, Slovenia – barbara.gnidovec@mf.uni-lj.si*

Objective: In contrast to point mutations and deletions, duplications of multiple sodium channel genes are less frequent cause of epileptic disorder. So far only nine patients with early onset epilepsy and 2q24 duplication involving the sodium channel gene cluster were described. They all presented with severe seizures that were refractory to antiepileptic treatment. We report another case of early onset epilepsy in association with 2q24 microduplication in whom seizure were well controlled in less than three-week time. **Case report:** Patient presented with tonic seizures shortly after birth. Despite several seizures daily the episodes were firstly not recognized as convulsions. Her first EEG was performed at the age of 5 weeks and showed prominent slowing and asymmetry of the background activity with multifocal epileptic discharges. The seizures were resistant to levetiracetam but with the introduction of topiramate and vigabatrin seizure remission was achieved in less than three weeks. Background EEG activity improved significantly with epileptiform discharges becoming less prominent and finally disappearing. Despite that she experienced mild developmental delay. Extensive neurometabolic evaluation was normal and early MRI showed thinning of the corpus callosum. Subtelomeric FISH analysis showed a microduplication in the 2q24.2q24.3 region that was later confirmed with array comparative genomic hybridization revealing a 11.64-Mb duplication of 2q24.2q31.1 region that included also a cluster of voltage-gated sodium channel genes (SCN1A, SCN2A, SCN3A). **Conclusion:** Our case confirms that duplication involving the sodium channel gene cluster on 2q24 is associated with early onset epilepsy, which however may not be always very resistant since we were able to achieve early seizure remission despite late introduction of antiepileptic treatment.

P58 - 1716

Management of epilepsies combining antiepileptic drug therapy and various modalities of alternative therapies

Zubcevic S, Sabic A. *Paediatric Hospital, Clinical Centre, University of Sarajevo, Bosnia and Herzegovina – smail.zubcevic@gmail.com*

Management of epilepsies combining antiepileptic drug (AED) therapy and various modalities of alternative therapies is still common, but scientifically ignored. The aim of this study (part of ongoing study on socioeconomic aspects of epilepsy) was to examine profile of parents applying such approach. Educational level, socioeconomic status, alternative treatments, factors involved in the formation of such a decision were investigated, and multivariate analyses were done. Compliance with AED regime was assessed by interview and measurement of AED serum concentrations where appropriate. 84 parents filled structured questionnaires in this part of study. 56% parents considered such management approach, only 27% actually applied it. There was one case where child promptly gained complete control of seizures with AED, in others epilepsy control was not gained in first 3 months. There was no significant difference of educational level. Slightly higher proportion of such practice was observed in rural areas, but the difference was not significant. Decision to try with alternative treatments was often result of

multiple influences, mainly by friends and relatives (52%), and visiting internet portals (38%). Compliance with regime of AED therapy was in 70% of cases assessed as good. Most frequent modality of alternative treatments were various diets and vitamins, some form of exorcism and talismans (usually connected with visiting clergypersons of different denominations), herbal medicines. Satisfaction with simultaneous AED and alternative therapy was described as good in 26% cases, fair in 43% cases. Common explanation for starting such combined treatment was “it can not hurt” and fear of side-effects of AED therapy was stated as a main reason in cases of poor compliance. We conclude that combination of AED and alternative treatment is quite common, in children of different socioeconomic and educational backgrounds, but sincerity of answers in questionnaires has to be scrutinized for better understanding of this problem.

P59 - 1708

Parental education predicts IQ change after epilepsy surgery in children

Meekes J, van Schooneveld MMJ, Braams OB, Braun K, Jennekens-Schinkel A, van Nieuwenhuizen O. *University Medical Center Utrecht, The Netherlands – meekes.joost@gmail.com*

Objective: To determine whether IQ change after epilepsy surgery in children is associated with environmental factors, specifically parental education (PE) or socio-economic status (SES). We focused on change (rather than pre- or post-surgical IQ per se) because cognitive effects of surgery are increasingly considered in the decision to operate. **Methods:** Retrospective cohort study of children (<18 years) who underwent epilepsy surgery between January 1996 and September 2010. Multiple regression analysis was used to identify predictors of change in IQ after surgery. To enhance interpretation of the results, we applied the same analysis to pre-surgical and post-surgical IQ. **Results:** The sample included 118 children (median age at surgery 9.73 years [range 0.47–17.70 years]). IQ change after surgery was significantly predicted by a model only including PE. Although there was large variation between children with equal PE, the average difference between lowest and highest levels of PE amounted to 12.18 IQ points (95% CI: 1.20–23.16). SES was also significantly associated with IQ change after surgery, but inclusion of SES in the model already containing PE yielded no further contribution to prediction of IQ change. A model including age at surgery, duration of epilepsy, etiology, and type of surgery significantly predicted pre-surgical IQ. The only significant predictors of post-surgical IQ, however, were pre-surgical IQ and PE, confirming the results concerning IQ change. **Conclusions:** For the first time, we demonstrate that, after paediatric epilepsy surgery, IQ increases most in children with highest PE or SES, whereas children with low PE or SES had smaller IQ increases or even decreases. Further study is required to determine whether this is due to differences in medical management, pre-existing disposition of the child or heterogeneity in post-surgical environments.

P60 - 1698

Survey on infantile spasm management and treatment outcomes in a tertiary hospital in Hong Kong

Yau MLY, Yam K-M, Fung ELW. *Department of Paediatrics, Prince of Wales Hospital, The Chinese University of Hong Kong, Hong Kong – maggie8419@yahoo.com*

Infantile spasm is usually refractory to conventional anti-convulsants. This study aims to study the management of patients with infantile spasm, their outcome and possible contributing factors. **Methods:** All newly diagnosed patients with infantile spasm from June, 2006 till December 2012 in Prince of Wales Hospital Hong Kong were reviewed. Their underlying eti-

ology, choice of treatment and seizure outcome were studied. **Results:** Total 12 patients were diagnosed with infantile spasm. The age of diagnosis ranged from two months to three years old (median: seven months). Majority (67%) of patients have underlying primary neurological disorders. Two of them have delayed treatment (five and six months) due to parental concerns on possible significant side effects. For initial treatment choice, four chose prednisolone, while seven chose vigabatrin and one chose conventional anti-convulsants. No patient was required to discontinue treatment due to side effects experienced. Four patients have achieved remission after one month of treatment (One in steroid group and three in vigabatrin group). Three with refractory seizure required ACTH treatment (not readily available in Hong Kong) with good response, achieving seizure remission on day four and day nine of treatment. Depending on etiology, three in idiopathic group (75%) remained seizure free (ranging from seven months to 47 months; median 25 months). However in those with primary neurological disorder, four remained seizure free (50%) (ranging from 17 months to four years; median 17 months). One who was refractory to anti-epileptic achieved remission after surgery was performed for removal of primary etiology. **Conclusion:** Idiopathic infantile spasm is a good prognostic indicator for outcome. In Hong Kong steroid phobia and ACTH availability remains an important issue towards the choice of treatment, which may have significant impact on seizure outcome.

P61 - 1697

Postictal psychosis: a rare entity in childhood epilepsy

Iqbal M, Prasad M, Baxter P. *Sheffield Childrens Hospital, Sheffield, UK – drmehtabch@yahoo.com*

Objective: To describe clinical presentation of Postictal Psychosis in a child who presented with a change in behaviour, hallucinations and confusion following cluster of seizures. **Material** (case description): 15 years old boy, known epileptic on Levetiracetam, presented with hallucination and confusion after having cluster of seizures. Interestingly there was a clear history of him remaining well for nearly 24 hour followed by onset of hallucination where he was complaining of seeing “red blood on arm” and seeing flashing lights and at times shouting. On examination his GCS was 15/15, looked confused, not answering questions but following commands. Rest of neurological examination was unremarkable. Initial investigations including ammonia, CSF and blood lactate, CSF/plasma glucose ratio, plasma aminoacids were all normal. EEG didn’t show any epileptic discharges or evidence of subclinical status and background EEG showed rhythmic slow waves mostly in posterior region. Levetiracetam level came back as nearly 2 times the normal range. However he was on the same dose (2 gm) for nearly 3 months with no reported side effects. He remained in-patient for 2 days; his psychotic symptoms slowly improved and didn’t need any specific treatment. His dose of Levetiracetam was subsequently reduced in view of the high levels. **Results:** Postictal psychosis is well known in adults but only sparsely reported in paediatric population. It usually occurs after prolonged partial complex seizure clusters with or without secondary generalisation. The psychosis commonly appears following a lucid interval, ranging from a few hours to days after seizure termination. Early recognition is important as suicidal tendencies have also been reported in adults. **Discussion:** We believe that the Paediatric Neurologist should be aware of this rare but distinct entity as early diagnosis helps in treating the patient effectively and alleviating patient and parents anxiety and also prevent unnecessary investigations.

P62 - 1678

Benign convulsions with mild gastroenteritis in young children: a retrospective clinical study

Kim DW, Kwon YS. *Department of Pediatrics, Inje University Ilsan Paik Hospital, Goyang, Korea – dwkim@paik.ac.kr*

Objectives: The so-called Benign convulsions with mild gastroenteritis (BCwMG), known as non-febrile seizures associated with gastroenteritis without dehydration or electrolyte imbalance in young children aged almost 6 months to 3 years, has been reported relatively more frequently in the Far East. Because its seizures are non-febrile and can occur repeatedly, it can be misdiagnosed as epilepsy. Therefore, understanding of its clinical characteristics is thought to be important. This study was carried out to investigate clinical features of BCwMG. **Material and methods:** From January, 2008 to December, 2012, thirty-four patients with BCwMG were admitted at Department of Pediatrics, Inje University Ilsan Paik Hospital in Korea. We reviewed their medical records to investigate and analyze their clinical features. **Results:** Out of 34 patients with BCwMG, 26 were boys and 10 girls. Of 34 patients, 28 (82.4%) patients were between 1 and 2 years of age. Generalized seizure was observed in all 34 patients. The duration of seizure was between 10 seconds and 10 minutes. Mean seizure frequency was 1.9 times (range, 1–5 times). Two or more seizures occurred in 20 patients (58.8%). All patients had seizures after the onset of gastroenteritis. All seizures occurred within the first 5 days of gastroenteritis. Rotavirus antigen was positive in stools in 16 out of 24 patients (66.7%). **Conclusions:** From our results, seizures in BCwMG were mostly brief and generalized and usually occurred as a cluster of episodes in young children aged 1 to 2 years. Seizures occurred within the first 5 days of gastroenteritis. The proportion of positive Rotavirus antigen was more than half.

P63 - 1669

Rufinamide as adjunctive drug in refractory epilepsy due to neuronal migration disorders

Coppola G, Moavero R, Cusmai R, Spalice A, Battaglia D, Verrotti A, Matricardi S, Pruna D, Parisi P, Curatolo P. *Salerno University, Italy – rominamoavero@hotmail.com*

Objective: To evaluate the efficacy and tolerability of add-on Rufinamide in children with refractory epilepsy symptomatic of neuronal migration disorders. **Material and methods:** We recruited 69 patients in a prospective, open-label, add-on treatment study from 8 Italian centers for pediatric and adolescent epilepsy care according to the following criteria: age 3 or above; focal or generalized seizures refractory to at least three previous antiepileptic drugs (AEDs), alone or in combination, secondary to neuronal migration disorders; two or more seizures per month in the last 6 months; use of another AED, but no more than three, at baseline. Informed consent from parents and/or caregivers was obtained at the time of enrollment. **Results:** We enrolled 69 patients with a mean age of 15 years (range 3–43). Forty-three patients (62%) had a 50–99% seizure reduction, and two (3%) became seizure-free. Seizure frequency was unchanged in 18 (26%) and worsened in 6 (8.7%). Twenty-nine patients (42%) reported adverse side effects, whilst taking rufinamide. Irritability was the most common side effect (11 patients), followed by decreased appetite (10), mood shift (6), vomiting (5), drowsiness (4), and decreased attention (2). Blood levels of concomitant anticonvulsive drugs were transiently abnormal in 5 patients. **Conclusion:** In our population of severely refractory epilepsy due to neuronal migration disorders, Rufinamide appeared to be effective and generally well tolerated.

P64 - 1656

Clinical course and outcome of idiopathic childhood epilepsy: determinants of early and long-term prognosis

Dragoumi P, Tzetzis O, Vargiami E, Pavlou E, Krikonis K, Kontopoulos E, Zafeiriou DI. *1st Department of Pediatrics, Aristotle University of Thessaloniki, Greece – jeff@med.auth.gr*

Objectives: To study the clinical course and outcome of idiopathic childhood epilepsy and identify variables determining both the early and long-term prognosis. **Methods:** We followed 303 children with newly diagnosed idiopathic epilepsy both prospectively and retrospectively. Outcome was defined at one, 2 and 4 years of follow-up, as well as at the end of the study period for all patients. Based on the data collected, patients were classified in four patterns of clinical course: “excellent”, “improving”, “relapsing” and “poor”. Variables defined at intake and after the initial year of treatment were analyzed for their prognostic relevance towards the clinical course and outcome of the patients, using both univariate and multivariate statistical analysis. **Results:** The mean age at seizure onset was 6.7 years and the mean duration of follow-up was 8.3 years (range 2.0–22.0, SD 4.24). During the initial year of treatment, 70.3% of patients were seizure-free. The course of epilepsy was “excellent” in 53.1% of the subjects, “improving” in 22.8%, “relapsing” in 22.1% whereas only 6 children with idiopathic epilepsy (2%) had a “poor” clinical course exhibiting drug-resistance. Variables predictive of a poor initial response to therapy ($p < 0.05$) were early seizure onset, multiple seizure types, history of febrile seizures, status epilepticus and sleep disorders. At the end of follow-up, variables of predictive value were the presence of multiple seizure types and a history of migraine or sleep disorders. **Conclusions:** In the vast majority of children, the long-term prognosis of idiopathic epilepsy is favorable. More than half of the patients attain seizure freedom immediately and their clinical course is considered “excellent”. About one fifth exhibit either an improving or a fluctuating course. Early seizure onset, multiple seizure types, history of febrile seizures, status epilepticus and sleep disorders are predictive of an initial poor response to treatment in children with idiopathic epilepsy.

P65 - 1653

Neurodiagnostic evaluations for differential diagnosis of syncope or epilepsy

Kim M-J, Yum M-S, Kim E-H, Choi H-W, Ko T-S. *Division of Pediatric Neurology, Department of Pediatrics, Asan Medical Center Children's Hospital, Seoul, Korea – tsko@amc.seoul.kr*

Background: In children who visits outpatient clinic with history of loss of consciousness (LOC), the clinical diagnosis of seizure or syncope is always challenging issues to the pediatricians and child neurologists. We evaluated the differences between epilepsy and syncope in clinical features and laboratory tests to find a clue to help the diagnosis. **Methods:** We retrospectively reviewed the medical records of children who visited pediatric neurology in Asan Medical Center with history of LOC from 2007 to 2011. Patients with insufficient clinical history or laboratory data were excluded. Diagnosis of syncope or epilepsy was done in three different steps; clinical diagnosis by history taking, laboratory diagnosis depended on EEG and tilt test, and final diagnosis putting laboratory results, treatments and follow-up episodes together. The clinical symptoms, result of EEG, EKG and tilt tests and prognosis of each final diagnosis were compared. The correlation between final diagnosis and clinical or laboratory diagnosis was also calculated. **Results:** Total 86 children (45 boys, mean age; 13.2 years) were reviewed. Seventy of 86 children (83%) were diagnosed as syncope, 8 (10%) syncope with epilepsy, 6 (7%) epilepsy, and 2 unclassified. Mean age at diagnosis, underlying disease, preceding symptoms, EKG and brain MRI findings were not significantly different among groups. Before diagnosis,

the mean number of episodes was 3.2 ± 5 without significant difference between groups. During follow-up periods after final diagnosis, the mean number of episodes were more frequent in epilepsy group (1.2 ± 3.8 vs 10 ± 10.3 , $p < 0.001$). The correlation coefficient of final and clinical diagnosis was higher than that of final and laboratory diagnosis ($k = 0.580$ vs $k = 0.425$, $p = 0.001$). **Conclusion:** In this study, clinical history is more helpful than the laboratory data for the diagnosis of patients with LOC. However history taking and laboratory data are not definitive but important for the differential diagnosis of seizure or syncope.

P66 - 1652

Benign familial neonatal seizures was confirmed through array CGH in twins

Kim SK, Lee JH. Hwa sung, Korea – pedkimsk@gmail.com

Introduction: Benign familial neonatal seizure (BFNS) is an autosomal dominant inherited form of epileptic syndromes in newborns. It begins in the first few days of life and usually goes away within 4 to 6 months. Mutations in two genes, KCNQ2 and KCNQ3 that are related to potassium channels, have been found to cause BFNS. The authors came across a case of BFNS in twins whose mutations of KCNQ2 genes were confirmed through array CGH. **Case:** Twin brothers were healthy boys without any medical findings, but they had been hospitalized in neonatal center after their birth. From the fourth day of life, more than 10 times asymmetric tonic seizures daily with apnea were observed in the twins. The blood gas analysis and blood tests including electrolyte and biochemistry tests during the seizures were all normal. The MRI result showed normal findings. A significant epileptiform discharge was not observed in EEG reading. The result of tandem mass screening, which could exclude any metabolic diseases, was also normal in both of them. The BFNS was suspected considering clinical findings, so array CGH was performed using twin's peripheral blood. The result showed KCNQ2 gene partial deletion was confirmed on chromosome 20 and they were diagnosed as BFNS. Phenobarbital was injected intravenously on the first day from the seizure for both of them and changed to oral medication upon their discharge from the hospital, as there had been no seizure. Both have been observed through outpatient clinic without any medication so far. **Conclusion:** The authors report that the BFNS case in twins whose partial deletion in KCNQ2 gene on chromosome 20 was confirmed through array CGH.

P67 - 1636

Generalized seizures in early childhood: clinical features and differential diagnosis

Nechay A. Neurology department, Paediatric Hospital No1 of c.Kiev, Ukraine – allanechay@ukr.net

Objectives: Diagnosis and differential diagnosis of generalized seizures in early childhood is one of important task for paediatric neurologist. Hyperdiagnosis of epilepsy still happen in up to 30%. **Material and methods:** Retrospective study of medical notes of 142 children aged 1 month–3 years hospitalized to tertiary medical institution for evaluation of generalized paroxysms suspicious for epilepsy during 2009–2011. **Results:** Generalized epileptic seizures were diagnosed in 73 (51.4%), in 69 (48.6%) – non-epileptic events. Generalized epileptic seizures mainly started during first 6m of life (56.2%); non-epileptic events – mainly between 7 and 12m – 44.9%. 56 (76.7%) children with generalized epileptic seizures had neurological deficit, whereas all but one with non-epileptic events performed normal neurological examination. Frequency of events was statistically higher in children with epileptic seizures (>1 per day in 72.6%). Provoking factors were typical for non-epileptic events (94.2%), but also happen in children with epileptic seizures (12.3%). Family history was

positive for same condition in 20.2% with non-epileptic events and in 6.8% with epilepsy. 67 (91.8%) children with epileptic seizures and 12 (17.4%) with non-epileptic events had abnormal interictal EEG. Early debut and brain abnormality correlated with severer epilepsy. In 40 children specific electro-clinical syndromes were diagnosed: in 33 (82.5%) – West syndrome, in 3 (7.5%) – Othahara syndrome, in 2 – Lennox-Gastaut syndrome in 1 – Doose syndrome, in 1 – benign myoclonic epilepsy. Among non-epileptic events prolonged expiratory apnea was the most frequent condition (72.5%), reflex anoxic seizures were diagnosed in 20.3%, gratification – in 5.8%, Sandifer syndrome – in 2.9%, stereotypical behavior, benign myoclonus of sleep, benign tonic upgaze – in 1.4% each. **Conclusions:** Paroxysmal events suspicious for generalized epilepsy happen often in early childhood, leading to hospitalization, though many are of non-epileptic origin. Careful anamnestic and clinical evaluation is essential for correct diagnosis especially in case of limited access to video-EEG and its low efficacy in children with rare events.

P68 - 1631

Fine motor skills in children with benign rolandic epilepsy

Ayaz M, Kara B, Soylu N, Ayaz AB. Sakarya Training and Research Hospital Child and Adolescent Psychiatry, Turkey – ayazmuhammed@yahoo.com

Fine motor skills in children with benign rolandic epilepsy Abstract The aim of the present study was to evaluate fine motor skills in children with benign rolandic epilepsy (BRE) and healthy controls in order to investigate the relationship between fine motor skills, and seizure and treatment parameters in children with BRE. The study included 44 children aged ≥ 8 diagnosed as BRE and 44 age- gender-, and level of education-matched controls. Fine motor skills were evaluated using the Purdue Pegboard Test (PPT) and intelligence was measured using the Wechsler Intelligence Scale for Children (WISC-R). All PPT subtest scores in the BRE group were lower than those in the control group. After performing covariance analysis to control for the effect of intelligence level (WISC-R overall score) on motor skills, the difference between groups in PPT dominant hand, both hands, and assembly subtest scores persisted. Epileptic focus, treatment status, the type of antiepileptic treatment, age at the time of first seizure, time since the last seizure, and the number of seizures did not affect motor skills. In the present study, it was demonstrated that BRE was associated with impaired fine motor skills, independent of intelligence level, and the observed impairment was not associated with seizure parameters.

P69 - 1630

Efficacy of sublingual lorazepam versus intrarectal diazepam for prolonged convulsions in Sub-Saharan Africa

Kaputu KMC, Mukeba KD, Walker TD, Mukampunga C, Mafuta ME, Kokolomani J, Dubru J-M, Mukendi KMR, Misson J-P. Service of Child Neurology, Mons, Belgium – ckaputukalalimalu@gmail.com

Background: In Sub-Saharan Africa, intrarectal diazepam (DZPIR) is the first-line recommended anticonvulsant agent used in the emergency management of children with convulsions. We aimed to assess this standard care to sublingual lorazepam (LZPSL), a drug that is potentially as effective, safer, and easier to administer. **Methods:** A randomized controlled trial was conducted in the paediatric emergency departments of 5 hospitals in Rwanda and 4 in Democratic Republic of Congo. 436 children aged between 5 months and 10 years with convulsions persisting for more than 5 minutes were randomly assigned to receive DZPIR (0.5mg/kg, $n = 202$) or LZPSL (0.1 mg/kg, $n = 234$). The primary outcome was cessation of convulsions within 10 minutes of administration of a single dose of the assigned medication. **Results:** LZPSL stopped

convulsions in 56.0% (131/234) of children treated and DZPIR in 79.2% (160/202; $p < 0.001$). The administration of LZPSL significantly increased the probability of treatment failure (OR=2.95, 95% CI 1.91–4.55). There was no statistically significant difference as far as 24 hour seizure recurrence and 24 hour mortality ($p=0$, 48 and $p=0$, 13 respectively) were concerned. **Conclusion:** LZPSL was less effective than DZPIR in terminating seizures within ten minutes of drug administration in this cohort of children with prolonged seizures. The ease of use of LZPSL still makes it an attractive treatment option where DZPIR is not rapidly available.

P70 - 1625

Vitamin B12, folic acid and homocysteine levels in children with febrile seizure

Ozkale Y, Erol I, Saygi S, Kılıçaslan B, Ozkale M, Sarıtürk C. *Baskent University Faculty of Medicine, Department of Pediatrics, Adana Teaching and Medical Research Center, Adana, Turkey – ilknur_erol@yahoo.com*

Objectives: Although febrile seizure is the most common brain-related disease in children, its pathophysiology is still unknown. Several studies have indicated that multiple factors can be involved in the pathogenesis of febrile seizure. This study was designed to address whether vitamin B12, folic acid and homocysteine have any role in developing febrile seizure. **Material and methods:** This prospective study enrolled 104 children who presented with febrile seizures and 73 children who presented with a febrile illness without seizures between October 2012 and March 2013. The serum levels of vitamin B12, folic acid and homocysteine were measured both from the febrile seizure and control groups. **Results:** The present study indicate that, the serum vitamin B12 levels of children with febrile seizure were significantly lower than that of febrile children without seizure. There was no significant difference in folic acid and homocysteine between the febrile seizure and control groups. On the other hand folic acid was significantly lower in the febrile seizure group who had more than three convulsion and who had a body temperature under 39 °C during convulsion. **Conclusions:** These data indicate that low body vitamin B12 levels may decrease the threshold of seizure and be a risk factor for the development of febrile seizures. In addition low folic acid levels appear to be associated with an increased risk of recurrence in febrile seizures.

P71 - 1624

Attention deficit and the associated clinical factors in children with benign childhood epilepsy with centrotemporal spikes (BCECTS)

Kim E-H, Yum M-S, Kim H-W, Ko T-S. *Division of Pediatric Neurology, Department of Pediatrics, Asan Medical Center Children's Hospital, Seoul, Korea – luke2178@naver.com*

Objectives: Children with epilepsy often experience attentional problems with less favorable outcomes. We assessed the attention in benign childhood epilepsy with centro-temporal spikes (BCECTS) and tried to identify the associated seizure variables which cause attentional problems. **Material and methods:** A total of 266 children were diagnosed with BCECTS at Asan Medical Center from 2004 to 2012. Among them, 93 children (57 males) who performed the formal attention test (ATA or CAT) were retrospectively reviewed. Clinical data including sex, age of seizure onset, seizure control, EEG findings, and response to treatment were analyzed to evaluate the association with attention deficit. **Results:** A mean age of seizure onset was 7.5 (3.3–13.3) years and mean follow-up duration after diagnosis was 3.4 (1–8.7) years. Of 93 patients, 63 (67.7%) were diagnosed as having attention deficit, including the inattentive type (32 cases, 50.8%) and the combined type (25 cases, 39.7%). The incidence of attention deficit was sig-

nificantly higher in children with a younger age of seizure onset (86.5% [3–6 years] vs 55.4% [7–14 years], $p=0.02$). However, other clinical factors, frequency and laterality of spike discharges on electroencephalogram (EEG), duration of treatment, seizure control were not associated with the incidence of attention deficit. And there was no factor related to attention quotient of visual or auditory selection. Eighteen patients (28.5%) were treated with central nervous system stimulants, and their epilepsy related factors and outcome were similar with those of patients without stimulant medication. There was no case with aggravated seizure after stimulants. **Conclusions:** Children with BCECTS have a high incidence of attention deficit and early onset of seizure was associated with this attention deficit. Therefore, systematic screening and proper management for attentional problems should be carried out in these patients.

P72 - 1622

Clinical experience of lacosamide as an adjunctive therapy in pediatric patients with refractory focal epilepsy

Kim JS, Park HJ, Kim H, Lim BC, Chae J-H, Choi J, Hwang YS, Kim KJ, Hwang H, Ryu HW. *Department of Pediatrics, Eulji University Hospital, Daejeon, Republic of Korea – pedneuro@eulji.ac.kr*

Purpose: To evaluate the efficacy and safety of lacosamide in pediatric patients with refractory focal epilepsy. **Methods:** We retrospectively reviewed the medical records of children younger than 18 years of age with oral lacosamide as an adjunctive treatment for refractory focal epilepsy at the Seoul National University Bundang Hospital. Clinical information regarding the characteristics of patient's epilepsy and outcome of lacosamide treatment was gathered and analyzed. **Results:** Twenty-two patients (17 boys and 5 girls) were included in the study, a mean age of 12.9 (range, 1.2–18.9 years). The mean number of concomitant AEDs was 3.0 (range, 1–6) and mean duration of follow-up was 10.1 months (range, 6.1–13.0 months). The mean maintenance dose was 5.4 mg/kg/day (range, 1.4–9.8 mg/kg/day). Fourteen patients (64%) were responder, four of these patients were seizure free at the latest follow-up. Six patients (27%) were non-responder: two of these presented with <50% seizure reduction and six had no change in seizure frequency. Two others (9%) discontinued the oral lacosamide because of adverse events (aggressive behavior and depression). Mild transient treatment-related adverse events were observed in 8 of the 22 patients (36%). **Conclusions:** Lacosamide represented a useful drug that is effective for a wide range of pediatric refractory focal epilepsy and was well tolerated.

P73 - 1621

Frequency of prenatal and neonatal complications in children with epilepsy in a tropical country

Dalbem JS, Siqueira HH, Alvarenga RP. *Federal University of Mato Grosso and Federal University of State Rio de Janeiro, Brazil – jsdalbem@hotmail.com*

Background: Epilepsy affects approximately 50 million individuals around the world, 90% of whom live in developing countries. It is estimated that 2.4 million new cases occur each year worldwide, with around 50% of these cases occurring in childhood and adolescence. **Objective:** Determine the frequency of prenatal and neonatal complications in a sample of children with epilepsy in a small town of Brazil. **Methods:** A cross sectional study was conducted in the mid-northern area of Mato Grosso, Brazil, in children of 0–14 years of age who had been diagnosed with epilepsy during 2010. **Results:** Sixty-five children with a diagnosis of epilepsy were evaluated, 53.8% males. The average age was 6.98 years. About 88% of whom lived in an urban area. In 73.9% of the patients, the first epileptic seizure occurred within

the first two years of life. In the prenatal and neonatal periods, 40% of the children had suffered complications such as hypoxia and epileptic seizures. Regarding the sex of the child, found a lower prevalence of complications in male children, this being statistically significant association (PR=0.51, CI95% = 0.29–0.96). Observed that lower maternal education and family income, the higher the frequency of neonatal complications (PR=0.60; CI95% = 0.33–1.08 and PR=0.45; CI95% = 0.26–0.78). Founded 2.34 times more the occurrence of neonatal complications among children with low birth weight (IC95% = 1.43–3.84). There were 1.51 times more occurrence of neonatal complications among children who were born at cesarean section, although not statistically significant. **Conclusion:** In developing countries improve in primary healthcare, including high quality prenatal care, care for the pregnant woman during delivery, and care and follow-up for the newborn infant may reduce structural and metabolic abnormalities and therefore the number of cases of epilepsy.

P74 - 1619

Clinical characteristics of gastroenteritis associated afebrile seizure in a tertiary hospital in Hong Kong

Yam K-M, Yau L-Y, Fung ELW. Department of Paediatrics, Prince of Wales Hospital, The Chinese University of Hong Kong, Hong Kong – ykkmkaren@gmail.com

Objective: To study the clinical characteristics of gastroenteritis associated afebrile convulsions in Hong Kong. **Method:** Medical records of healthy children who suffered from acute gastroenteritis with afebrile seizure from January 2011 to December 2012 in Prince Of Wales Hospital in Hong Kong were reviewed. Their demographic data, clinical features, pathogen identification and neurological outcome were studied. **Results:** Nineteen children with normal premorbid status suffering from gastroenteritis with afebrile convulsion were identified, including 9 males (47%) and 10 females (53%). Age ranged from 13 months to 12 years old (Median=18 months). All children enjoyed good past health except one had history of febrile convulsion. 14 (74%) were affected during summer months (June to September) with clustering of 7 cases (36%) in August 2012. All had satisfactory hydration except one with mild dehydration. Seizure occurred on day 2 to 5 of illness with 12 children (63%) having generalized tonic-clonic seizure and 7 (37%) having tonic seizure. 11 children had seizure recurrence, ranging from 1 to 4 times. They recurred within first 24 hours except 1 child had an attack 3 days later. The duration of seizure ranged from 10 seconds to 15 minutes (median=3 minutes). All children had serum electrolytes checked and only 2 had hyponatraemia down to 118mmol/L and 132mmol/L respectively. 17 children (89%) had stool results available with Norwalk virus isolated in 11 children (65%) and Rotavirus in 2 children (12%). 15 had neuroimaging, 6 had cerebrospinal fluid assay and 13 had electroencephalogram recording, which were all normal. All children did not require long term anti-epileptic treatment and had no subsequent admission for convulsion. **Conclusion:** Afebrile seizures associated with gastroenteritis are relatively common in Hong Kong. It comes in clusters and is mostly associated with Norwalk virus infection. The neurological outcome at discharge is generally favorable. But long-term follow up studies may help to clarify the outcome, especially in cases with prolonged seizures.

P75 - 1611

Midazolam oromucosal solution versus rectal diazepam for prolonged acute convulsive epileptic seizures: Italian cost-effectiveness analysis

Lee D, Anelli M, Gladwell D, Saunders A. BresMed, Sheffield, UK – dlee@bresmed.co.uk

Objectives: Current care in Italy for first-line treatment of

seizures in the community is rectal diazepam, but carers are reluctant to use this due to patient dignity and social acceptability issues. BUCCOLAM® (midazolam oromucosal solution) is indicated for the treatment of prolonged, acute, convulsive seizures (PACS) in children and may be used by parents and other carers in a community setting where a child has been diagnosed with epilepsy. A decision-tree model was developed to assess the cost-effectiveness of BUCCOLAM compared to rectal diazepam for the treatment of PACS occurring in the community. **Material and methods:** The model allows different treatment options, including whether or not (1) a carer administers treatment, (2) an ambulance is required and patients are taken to hospital, and (3) inpatient stay is required. The primary outcomes are the cost impact of PACS, including emergency care and hospitalisation costs, and health-related quality of life. Efficacy and effectiveness data were obtained from McIntyre et al (2005) and a Delphi panel. Costs were taken from Italian national databases. The price of BUCCOLAM was taken from the Gazzetta Ufficiale. Rectal diazepam is not reimbursable therefore its cost is not included. **Results:** Clinicians estimated that compared to rectal diazepam BUCCOLAM would increase the likelihood of successful treatment, and therefore reduce ambulance call-outs and hospital stays. It is predicted to save €1,540 per patient and improve quality-adjusted life years by 0.003 over 1 year. At an uptake of 10% of eligible patients this would deliver cost savings of €8–17 million over 1 year. **Conclusions:** Treatment with BUCCOLAM reduces the requirement for emergency and hospital care and is cost saving compared to rectal diazepam. More patients are successfully treated at seizure onset in the community due to reduced concerns surrounding patient dignity and an easier administration route.

P76 - 1607

Guidelines on the management of prolonged acute convulsive seizures in out-of-hospital settings: a gap to be filled

Lagae L, Arzimanoglou A, Beghi E, Bennett C, Cross HJ, Mifsud J, Schmidt D, Wait S, Harvey G. KULeuven, Neuro-musculo-skeletal Research Unit, Leuven, Belgium – suzanne@shwhealth.co.uk

Objectives: Prolonged acute convulsive seizures require immediate treatment with benzodiazepines in order to prevent their progression to status epilepticus. Most seizures occur outside of the hospital, thus practical guidance is needed for non-medically trained caregivers who wish to administer rescue medication in out-of-hospital settings. The purpose of this paper is to determine whether existing clinical guidelines on the management of prolonged acute convulsive seizures in children contain such guidance. **Material and methods:** As part of the Practices in Emergency and Rescue medication For Epilepsy managed with Community administered Therapy (PERFECT) initiative, a pragmatic review of the published literature and of professional society websites was undertaken to identify national relevant clinical guidelines in France, Italy, Germany, Spain, Sweden, and the United Kingdom. All searches were conducted in English and local languages. **Results:** Most existing guidelines focus on the hospital setting. Only the UK guidelines specify that all non-medically trained caregivers should receive dedicated training and that all children with a history of prolonged seizures should have an individualised healthcare plan. All guidelines recommend treatment of prolonged seizures after 5 minutes with either rectal diazepam or buccal midazolam, depending on availability of these medicines and, in some countries, on patient preferences. Different specialties (neurology, paediatric neurology, intensive care medicine) were involved in drafting guidelines depending on the country. **Conclusions:** Most existing guidelines do not provide practical recommendations to caregivers in out-of-hospital settings on the administration of rescue medication. Filling this gap is critical to ensure that children at

risk of prolonged acute convulsive seizures receive their rescue medication quickly and safely regardless of where their seizure occurs, thereby avoiding unnecessary treatment delays, clinical sequelae and costly admission to hospital.

P77 - 1597

Clinical spectrum and treatment outcome of children with West syndrome in children from northern India

Kaushik JS, Patra B, Sharma S, Aneja S. *Department of Pediatrics, Lady Hardinge Medical College and Kalawati Saran Children Hospital, New Delhi, India – jayashankarkaushik@gmail.com*

Objective: This study was intended to document the clinical profile and treatment outcome of West syndrome in children attending a tertiary care center in Northern India. **Material and methods:** Data were collected by a retrospective chart review of children admitted with a diagnosis of West syndrome between January 2008 and January 2012. Information was recorded pertaining to clinical profile, age at onset and presentation, etiology, and associated co-morbidities; result of electroencephalography (EEG) and neuroimaging; treatment given; and final outcome. The following drugs were used to control spasms: pyridoxine, prednisolone, vigabatrin, sodium valproate, nitrazepam, topiramate, and levetiracetam. The response to drugs was categorized as spasm cessation, partial improvement (>50% improvement), or no improvement. The final outcome was considered favorable when there was a complete cessation of spasms; with absence of relapse and no progression to other seizure types for at least subsequent 6 months. **Results:** Records of 148 children (120 boys) were retrieved and analyzed. The mean (SD) age at onset and presentation was 5.3 (4.6) months, and 13.1 (7.3) months, respectively. The majority of the children had delayed development (92.5%). Perinatal asphyxia (61.4%), neonatal sepsis/meningitis (10.6%), and postnatal meningitis (11.4%) were the predominant causes. The etiology could not be ascertained in 16.6% of children. Favorable outcome was observed in 45 (30.4%) children with spasm cessation rate of 25.4% with prednisolone. Age at onset, gender, time lag to treatment, presence of perinatal asphyxia, or comorbid cerebral palsy did not affect the final outcome. **Conclusion:** This study highlights the developing country perspective of children with West syndrome, including delayed presentation, adverse perinatal events as the predominant etiology, and modest response to oral steroids.

P78 - 1596

The cost effectiveness of midazolam oromucosal solution for the treatment of prolonged acute convulsive epileptic seizures in France

Lee D, Porter J, Tate E, Saunders A. *BresMed, Sheffield, UK – dlee@bresmed.co.uk*

Objectives: BUCCOLAM® (midazolam oromucosal solution) is indicated for the treatment of prolonged acute convulsive seizures (PACS) in children. A cost-utility model demonstrates the incremental value of BUCCOLAM compared to current treatments administered in the community setting for children with epilepsy in France. **Material and methods:** Clinical events following seizure onset were simulated using a decision-tree model. The primary outcomes are the cost impact of PACS, including expected ambulance call-outs, emergency hospital visits and inpatient hospitalisation, and health-related quality of life (HRQL). Efficacy data were obtained from a published study of 177 children suffering 219 separate seizure episodes. A Delphi survey of French clinical experts provided estimates of how choice of rescue medication influences events in the community setting. Resource use costs were obtained from the National Security Agency of Medicines and Health Products and French social security databases.

Results: Clinician responses defined current care as rectal diazepam (92%) and clonazepam (8%) and estimated that treatment with BUCCOLAM would result in an increased chance of successful treatment in the community setting compared to current care, reducing the requirement for emergency services and hospital resource use. Compared to current care, BUCCOLAM showed a cost saving of €2,637 and an increase in HRQL by 0.0002 quality-adjusted life years over 1 year. Similar savings were expected compared to rectal diazepam alone. **Conclusions:** Treatment with BUCCOLAM reduces the requirement for emergency and hospital care and is cost saving compared to current medications. More patients are successfully treated at seizure onset due to: Fewer dignity concerns and an easier administration route compared to rectal preparations. Licence wording that specifically allows caregivers and teachers to administer treatment; previously they may not have felt able to do so or were not permitted to. Improved or equal efficacy in stopping seizures and preventing recurrent seizures.

P79 - 1579

Role of EEG in diagnostic of focal epilepsy

Kušar M, Kirevski M. *Ljubljana, Slovenia – marija.kirevski@gmail.com*

Aim: Up to 60% of patients with focal epilepsy may manifest pharmacoresistance and more than half of them may be candidates for epilepsy surgery. Goal of resective surgery aims at the complete resection of epileptogenic zone while sparing eloquent cortex. Epileptogenic zone is the cortical area responsible for generating epileptic seizures. The neurophysiology assistant should have enough knowledge and experience and above all must be able to identify and recognize all abnormalities of brain electrical activity, observe patient clinical manifestation and perform age appropriate testing of patient during the seizures. For this presentation we reviewed focal epileptic discharges in EEG recordings of paediatric patients who underwent resective surgery. **Methods and patients:** By assessing ictal and interictal EEG, as well as ictal semiology the neurophysiology assistant can help to predict possible epileptogenic zone. Careful analysis of patient's symptoms and signs during seizure allows neurophysiology assistant to estimate the putative symptomatogenic zone. With scalp EEG he can record interictal and ictal epileptiform discharges that gives us information of epileptogenic zone, but if epileptogenic focus is restricted, obscured or inaccessible to recording scalp electrodes, we can use additional scalp electrodes and/or invasive recording is required. Some examples of different types of ictal and interictal EEG patterns in focal epilepsies in children will be presented. All EEG studies were recorded in patients who were referred from Ljubljana, Department of Child, Adolescent and Developmental Neurology, for resective surgery to major epilepsy centers in Europe. **Conclusions:** Diagnosing of focal epilepsy in children is challenging because of EEG maturation and also because of occurrence of specific focal epileptic patterns during different paediatric periods. From our review of cases we aim to present all the complexity of various patterns of focal epilepsy in different age group.

P80 - 1574

Dyskinesia as a new adverse effect of hormonal treatment in West syndrome

Sukhudyan B, Dimova P, Vigevano F. *"Arabkir" Medical Complex and Institute for Child and Adolescent Health, Yerevan, Armenia – biayna_sukh@yahoo.com*

Objectives: West syndrome is an age-dependent epileptic encephalopathy. Besides its potential harm, hormonal therapy remains main treatment in West syndrome. Here we report on 9 patients with appearance of unusual mostly hyperkinetic move-

ments on treatment. **Material and methods:** In this retrospective observational study we looked at patients who developed unusual movements during steroid therapy for West syndrome. Inclusion criteria were infants with spasms, hypsarrhythmia in EEG and occurrence of hyperkinetic movements on hormonal therapy. **Results:** Facial grimacing, repetitive mouth opening, adduction and abduction of upper and lower extremities and periodical strabismus in different combinations were observed in all patients independently on formulation, dose, duration and efficacy of treatment. They disappeared in sleep and reappeared immediately on arousal. They interfered with feeding and emotional smile; involuntary eye muscle movements made an impression of absent visual fixation. However, tube feeding was never required. Hyperkinesia in extremities interfered with voluntary movements. Dyskinesias stopped gradually in a month after discontinuation of treatment. Repeated EEGs did not show correspondent epileptiform activity. In 3 patients, besides dyskinesic movements we observed sustained retro- and torticollis. In all cases we registered disappearance of hypsarrhythmia, although control of spasms was not always satisfactory. A specific cause of West syndrome was identified in only 4 patients. Genetic testing in one and medical history (severe birth asphyxia) and clinical data (microcephaly, spastic tetraparesis) in another helped to establish genetic and structural causes of West syndrome, respectively. A structural origin of West syndrome was proved by brain MRI investigations in 2 patients with multiple focal dysplasias and severe brain atrophy of unknown origin, respectively. **Conclusion:** We conclude these abnormal movements can be attributed to side effect of hormonal treatment.

P81 - 1571

Intravenous levetiracetam for continuous spike and wave during slow sleep

Shinhye K. Myongji Hospital, Goyang, Korea – shine7991@naver.com

A 6-year-old girl visited the pediatric clinic for hematemesis during sleeping. She had been grown up without significant health problems until she was rescued from drowning in swimming pool two weeks before having seizure. She was performed cardiopulmonary resuscitation for 7 minutes immediately after noticed by lifeguard. On brain MRI after treated for aspiration pneumonia, no abnormal signals were seen. On neurologic examination, abnormal focal neurologic signs were not shown. Her mother reported her hematemesis with decreased responsiveness during sleeping, only two weeks later, when she visited my clinic second time. On electroencephalography, nearly consistent spike and wave discharges was seen during sleeping, her mental status was stupor, that we urgently started intravenous levetiracetam, 20 mg/kg and maintained it with 20 mg/kg/day and titrated with 10 mg/kg/day until 40 mg/kg/day. After two days of intensive care, epileptiform discharges disappeared and she could communicate fluently and was improved to alert mental status. On the second brain MRI on recovering state, abnormal signals were not found on T1, T2 and FLAIR images, either. **Conclusion:** Levetiracetam can be effective treatment option in children for continuous spike and wave discharges during slow sleep as we described.

P82 - 1567

The efficacy and safety of levetiracetam in pediatric patients treated with chemotherapeutic agents for hematologic disorders

Bayram E, Topcu Y, Tufekci O, Karaoglu P, Yis U, Oren H, Hiz SK. Dokuz Eylul University Hospital, Division of Pediatric Neurology, Izmir, Turkey – dr.erhanbayram@yahoo.com

Purpose: We aimed to describe the efficacy and safety of levetiracetam in pediatric patients receiving chemotherapy for hema-

tologic disorders. **Material and methods:** Children with hematologic disorders who were receiving chemotherapy agents and developed seizure during treatment and treated with levetiracetam were included in the study. The clinical data of the patients were retrospectively evaluated. Primary hematologic diagnosis, chemotherapeutic agents, age at first seizure, seizure type, interictal electroencephalography findings, magnetic resonance imaging findings, response to the levetiracetam treatment, dose of levetiracetam, levetiracetam side effects and treatment period were recorded. **Results:** Ten patients with a mean age 12.4 ± 2.96 years were included in the study. Possible triggering factors for seizures were chemotherapeutic agents in 60% (n=6), posterior reversible encephalopathy syndrome in 20% (n=2) and central nervous system involvement of the primary disease in 20% (n=2). Nine patients received levetiracetam monotherapy and one patient received levetiracetam that was added on oxcarbazepine due to the intractable seizures. The mean duration of antiepileptic treatment that overlapped with chemotherapy was 7.3 ± 3.5 months. Nine patients (90%) were seizure free after levetiracetam monotherapy and one patient (10%) had $\geq 50\%$ seizure reduction after levetiracetam who was previously treated with oxcarbazepine. No side effects were observed for levetiracetam during treatment. **Conclusion:** Levetiracetam treatment is safe and effective to prevent seizures in children receiving chemotherapy for hematologic disorders.

P83 - 1562

Epilepsy and autoimmunity in pediatric patients

Bektaş Ö, Jacobson L, Tutkak H, Karagöl S, Lang B, Clover L, Vincent A, Deda G. Department of Pediatric Neurology, Ankara University Medical School, Ankara, Turkey – gulhisdeda@gmail.com

Aim: Anti-epileptic drugs are used as the main treatment of epilepsy. However, one-third of epilepsy patients do not respond to antiepileptic drugs. In addition, a large portion of epilepsy etiology is still unknown. Our aim was determine the role of the autoantibody, and autoimmunity in epileptic patients with undetermined etiology. **Material and methods:** One hundred subjects (80 patients, 20 healthy controls), who were referred to the Pediatric Neurology Department at Ankara University between November 2011 and April 2012, were enrolled in the study. ANA, anticardiolipin IgG, antiphospholipid, anti-thyroid peroxidase, anti-paraneoplastic antibodies (Hu, Ma2, CV2/CRMP5, Yo, Ri ve amplicilin), GAD, and anti-N-methyl-D-aspartate receptor antibodies were studied in our university laboratory. Additionally anti-NMDA and voltage-gated potassium channel-complex antibody (LG11 and CASPR2 in the VGKC antibody) were studied by Oxford University Immunology Laboratory. **Results:** The study included 44 girls (44%) and 56 boys (56%) with a mean symptom age of 8.6 ± 4.53 years (range: 9 months–18 years). ANA was positive in 15 (18.8%), antiphospholipid Ab in 3 (3.75%), anticardiolipin Ab in 1 (1.25%), anti-thyroid peroxidase in 3 (3.75%) epilepsy patients. Additionally anti-GAD Ab was positive in 7 (8.75%), anti-Yo Ab 3 (3.75%), and anti-Ma2 in 3 (3.75%) epileptic patients. Anti-VGKC was positive in 6 (7.5%) epileptic patients. None of the patients were positive for anti-LG11, CASPR2 and NMDA. In 32 (40%) of 80 patients with epilepsy had at least one antibody positivity, whereas it was 3 (15%) in control patients ($p=0.039$). **Conclusion:** We performed a pioneer study to investigate the association of autoimmunity and pediatric epilepsy and we believed that autoimmunity should be considered in epileptic patients with undetermined etiology.

P84 - 1546

Metabolic syndrome in children with epilepsy on valproate and phenytoin monotherapy: a cross-sectional study

Dhir A, Sharma S, Aneja S. *Lady Hardinge Medical College and Kalawati Saran Children's Hospital, Gurgaon, India – aditi.dhir0201@gmail.com*

Background: Metabolic syndrome is a well recognized complication of valproate therapy. However there is paucity of data on the prevalence of metabolic syndrome in children with epilepsy on valproate monotherapy. **Objective:** To compare the prevalence of metabolic syndrome between children on valproate and phenytoin monotherapy. **Methods:** Children aged 3–16 years with epilepsy on valproate or phenytoin therapy for at least 6 months were enrolled. They were evaluated for the presence of abdominal obesity, dyslipidemia, glucose intolerance and hypertension. Metabolic syndrome was diagnosed when 3 of the following criteria were met: elevated fasting glucose (>100 mg/dl), hypertension, high triglyceride levels or abdominal obesity. The prevalence of metabolic syndrome and abnormalities in the individual parameters were compared between the two groups. **Results:** Four out of 57 valproate-treated children (41 males, 16 females) and none of the 53 phenytoin-treated children (37 males, 16 females) had metabolic syndrome. The baseline characteristics including age and duration of therapy were comparable in both groups. Mean serum triglyceride levels were higher in the valproate group as compared to the phenytoin group (94.97 ± 38.58 mg/dl versus 77.60 ± 11.44 mg/dl, $p < 0.05$). The total cholesterol values were also significantly greater in valproate treated children as compared to the phenytoin group (148.28 ± 25.95 mg/dl versus 132.83 ± 23.51 mg/dl, $p < 0.05$). The serum fasting glucose was not significantly different in the two groups. **Conclusion:** The prevalence of metabolic syndrome and dyslipidemia was higher in valproate treated children as compared to phenytoin treated children with epilepsy. Children on valproate treatment need to be monitored for the development of metabolic syndrome.

P85 - 1545

Myoclonic-astatic epilepsy: seizures outcome

Shoukry I, Girgis MY, Abdel Ghaffar HM. *Cairo University, Egypt – npcibrahim@yahoo.com*

Objectives: Myoclonic astatic seizures have variable course and outcome. Spontaneous remission with normal development has been observed in some untreated cases of MAE. The purpose is to follow the outcome of MAE in relation to treatment modalities and associated seizure phenotypes. **Material and methods:** Thirty children with MAE of idiopathic etiology with mean age at seizure onset 27 ± 11.6 months; (24 males, 6 females) from neuropediatric unit Cairo University. Twenty percent had family history for epilepsy and 13.3% for febrile seizures. Digital EEG and MRI brain were done for all. **Results:** Patients were classified into 2 groups, group1 with complete seizure remission (76.6% $n=23$) and group2 (23.3% $n=7$) with ongoing seizures despite appropriate treatment over at least 6 months. Presenting seizure type was MAE in 66.6%, while GTCs and astatic seizures in 23.3% and 6.6% respectively. In group1, 44% had only one type of seizure namely myoclonic astatic while 56% had more than one type GTCs, absence or atonic fits. In group 2, 100% had more than one seizure type (p -value 0.033). EEG was normal in 40% of group1. Valproic acid was the most frequently used AED (83.3%) with the highest remission rate (80%) followed by clonazepam, lamotrigine, ethosuximide respectively. In group 2, 100% were on polytherapy while 26% of patients in group1 achieved complete remission on monotherapy. Sixty four percent were achieving normal development; most of them belonging to group1. **Conclusion:** The overall prognosis, despite initial resistance to treatment, is good. The outcome is not dependant on age of seizure onset, severity of EEG findings

or duration of disease before remission. It is highly dependent on variability of seizures with worse prognosis when more than one seizure type occurred. The seizures switch off (remission) can occur at any time of the disease.

P86 - 1541

Prevalence of genetic polymorphisms of UGT1A6 and their association with serum valproate levels in north Indian children with epilepsy on valproate monotherapy

Jain P, Gulati S, Shastri S, Kabra M, Gupta YK, Pandey RM, Gupta N. *Division of Pediatric Neurology, AIIMS, Delhi, India – puneet_mpa@yahoo.com*

Objectives: There is marked inter-individual variability in the pharmacokinetics and pharmacodynamics of valproate. Polymorphisms in UGT1A6, one of the major enzymes involved in the hepatic glucuronidation of valproate, may partly explain this. This study aimed to assess the association between the genetic polymorphisms of UGT1A6 in Indian children with epilepsy and the pharmacokinetics of valproate. **Methods:** This cross-sectional study was carried out in the Department of Pediatrics, AIIMS, New Delhi, between March 2011 and July 2012. Children aged 3–12 years of North Indian Origin diagnosed as epilepsy on valproate monotherapy for at least 1 month were enrolled. They underwent a detailed clinical examination as per a pre-designed proforma. The UGT1A6 polymorphisms were detected by PCR-restriction fragment length polymorphism. Random samples were checked by genetic sequencing. The steady state plasma concentrations of valproate were measured by High Performance Liquid Chromatography (HPLC) and associated with UGT1A6 polymorphisms. **Results:** The most common etiological causes of epilepsy were neurocysticercosis (37.5%) and cerebral palsy (30%). The mean age at seizure onset was 5.6 ± 3.4 years. The mean dose of valproate was 21.8 ± 9.1 mg/kg/day. The prevalence of UGT1A6 T19G was as follows: TT (45%), TG (38.8%) and GG (16.3%); that of UGT1A6 A541G was: AA (48.8%), AG (38.8%) and GG (12.5%); and that of UGT1A6 A552C was: AA (43.8%), AC (40%) and CC (16.3%). There was no significant association between valproate doses or standardized serum valproate concentration and the various UGT1A6 genotypes. **Conclusions:** Although no significant association was found between valproate doses or standardized serum valproate concentration and the various UGT1A6 genotypes, larger studies, studies in different ethnic backgrounds and meta-analyses of current data will help clarify the functional impact of UGT1A6 polymorphisms.

P87 - 1529

Evaluation of adherence to a convulsion management protocol for children in Rwanda

Kaputu KMC, Birindabagabo J-D, Mafuta ME, Walker TD, Misson J-P. *Service of Child Neurology, Mons, Belgium – ckaputukalalalamu@yahoo.fr*

Background: Prolonged seizures occur frequently among children in sub-Saharan Africa and are known to be associated with high morbidity and mortality. Inappropriate treatment may be one of the causes of this tragic situation. **Objective:** Assess the adherence of health professionals in southern Rwanda to a national protocol for pharmacological management of seizures in children. **Method:** A questionnaire featuring a 5 year old child with generalized seizures lasting longer than 5 minutes was administered to doctors and nurses working in hospitals in the Southern Province of Rwanda. The questions focused on the choice of initial treatment and the sequence of management following failure of the initial treatment choice. **Results:** The questionnaire was answered by 60.5% (129/213) of those surveyed. On substantive issues, there was no statistically significant difference in responses

between physicians and nurses. Benzodiazepine was chosen as initial therapy by 93.7% of physicians and 90.9% of nurses. Only 49.2% of physicians and 41% of nurses would repeat the initial treatment in case of failure of the first dose and 47% of doctors would wait 30 minutes to intervene. 34% of physicians would give 3 doses of benzodiazepine. 57% of them were unsure of the time to wait between the second and third dose of anticonvulsant, while 19% did not know what to do in case of refractory status epilepticus. **Conclusion:** These results suggest poor adherence to national protocol. Further education would contribute to improved management of prolonged convulsions in Rwanda.

P88 - 1520

Hormonal treatment in the management of infantile spasms

Jaxybayeva A, Kenzhegulova R, Kazhaparova D. National Research Center for Mother and Child Health, Astana, Kazakhstan – altynshash@gmail.com

Background: Infantile spasms (IS) is an uncommon epilepsy syndrome that typically begins in infancy. IS are considered to be a “catastrophic childhood epilepsy” due to the difficulty in controlling its symptoms and the developmental problems that can occur as a result of the condition. The triad of spasms, arrest of psychomotor development, and hypsarrhythmia is known as West syndrome. The goal of treatment is to eliminate the spasms and hypsarrhythmia as quickly as possible. Awareness and proper identification can result in the selection of appropriate therapy that can improve a patient's developmental outcomes. There is no consensus on the best initial approach for infantile spasms. Many experts recommend a short course of hormonal therapy (ACTH) but others use oral antiepileptic drugs (vigabatrin or topiramate) or oral steroids (prednisolone). **Purpose:** to identify a most appropriate way for management of IS in Kazakhstani patients and compare cognitive development and seizures control between subgroups with and without hormonal treatment (ACTH or dexametazone and valproates). **Patients and methods:** 25 children 3–11 month of age with IS (most of them diagnosed as a West syndrome, one had an Aicardi syndrome) were analyzed during 2011–2013. **Results:** we had three groups of patients who were treated with different ways. One group had a treatment with ACTH. Second group were treated with dexametazone and third group were treated by valproates. **Conclusion:** First and second group had a reduction of seizure activity during first week of hormonal treatment in 80%. Cognitive improvement after 5th day of treatment was reported by all mothers. Long term seizures free period at first and second group during 6 months – 80% and during 12 month- 60%. At third group we got positive results after three weeks of treatment by valproates. Seizures free period were not be reached.

P89 - 1517

Clinical audit of an established paediatric transient loss of consciousness (“blackouts”) clinic

Randhay AS, Thakker P, Whitehouse WP. School of Clinical Sciences, University of Nottingham, UK – mzyasra@nottingham.ac.uk

Objectives: The study intended to highlight processes that could be improved and evaluate the usefulness of paediatric transient loss of consciousness (TLoC) clinics. It also explored the management of patients with neurally mediated syncope (NMS). **Methods:** Clinical documents were examined and evaluated against a compiled list of processes deemed necessary in a TLoC clinic. The outcome measure was change in frequency of symptoms after one year of follow-up. **Results:** 57 patients aged 1 to 17 years (median 13) were audited. The rates for the clinic's documented processes were: 100% for history of presenting complaint and description of events; 98% for drug and medical history; 93% for

triggers and blood pressure; 91% for family history, 82% for lying and standing blood pressure and heart rate; 79% for neurological examination; 68% for cardiovascular examination; 70% for a standard 12-lead electrocardiogram. In addition 46% had an EEG and 44% a head-up tilt test. In 33% of patients the diagnosis changed significantly by one year of follow-up. 32/46 (70%) patients with TLoC had 50% or fewer events after one year including 23/46 (50%) symptom-free for the last 6 months of follow-up. 16/35 (46%) patients with pre-syncope had 50% or fewer episodes after one year of follow-up, including 6/35 (17%) who were symptom-free in the last 6 months. **Conclusions:** The documentation rate should have been 100% for the processes listed (excluding EEG and head-up tilt test) as they are recommended in the existing literature. Better documentation and the use of a checklist could improve these rates. The clinics' promising outcomes pave the way for future studies and drug trials. The audit showed the need for paediatric TLoC guidelines to help general practitioners and paediatricians manage TLoC more actively. It also highlights the importance of using the right diagnostic tests to increase the quality of diagnoses.

P90 - 1515

Effects of oxcarbazepine on the language and problem solving abilities in newly diagnosed pediatric epileptic patients

Kim SJ, Min JH, Kim KS. Department of Pediatrics, Chonbuk National Univ Medical School, Korea – sunjun@jbnu.ac.kr

Purpose: The purpose of this study was to determine the effects of oxcarbazepine on the problem solving abilities in newly diagnosed pediatric epileptic patients. **Patients and methods:** Thirty newly diagnosed pediatric epileptic patients (Male:Female = 14:16, Mean age: 10.5±3 y), who were investigated from April 2006 to Oct 2012. We performed a standardized full articulation tests and Peabody picture vocabulary test-revised (PPVT-R). Test of Problem Solving (TOPS), Mean Length of Utterance in words (MLU-w), comparison of Precise Articulation, Computerized Speech Lab were used to assess the language function before and after initiation of oxcarbazepine. Starting dosage of oxcarbazepine was 10 mg/kg for the first 7 days; increased to 20 mg/kg for the next 7 days and increased up to 30 mg/kg/day (or 1,200 mg/day). The mean dosage of oxcarbazepine was 25 mg/kg/day. **Results:** First, TOPS showed that the abilities of problem solving were improved after initiation of oxcarbazepine [(total score: 35.6±14.8 vs 40.1±13.2, P<0.05), Causal reason parameter (11.0±4.3 vs 12.1±4.2), solution ratiocination (15.3±6.2 vs 16.9±6.9), beginning guess (9.3±5.3 vs 10.9±4.3)]. Second, MLU-w did not reduce after taking medicine (4.8±1.4 vs 4.9±1.4). Third, the receptive language function was significantly improved after taking oxcarbazepine in PPVT (9y 6m±3y 3m vs 10y 2m±3y 5m, P<0.05). **Conclusion:** Our results suggest that oxcarbazepine can be used without significant negative effects on language function. Moreover, language functions, especially receptive language, were improved after oxcarbazepine initiation.

P91 - 1510

Polymorphism of SCN1A and SCN2A gene in pediatric refractory epilepsy patients

Lee KS, Kang JW, Kim DW. Department of Pediatrics, Chungnam National University Hospital, Chungnam National University School of Medicine, Daejeon, Korea – ksulee@cnu.ac.kr

Objectives: Epilepsy is a common chronic neurological disorder characterized by recurrent unprovoked seizures. While there have been many break throughs in development of antiepileptic medications, the cure for epilepsy still needs many answers, such as genetic aspects of the illness. Gene mutation may contribute to this situation. In this study, we have evaluated children

with single nucleotide polymorphisms (SNP) of SCN1A c.3184 A→G (rs2298771) and SCN2A c.56 G→A (rs17183814) to analyze these genes were associated with refractory seizure. **Material and methods:** Three hundreds and eleven children who visited the outpatient clinic in Chungnam National University Hospital, were retrospectively reviewed and, the data for their demographic profiles, clinical characteristics, and the results for SNP of SCN1A and SCN2A gene were collected. We divided them into three groups of control, response, and refractory groups. **Results:** There was no statistical difference in demographic profiles of the patients. A variant of SCN2A c.56 G→A polymorphism was associated with refractory seizure in pediatric patients with epilepsy ($p=0.004$; odds ratio 2.78, 95% confidence interval 1.39–5.56). **Conclusions:** SNP of SCN2A c.56 G→A could be suggested as one of the causes of pediatric refractory epilepsy.

P92 - 1507

Association between hypocapnia and febrile seizures

Kılıçaslan B, Erol I, Ozkale Y, Saygi S, Sarıtürk C. Baskent University Faculty of Medicine, Department of Pediatrics, Adana Teaching and Medical Research Center, Turkey – ilknur_erol@yahoo.com

Objectives: The pathogenesis of febrile seizures is not clear even today. Despite evidence from both animal models and adult humans, this is only the second study to measure pCO₂ and pH values in children with febrile seizures. The purpose of this study is to determine whether hyperthermia-induced hyperventilation with subsequent hypocapnia is relevant to febrile seizures in children. **Material and methods:** This prospective case-control study enrolled 18 children who presented with febrile seizures and 18 children who presented with a febrile illness without seizures between October 2012 and January 2013. Blood gas analyses were measured both from the febrile seizure and control group. **Results:** There was no significant difference in mean blood pH between the febrile seizure and control groups but blood pCO₂ was significantly lower in the febrile seizure group. Patients with complex febrile seizures exhibited significantly lower pCO₂ levels within 1 hour of seizure onset than patients with simplex febrile seizures. **Conclusions:** These data indicate that febrile seizures may be associated with hyperventilation and that the ensuing hypocapnia may contribute to the development of a seizure disorder.

P93 - 1504

New cases of triple syndrome

Popova VA, Afonin AA, Shokarev RA, Baybikova GSh, Timolyanova EK. Rostov Scientific-Research Institute of Obstetrics and Pediatrics, Rostov-on-Don, Russia – mliap@yandex.ru

TRIPLE syndrome is a rare autosomal-recessive pathology which is characterized by hypocorticism, melanoderma, achalasia of esophagus, alacrimia. Proband D, 5 years old. Parents came for a consultation as the child had convulsive disorder, melanoderma and had no tears when crying. Skin pigmentation was recorded for the first time at the age of 2, it gradually increased, at the age of 2.5 the boy was operated for achalasia of the cardiac part of esophagus. At the same age a low level of blood cortisol with the normal range of glycemia was detected, chronic adrenal insufficiency was diagnosed. By diagnosis specification blood cortisol decrease reached 0.2 MOM. The first convulsive clonicotonic attack with the loss of consciousness was also registered at the age of 2.5. Further on it repeated approximately once in a year in spite of the therapy conducted. According to EEG data epiactivity was not registered. Proband Z., 8 years old, was sent for examination concerning convulsive disorder, hypomnesia, melanoderma and alacrimia. Swarthy skin pigmentation was noticed at the age of 5. At the age of 6 and 7 – two episodes of clonicotonic

convulsions with long impairment of consciousness (up to 12 hours) on the background of a normal level of blood glucose. EEG registered moderate paroxysmal activity of subcortical genesis. By laboratory examination a very low level of blood cortisol (0.2 MOM), increase of ACTH (5.1 MOM) and TSH (4 MOM) were detected. On the background of treatment with hydrocortisone children's condition improved, content of cortisol in blood increased up to 0.8 – 1.0 MOM, biorhythm of its secretion restored. It is of interest that both children have the episynndrome which is refractory to standard anticonvulsive therapy in the absence of substantial changes of EEG, earlier it was not described in case of such pathology.

P94 - 2054

Two patients with infantile epileptic dyskinetic encephalopathy and late diagnosis of focal cortical anomaly

Kara B, Maras H, Yalcin EU, Aktan F, Demirbas F. Kocaeli University Medical Faculty, Department of Pediatrics, Division of Child Neurology, Kocaeli, Turkey – hulyamaras@gmail.com

“Early-Infantile Epileptic Encephalopathy (EIEE) with Suppression-Burst” is the most severe and earliest form of age-related epileptic encephalopathy with heterogenous group of etiology including cortical malformations, hypoxic ischemic encephalopathy, inborn errors of metabolisms and specific genetic defects. We present two patients with EIEE and severe dyskinetic movements. Patient 1 is 21-month-old-boy and patient 2 is 2.5 year-old boy. Both patients had uneventful prenatal and natal history. The intractable seizures started on the first day of their lives, severe dystonic posture was relevant and “burst-suppression” pattern was seen on the EEG. Extensive metabolic work-up including blood chemistry, complete blood count, serum ammonia and lactate levels, serum and cerebrospinal fluid (CSF) quantitative amino acid levels, Tandem MS/MS, urine organic analysis, CSF neurotransmitter levels were normal. Initial cranial magnetic resonance imaging (MRI) taken during the neonatal period was normal. Aristaless-related homeobox (ARX) gene was not found in both patients. We thought that the patients had a genetic defect causing infantile epileptic dyskinetic-encephalopathy and planned to study other genes reported to be responsible in EIEE. However, the video-EEG in the first patient recorded when he was 17-month-old revealed multiple seizures originating from the left temporal lobe. The repeated cranial MRI revealed cortical anomaly in the left temporal lobe. Positron emission tomography (PET) study of the second patient revealed right fronto-temporal hypermetabolism and MRI revealed a probable right fronto-temporal cortical anomaly. The first patient underwent lesionectomy and the second patient has been prepared for epilepsy surgery.

P95 - 1984

Treatment of epilepsy in 6 patients with MECP2 duplication syndrome

Hasse A, Haberl C, Betzler C, Hasselmann O, Maier O, Shimada S, Biro A, Selch C, Staudt M, Kluger G. Neuropädiatrie, Schön Klinik Vogtareuth, Germany – ahasse@schoen-kliniken.de

Objectives: Increasing use of Array CGH leads to increased diagnosis of MECP2 duplication syndrome. Male and female patients can be affected with different phenotypes (Bijlsma et al. 2012). The most common features in affected boys are infantile hypotonia, global developmental delay, intellectual impairment, autistic traits, poor or absence of speech, recurrent respiratory infections and seizure (Ramocki et al. 2010). Seizures occur in >50% of children and >90% of adolescent patients. Age of onset, inter- and intraindividual types are variable. Until now, no antiepileptic drug has been found to be particularly suitable. Anecdotically

benzodiazepines do offer the best treatment to drop attacks (Ramocki, pers. com.). Swallowing difficulties are although frequent (>50%, Ramocki et al. 2010) and from our own experience, could be associated with seizure frequency. **Material and methods:** Retrospective case evaluation of 6 male patients (age: 3–14) with MECP2 duplication syndrome with regard to seizure type, antiepileptic drugs and swallowing difficulties. **Results:** The following seizure types were observed: Drop attacks/head dropping (6/6), generalized-tonic-clonic seizures (6/6), focal tonic seizures (4/6), atypical absences (2/6), myoclonic seizures (2/6). All patients had swallowing difficulties. 12 different AEDs were used as monotherapy or in combination: TPM, VGB, ZNS, AZA (1/6), RUF, LEV, CLB, STM, CZP (2/6), LTG, ESM (3/6). 6/6 were treated with VPA, 1/6 showed seizure reduction for some weeks, the others no lasting success. 3/6 patients had benzodiazepines. One patient became seizure free for at least 6 month with Rufinamid and Clonazepam associated with increased swallowing ability. None underwent epilepsy surgery, none were treated with ketogenic diet or VNS. Aggravations are not described. **Conclusions:** Epilepsy in children with MECP2 duplication syndrome is difficult to treat. Further collaborated clinical observations and data collections are needed in order to develop treatment recommendations.

Headache

P96 - 2079

Significance of continuous performance test in children with headaches

Lee K-H, Woo SB. Hallym University Medical Center, Korea – headaches77@gmail.com

Purpose: The study examines the continuous performance test (CPT) in children with headaches. Headaches in children have known to be associated with the difficulty in concentration or school performance. But limited data are available for the measurement of attention deficit or changes of attention after treatment in relation with pediatric headaches or CPT. **Material and methods:** We enrolled 14 children and adolescents at Kangnam Sacred Heart Hospital during March to August in 2012, suffering from primary headaches according to diagnostic criteria of the international classification of headache disorders (ICHD-II). The control group was 14 patients with ADHD and no history of recurrent headaches. All of them were assessed using advanced test of attention (ATA), one of CPT, during the headache attacks and after medication for treatment. **Results:** The auditory ADHD indexes (AI) of headache patients were as high as that of control ADHD group. The visual and auditory AI of the headache patients in some parts were improved after treatment. **Conclusion:** During the headache attacks, attention of children with headaches was as disable as ADHD patients in the CPT. The patients showed statistically improvement of clinical symptoms and AI after treatment. The CPT was efficient test to assess the degree of disability and improvement after treatment in attention of pediatric headaches.

P97 - 2066

Effectiveness of therapeutic measures in paediatric migraine

Legisa S, Krvavica K, Rogac M, Renner Primec Z. Department of Child, Adolescent and Developmental Neurology, Children's Hospital, University Medical Centre Ljubljana, Slovenia – zvonka.rener@mf.uni-lj.si

Objective: The aim of the study was to determine the effectiveness of therapeutic measures in paediatric migraine. **Patients and methods:** 150 children who were diagnosed with migraine

with or without aura by International Headache Society criteria in a period of one year in our tertiary hospital were included in the study. Questionnaire about therapeutic measures and outcome of migraine in this group was sent to all children. Data received from 79 children were evaluated. **Results:** Therapeutic measures that were most effective in acute treatment of migraine headache were sleep in 75% (59/79), NSAID in 71% (32/45) and acetaminophen in 61% (42/69). More than 85% of children took the drug the right time and in appropriate dose. 22% (17/79) of children were prescribed with migraine-specific treatment (sumatriptane in 88% (15/17), aspirin migran 6% (1/17) and pizotifen 6% (1/17)). Migraine prophylaxis was prescribed in 28% (22/79). Most common measures were 50 mg of riboflavin in 55% (12/22), acupuncture in 27% (6/22), and 50 mg of coenzyme Q10 in 9% (2/22). Riboflavin prophylactic treatment was effective in 42% (5/12), acupuncture in 67% (4/6) and coenzyme Q10 in 50% (1/2). **Conclusions:** The most effective treatment for treatment of acute migraine headache with or without aura in our study was sleep, with NSAIDs and acetaminophen as most common used effective analgesics. Relatively low percentage of children was prescribed migraine-specific treatment and/or prophylaxis. Riboflavin, acupuncture and coenzyme Q10 show promising results for migraine prophylaxis in children, but were used in a small subgroup of children.

P98 - 2037

Une crise de migraine hémiplégiante familiale atypique et réaction paradoxale au Topiramate

Loiseau Y, Comte A, Amsellem D, Altuzarra C. Service de médecine Pédiatrique CHRU de Besançon, France – cecilia.altuzarra@orange.fr

Resume: La migraine hémiplégiante familiale (MHF) peut se révéler par diverses présentations cliniques, parfois atypiques. Nous en rapportant une nouvelle observation clinique caractérisée par la survenue d'un coma. **Sujet:** Il s'agissait d'une patiente de 2 ans et demie aux antécédents personnels et familiaux de MHF avec mutation du gène ATP1A2. L'enfant a présenté un épisode d'hémiparésie à bascule dans un contexte fébrile à 40°C associé à un état de coma vigile. Le bilan para-clinique (EEG, IRM encéphalique, ponction lombaire avec PCR herpès, fond d'œil) était normal en dehors de quelques lésions ischémiques corticales de petite taille, mises en évidence à l'imagerie cérébrale. L'évolution était favorable sous traitement symptomatique et Topiramate. Secondairement, la patiente a présenté des troubles du comportement avec régression du langage, irritabilité et cris stridents. Ces symptômes n'ont alors régressé qu'à l'arrêt du traitement. **Conclusion:** L'état de coma est une manifestation clinique rare dans les crises de MHF. Différents médicaments antiepileptiques peuvent être utilisés pour limiter la fréquence des crises. Dans cette observation, le traitement par Topiramate était responsable de troubles du comportement régressant dès l'arrêt de celui-ci.

P99 - 1850

Altered pain perception in children with chronic tension-type headache: is this a sign of central sensitisation?

Soe AL, Thomsen LL, Tornøe B, Kreiner S, Skov L. Department of Paediatrics, Children's Headache Clinic, Copenhagen University Hospital Herlev, Denmark – annbritt@dadlnet.dk

Aim: To investigate if children (7–17 years) with frequent episodic tension-type headache (FETTH) or chronic TTH (CTTH) have an altered pain perception compared to healthy controls. **Methods:** We applied a pressure of 5 increasing intensities to m. trapezius and m. temporalis with a Somedic Algometer II. Visual analogue scale-score was rated and Area under the curve (AUC) calculated. An average AUC in each person was used as outcome variable

in further univariate multiple linear regression analysis, because factor analysis showed that AUC represents only one dimension underlying both muscles. **Results:** Participants: 22 children with FETTH, 36 children with CTTH and 57 controls. The CTTH group had a significantly higher AUC compared to the control group ($P < 0.001$). The FETTH group represented an intermediate state. AUC did not change with increasing age, headache years, headache intensity, headache frequency or sex. **Conclusion:** Children with CTTH show significantly increased pain sensitivity in a range of pressures compared to the FETTH group and the controls. Since AUC in m. trapezius and m. temporalis represents only one general latent tenderness, it might indicate that the altered pain perception is mainly due to central sensitisation.

P100 - 1629

TGFB1 genetic polymorphisms in pediatric migraine patients

Saygi S, Alehan F, Erol I, Ataç FB. Baskent University Faculty of Medicine, Department of Pediatrics, Division of Child Neurology Adana Teaching and Medical Research Center, Turkey – semra_saygi@yahoo.com

Objectives: The pathogenesis of migraine is known to be related to the presence of genetic polymorphisms, including those of cytokine-related genes. However there is no information about the role of Transforming growth factor- β 1 (TGF β 1) in the pathogenesis of pediatric migraine. Therefore we investigated polymorphisms in the TGF β 1 gene in relation to the migraine. **Material and methods:** The study included 100 consecutive children and adolescents in whom migraine was diagnosed according to the International Classification of Headache Disorders, as well as 98 healthy children and adolescents at the Baskent University Ankara and Adana hospital. Genomic DNA was investigated for 4 polymorphisms in the TGF β 1 gene 800 G/A, 509 C/T, codon 10, and codon 25. **Results:** In total 28 patients were defined as migraine with aura (MWA), 72 were defined as migraine without aura (MWOA). The mean ages of the children in the MWA group, MWOA group and control group were 14.36 ± 1.93 , 12.97 ± 2.63 , and 10.67 ± 3.44 years, respectively. No significant differences in genotypic distributions among MWA or MWOA patients and controls were observed in the polymorphism of 800 G/A and C25. Genotypic distributions of 509 C/T among patients with migraine and control groups also were not significant. However, the genotypic distribution of 509 C/T, was significantly different between control and MWOA patients. The C10 C/T genotypic and C10 C allelic frequency of TGF β 1 polymorphism was significantly higher in MWA or MWOA patients than healthy controls. **Conclusions:** In conclusion, the present results indicate the possible contribution of TGF β 1 gene polymorphisms to migraine headache generation in children. To our knowledge it is the first time that a relationship between TGF β 1 gene polymorphisms and migraine is shown in pediatric age group. Further studies on this subject are needed, along with a search for new therapeutic agents with anti-inflammatory properties.

P101 - 1628

Body mass index and headache in school children: a nation-wide survey

Rho Y-I, Chung H-J, Lee K-H, Eun B-L, Eun S-H, Nam S-O, Kim W-S, Kim Y-O, Park H-J, Kim H-S. Department of Pediatrics, School of Medicine, Chosun University, Gwangju, Korea – ryoung@chosun.ac.kr

Background: Body mass index (BMI) is associated with headache prevalence, frequency and severity of headache and disability, but it is controversial. Obesity is risk factor with chronification within subjects with episodic headaches. Recently, it was reported that obesity occurs at a higher rate in children pre-

senting to tertiary pediatric headache center compared with the general population. **Purpose:** To access the relationship of BMI to the prevalence, frequency, duration, severity of headache, and chronic headache in school children in Korea. **Methods:** We conducted a cross-sectional school-based study of randomized and proportional sample of 3493 boys and girls. The questionnaires collected demographic data in addition to specific questions about headache according to the ICHD-2 criteria. The BMI calculated and the BMI percentile determined. **Results:** The prevalence of headache was 29.0% (1013/3493) among in South Korea. The prevalence of headache in girls (33.2%) was significantly higher than in boys (25.0%) ($P < 0.001$). The prevalence of chronic headache in girls (3.2%) was significantly higher than in boys (1.3%) ($P = 0.013$). The prevalence of overweight school children with headache (9.8%) did not significantly differ from the overweight school children (11.9%). The prevalence of chronic headache in overweight children (10.1%) was higher rate than in non-overweight children with headache (7.5%). BMI percentile was not significantly correlated with headache frequency, severity, and duration. **Conclusions:** The prevalence of overweight school children with headache did not significantly differ from the overweight school children without headache. Obesity was higher rate in school children with chronic headache in Korea, similar to findings of other studies. The frequency, duration, and severity of headache were not associated with obesity.

P102 - 1536

The role of vitamin D supply and its impact on headaches in children and teenagers

Potrykus AJ, Pilarska E. Department of Developmental Neurology, Medical University of Gdańsk, Poland – pilar@gumed.edu.pl

Objectives: There is little evidence on the impact of cholecalciferol on headaches despite the building evidence on its role in brain, and the widespread vitamin D deficiency. The aim of the study is to verify whether vitamin D supplementation reduces strength or frequency of headaches and if the used dosages and to assess the efficacy of the doses recommended by experts. **Material and methods:** Children and adolescents diagnosed with migraine and/or tension-type headaches, with no other co-existent neurological diseases, were tested for vitamin D serum level (25OHD=25-hydroxycholecalciferol) after obtaining written informed consent from parents. They were provided with prescription for cholecalciferol drug in liquid drops and advised to supplement vitamin D depending on the deficiency level. Levels and doses were defined as follows: below 10 ng/mL – 5000 IU/day; 10–20 ng/mL – 2000 IU/day; 21–29 ng/mL – 1000 IU/day; 30–60 ng/mL – 500 IU/day. The 25OHD levels were assessed at 3 and 6 months, additionally at 1 month if 5000 IU/day were given. Each patient received headache diary designed for the duration of the study – 6 months. **Results:** The study is on-going. Of 37 patients tested, 27 had 25OHD level below 20 ng/mL (considered deficiency), no one exceeded 30 ng/mL. The patient's parents generally declare a reduction in headaches strength after 3 months of vitamin D supplementation. The recommended cholecalciferol doses used in deficiency are not sufficient in some cases to observe the demanded increase in 25OHD level (> 30 ng/mL) after 3 months. **Conclusions:** Vitamin D deficiency is widespread among children with headaches from northern Poland. Further studies are needed on the impact of vitamin D on headaches in children, teenagers and adults.

Immunology

P103 - 2052

Acute subdural hematoma as a complication of varicella zoster virus infection in a 2 year old child

Aziz M, Kaliaperumal C, Allcutt D. *Children's University Hospital, Temple Street, Ireland – mohdazli@me.com*

A. Background: Intracranial haemorrhage (ICH) in varicella zoster virus (VZV) infection is rare. 2 cases have been reported as sub-arachnoid haemorrhage secondary to VZV vasculitis and ICH two months post varicella infection. To our knowledge this is the first case of acute subdural and intracerebral haemorrhage secondary to coagulopathy caused by VZV infection. **B. Case description:** A 2 year old previously healthy male child presented with 6 day history of chicken pox infection and bilateral facial and neck swelling. The oedema compressed his upper airway and child was intubated and ventilated. The neck swelling on the left was complicated by cellulitis and ulceration. The clinical course deteriorated to septicaemia and hypotension with renal and liver failure, coagulopathy and rectal bleeding. Two weeks later he developed bilaterally fixed pupils. **C. Results of investigations:** Peripheral blood culture and tests confirmed superimposed Group A Streptococcus (GAS) septicaemia and thrombocytopenia, abnormal liver function test and prolonged clotting time. Emergency MRI brain prior to neurosurgical intervention showed a very large left subdural hematoma associated with significant midline shift causing ischaemia to medial aspect of cerebral hemisphere, bilateral frontal lobes, left thalamus, midbrain, pons and contralateral occipital lobes. **D. Treatment:** Child underwent emergency left hemi craniotomy and evacuation of acute subdural hematoma and left occipito- parietal hematoma. Intra-operative findings were blood clot and products no pus seen. This was confirmed on analysis of theatre specimen. Post- operatively child underwent intensive multi- disciplinary rehabilitation and currently progressively recovering. **E. Discussion:** ICH is a severe complication of VZV infection. We infer that the superimpose infection of another micro-organism from the skin flora (GAS) as the main threat of ulcerated VZV infection that can lead to a catastrophic outcome.

P104 - 2146

Atypical presentation of subacute sclerosing panencephalitis

Yüksel D, Sonmez K, Boynukalin M, Kabataş EU. *Dr. Sami Ulus Children's Health and Diseases Training and Research Hospital, Ankara, Turkey – drdeniz_yuksel@yahoo.com.tr*

This report describes a patient with atypical features including hemiparesis, subacute vision loss, lack of myoclonus, and lack of specific electroencephalographic changes. Before admitted to our clinic with vision loss, 11 year old male had applied another hospital because of hemiplegia and misdiagnosed acute disseminated encephalomyelitis and steroid therapy had been started. On magnetic resonance imaging of brain, parieto-occipital cortico-subcortical regions white matter signal intensities had become higher and supratentorial cortical atrophy was observed. Our neurological examination revealed left hemiparesis, mild mental retardation, and decreased visual acuity. Fundus examination revealed bilateral optic atrophy and chorioretinitis. A periodic electroencephalogram complex was absent. The diagnosis was confirmed with the identification of measles antibodies in the cerebrospinal fluid. Isoprinosine therapy was started. Physicians taking care of children need to be aware of atypical presentations of subacute sclerosing panencephalitis and avoid unnecessary diagnostic and therapeutic interventions.

P105 - 2133

Acute encephalitis related to human herpesvirus type 6 (HHV6): two immunocompetent children with variable outcome

Amsallem D, Pâris C, Devys-Meyer N, Bévalot J, Camélio A. *Department of Pediatric Neurology, University Hospital Jean Minjoz, Besançon, France – damsallem@chu-besancon.fr*

Direct infections of the brain can be caused by many viruses, bacteria, parasites and fungi. We describe two previously healthy boys with primary infection caused by HHV- 6. A 18-month-old French boy presented in 04/2012, with high fever, cough treated since two days with Amoxicillin, hypotonia, whimpers, vomiting, impaired consciousness, tonico-clonic seizures. Previously, walk and some words were acquired. Neurological examination revealed no focal signs. Pneumonia interestingly the right upper lobe was confirmed by radiography. Initial laboratory tests were unrevealing, except CRP = 87 mg/ml. CSF was normal with no oligoclonal bands. Culture, antibody studies and polymerase chain reaction (PCR) of CSF were broadly performed. CSF contained high copy number of HHV-6 DNA (2044 copies/ml). All other investigations remained negative. He was treated, initially, with broad-spectrum antibiotics, acyclovir, clonazepam, phenytoin. MRI brain showed high signal intensities in diffusion-weighted images in fronto-parietal cortical and subcortical structures. The patient stayed in hospital for 15 days and recovered during six months in rehabilitation center from hypotonia, gait abnormality, mood disorder, poor swallowing and speech impairment. Motor impairment persists. A 6-year-old boy presented in 03/2013, with high fever, atonic seizure, comatose and pyramidal signs. Laboratory tests were unrevealing, except CRP = 20 mg/ml. CSF was normal with no oligoclonal bands. Culture, antibody studies and polymerase chain reaction (PCR) of CSF were broadly performed. CSF contained mild copy number of HHV-6 DNA (740 copies/ml). All other investigations remained negative. He was treated, initially, with broad-spectrum antibiotics, acyclovir, clonazepam, valproate. MRI brain showed high signal intensities in diffusion-weighted images throughout the entire cerebral hemispheres, involving cortical and subcortical structures. The patient stayed in hospital for 21 days with intravenous ganciclovir. He recovered rapidly without neurorehabilitation or evidence of neurologic sequelae. Primary HHV6 infection is not always a benign illness and may require specific treatment.

P106 - 2127

The importance of monitoring system epidemiologic acute flaccid paralysis for identifying cases of syndrome Guillain-Barré in the capital of Brazil: the period 2007–2011

Bomfim D, Melo MLA; Siqueira ES. *Neurologist Paediatric Hospital Regional da Asa Sul - Brasília, Brazil – denizebomfim2006@gmail.com*

Introduction: Polio is a contagious infectious disease caused by poliovirus, more common in children. The system of surveillance of Acute Flaccid Paralysis (AFP) aims to maintain polio caused by wild poliovirus eradicated allowing differential diagnoses to identify patients suffering from Guillain-Barré syndrome in pediatric patients to be among their differential diagnoses. **Objectives:** Describe the epidemiology of cases of Guillain-Barré syndrome reported in the period January 2007 to January 2012 by the surveillance system of the AFP. **Methodology:** Conducted a retrospective analysis of data collected in Sheets AFP-Epidemiological Research, available in SINAN, from January 2007 to January 2011. **Results:** There were 43 reported cases, the regional health Brasília greater number of cases were Ceilândia with 28.7% of cases; range with 14.28% and 9.52% in Santa Maria, the female was more prevalent with 52%, the most affected age group is 0–5 years old with 28.5%. Following the goals determined by the program found: 42 reported cases, 2 cases were diagnosed with open end. The 40 cases with a final diagnosis: 30% cases - Guillain

Barré syndrome, 17.5% - Acute encephalitis and 10% - Periodic Paralysis. Among the 43 reported cases, 30% was due to GBS, 17.5% for acute encephalitis and 25% of unknown etiology (Chart 4). The symptoms most frequently found were pain (55.8%), fever (48.8%) and vomiting (37.2%). **Conclusion:** The results demonstrate that the surveillance of AFP in Brasilia in the period 2007–2010 was very sensitive to achieve the targets set for the indicators and the majority of cases reported had the diagnosis of Guillain-Barré syndrome which is now the main differential diagnosis of poliomyelitis.

P107 - 2099

Posterior reversible encephalopathy syndrome in our paediatric population

Wang FSJ, Ong HT, Lin JBY, Tay SKH, Yap HK. Singapore – furene_wang@nuhs.edu.sg

Objectives: Posterior reversible encephalopathy syndrome (PRES) is defined as new-onset seizures, severe headaches, altered mental status or cortical visual changes. This may be accompanied by significant neuro-radiological changes. Common etiologies include hypertension, uremia and the use of calcineurin inhibitors such as cyclosporin A. There are few paediatric studies of posterior reversible encephalopathy syndrome as compared to adult studies. We aim to describe the clinical features, etiologies, neuroimaging changes and electroencephalogram findings in a group of patients with PRES. **Material and methods:** We analysed the data of six patients identified from August 2008 to July 2012 retrospectively. **Results:** 5 out of 6 patients had renal impairment and 1 had chronic liver disease. The patients with renal impairment presented with PRES due to uncontrolled hypertension and PRES in the child with liver disease was attributed to the usage of cyclosporin A. All 6 patients presented with seizures and 1 child had cortical visual changes, which completely resolved. Although most of the patients had neuroimaging findings of occipital and posterior parietal abnormalities, 2 of them had changes of the basal ganglia. Electroencephalogram performed showed abnormalities ranging from frontal sharp waves to generalized spike wave activity. Follow-up neuroimaging studies performed showed resolution of the abnormalities. **Conclusions:** PRES should be recognized early as a complication of varying etiologies, and it can respond favourably to appropriate treatment such as optimal control of hypertension. The neuroimaging changes may not always be in the posterior white matter but are usually fully reversible.

P108 - 1741

Anti-N-methyl-D-aspartate receptor encephalitis in a child

Aksoy A, Konuşkan B, Saygi S, Ozkan M, Çenesiz F, Yüksel D. Division of Pediatric Neurology, Department of Pediatrics, Dr. Sami Ulus Children's Health and Diseases Training and Research Hospital, Hacettepe University Children's Hospital, Baskent University Faculty of Medicine, Ankara, Adana, Turkey

Anti-N-methyl-D-aspartate (anti-NMDA) receptor encephalitis likely has a wider clinical spectrum than previously recognized. A wide variety of movement disorders, which stereotypic movements, ataxia, limb dystonia, limb myorhythmia, oromandibular dystonia, facial myorhythmia, blepharospasm, opisthotonus, athetosis, and tremor, often in combination, can be observed in children with anti-NMDA encephalitis. We report a 6-year-old boy with anti-NMDA receptor encephalitis without a detectable tumor who showed a nearly complete recovery after intensive immunotherapy.

P109 - 1522

Anti-NMDA receptor encephalitis: an unusual cause of autistic regression in a toddler

Scott O, Richer L, Forbs K, Eliyashevskaya M, Goetz H. Faculty of Medicine and Dentistry, University of Alberta, Edmonton, Canada – goez@ualberta.ca

Introduction: Anti-NMDA receptor encephalitis in children is typically associated with prodromal viral-like illness, followed by psychiatric changes (predominantly aggression), seizures, language dysfunction, dystonia, and dyskinesias. We present the first report of autistic regression in a toddler caused by anti-NMDA receptor encephalitis. **Case description:** A 33-month old boy presented with decreased appetite, irritability, and insomnia following an upper respiratory tract infection. Over the course of the next few weeks he lost previously-acquired language and social skills, finally becoming mute. Repetitive left hand movements and posturing appeared. Toe-walking and wringing movements of the left wrist were observed. Within a month, this previously-healthy patient came to fit the diagnostic criteria for Autistic Spectrum Disorder. Laboratory tests were normal, apart from mild elevation of liver enzymes, and increased CSF IgG index. Brain MRI was normal, and EEG revealed non-specific background slowing with no seizures. Upon further investigation, CSF serology was returned positive for NR1 anti-NMDA receptor antibodies. The patient was treated with intravenous immunoglobulins followed by 8 weeks of oral steroids, resulting in reacquisition of language and social skills, and resolution of hand posturing. **Discussion:** While most children diagnosed with Autistic Spectrum Disorder fail to attain communication and/or social skills in their first 2 years of life, up to one third of cases are characterized by loss of previously-acquired skills during toddlerhood. Given our incomplete understanding of the pathogenesis of Autistic Spectrum Disorder, it is possible that autistic regression in some children may stem from an underlying autoimmune process, as found in our patient. Our case emphasizes the significance of suspecting anti-NMDA receptor encephalitis as the cause of autistic regression. We caution physicians to maintain a high index of suspicion even in an age group where the diagnosis of Autistic Spectrum Disorder is typically made, and especially when presentation follows a febrile illness.

P110 - 1561

A different presentation of anti-N-methyl-D-aspartate receptor encephalitis: anti-N-methyl-D-aspartate receptor encephalitis that developed after herpes encephalitis

Bektaş Ö, Tanyel T, Aldemir B, Fitöz S, Ince E, Deda G. Department of Pediatric Neurology, Ankara University Medical School, Ankara, Turkey – gulhisdeda@gmail.com

Herpes encephalitis is one of the most common viral encephalitis. Brain abnormalities on MRI were significantly reduced in a mouse model of herpes infection when methylprednisolone was administered in combination with acyclovir, compared to treatment with acyclovir alone. Additionally, earlier publications reported that some patients developed choreoathetosis which was refractory to acyclovir after herpes encephalitis. These reports suggest the presence of secondary autoimmunity in the pathogenesis of herpes encephalitis. 19-month-old previously healthy girl presented with sudden onset of seizures and loss of consciousness. The initial HSV PCR was negative. Also limbic encephalitis antibodies were negative, we started steroids along with acyclovir due to the possible other autoimmune encephalitis and the patient had a history of varicella vaccine. HSV PCR was positive on the fifth day, but we continued the steroid treatment because the patient had benefit from the treatment. Because of the upper respiratory tract infection steroid was reduced on the 25th day of treatment and the patient developed orofacial dyskinesia

and choreoathetoid movements. The anti-N-Methyl-D-Aspartate Receptor antibodies was positive in serum and CSF on 28th day. This case supported the presence of autoimmunity in the pathogenesis of herpes encephalitis. Therefore we believe that the cases with previous herpes encephalitis who benefited from steroids should be re-evaluated in the light of this information.

P111 - 2090

VGKC antibodies: can become positive 4 weeks after presentation

Singh J, Kashyape P, Kirkham F. Southampton General Hospital, UK – jazzyrat79@yahoo.co.in

Objective: To report a previously unreported characteristic of Voltage Gated Potassium Channel (VGKC) antibodies. **Material and methods:** Retrospective review of case notes. **Results:** 11 year old boy presented with acute onset focal seizures with occasional secondary generalisation. This was preceded by an upper respiratory infection approximately 2 weeks before seizure onset. He was also reported to have behavioural problems in the form of aggression which continued after seizure onset. His initial investigations all done within 1 week of seizure onset showed mild hyponatremia and mildly high signal in the left hippocampus which was felt to be secondary to the seizures rather than the cause for seizures. The EEG was encephalopathic and a left hemispheric electrographic seizure was noted during the recording with a left temporal origin. Urine organic acids, blood for lactate, ammonia, amino acid, acylcarnitines were negative. As the presentation was consistent with Autoimmune Encephalitis, extended antibody screen including against NMDAR, VGKC, GAD and others were negative at this time. Child was empirically treated for Autoimmune Encephalitis with high dose IV Methyl Prednisolone for 5 days followed by a tapering course. There was initial good response but seizures recurred within the week and so Levetiracetam was added. The repeat autoimmune screen, sent 4 weeks after seizure onset, confirmed the diagnosis of VGKC Encephalitis as the positive antibody result was reported. In view of this he was treated with intravenous immunoglobulin and responded favourably. It seems likely that he will require further immunomodulatory drugs. **Conclusions:** Our literature search did not bring up any reports of a similar presentation in which the antibodies became positive >4 weeks after initial presentation on repeat sampling in the paediatric population. This case adds an important and valuable vignette in the investigation and hence the treatment of this rare condition.

P112 - 2064

Acute necrotising encephalopathy in two children

Diakogeorgiou A, Deconinck N, De Laet C, Dan B, Monier A. Department of Pediatric Neurology, HUDERF, ULB Brussels, Belgium – anne.monier@huderf.be

Acute necrotising encephalopathy (ANEC) is a rare rapidly progressive paediatric encephalopathy. The MRI hallmark of the disease consists of symmetric, multifocal lesions in the thalami with variable involvement of the white matter, basal ganglia, brainstem and cerebellum. Pathogenesis is supposed cytokine mediated after viral infection. Mutations in RANBP2 have been recently associated with familial and recurrent cases of ANEC. Two children aged 3 and 10 years old respectively, presented with high fever and respiratory tract infection. Both developed altered consciousness rapidly progressing to coma. The youngest presented focal seizures. Routine laboratory tests were unremarkable except a slight elevation of serum aminotransferase for the second patient. CSF evaluation showed mild proteinorachia in the first patient and pleiocytosis in the second. Extensive infectious work-up was negative, except a positive Rhinovirus

PCR on nasopharyngeal aspirate for the first patient. Successive brain MRIs of the first patient demonstrated symmetric T2 hyperintensity in the thalami extending to the basal ganglia, infracortical white matter, cortex, and cerebellar peduncles. MRI of the second patient demonstrated asymmetric T2 hyperintensity in the insular cortex, the mesencephalon and the basal ganglia. Autoimmune, mitochondrial, organic acid and urea cycle disorders were excluded. NMDA receptor antibodies were absent. Genetic test for RANBP2 is pending. Brain biopsy in the second patient was not pathognomonic. Diagnosis of ANEC was evoked and corticosteroids were administered, followed by immunoglobulins and ultimately plasmapheresis. Clinical outcome was poor, with dystonic quadriplegia and dysautonomic disorder in both patients and additional parkinsonism in the second. Patients are currently severely disabled and necessitate gastrostomy feeding. Acute encephalopathy after viral illness is a severe condition requiring prompt management to improve neurological outcome. However, prognosis remains poor. The typical imaging features of ANEC will be developed in the poster.

P113 - 2059

Recurrent acute disseminated encephalomyelitis in a child or multiple sclerosis?

Bouchaala W, Chaari D, Jemaa R, Sakka S, Kammoun F, Triki C. Child neurology department, Hedi Chaker Hospital, Sfax, Tunisia – chahnez08@gmail.com

Introduction: A number of clinical and para-clinical data are similar between multiple sclerosis (MS) and acute disseminated encephalomyelitis (ADEM), making difficult the distinguishing between these two diseases. The differentiation of these two conditions is still important both in diagnostic and therapeutic decision. **Aim:** Through the observation of a patient with recurrent neurological symptoms, we will try to find criteria to distinguish between these 2 entities. **Case report:** A 9 years old boy without any previous medical history presented at the age of 3 years an acute post infectious cerebellar syndrome spontaneously regressive. MRI showed T2 signal hyperintensity lesion at the brain stem, basal ganglia, temporal lobes and external capsule. Four months later, he had presented an episode of hemiplegia and brain MRI showed new hypersignal in spinal cord extended to more two vertebrae and in the cerebral white matter with regression of the lesions described above. The child received corticosteroids in bolus. Actually, the patient had left hemiparesis and MRI showed disappearance of brain and spinal lesion with spinal atrophy at three months and 6 years later. The visual evoked potentials showed bilateral retrobulbar optic neuritis. **Discussion:** The differential diagnosis between MS and ADEM is more difficult in child than in adult. Although, some clinical and radiological criteria are predictive of ADEM: recent post infectious motor disorder, lesions with same age and some specific location as the brain stem, cortex, subcortical white matter and with favorable radiological evolution. In case of recurrent ADEM, clinical and radiological symptoms are located in the same territory then the first episode. The diagnosis of MS is suggested by the appearance of other lesion in different territory and the presence of infraclinical retrobulbar optic neuritis.

P114 - 2049

Autoimmune limbic encephalitis and DRESS syndrome: is there an association?

Maras H, Ipekci B, Yologlu N, Aydogan M, Kara B. Kocaeli University Medical Faculty, Department of Pediatrics, Division of Child Neurology, Kocaeli, Turkey – hulyamaras@gmail.com

Autoimmune encephalitis (AE) is characterised by intractable seizures, cognitive impairment and psychiatric symptoms. The

non-paraneoplastic causes may be associated with systemic autoimmune disorders, and autoantibodies to cell membrane or intracellular antigens. “Drug Rash with Eosinophilia and Systemic Symptoms” (DRESS) syndrome is a rarely seen drug related acute hypersensitivity reaction, and characterized by fever, lymphadenopathy, eosinophilia, and single or multi-organ involvement. The pathogenesis of DRESS syndrome is not well known, but it is thought to be T lymphocyte mediated delayed hypersensitivity syndrome to toxic metabolites of drugs. Here, we report an 8-year-old boy developing DRESS syndrome after anti-epileptic drug use during the course of AE. He presented with focal seizures and behavioral change. The initial diagnostic work-up for encephalitis were negative. He was receiving phenytoin and clonazepam for intractable seizures. Three weeks after treatment, he developed DRESS syndrome. Antiepileptic drugs were stopped and steroid was started. He had no seizures during steroid treatment and psychiatric symptoms improved significantly. After steroid was withdrawn, his seizures and behavioural disorders restarted. After observing the clinical response to steroids during DRESS syndrome, AE was suspected and anti-glutamic acid decarboxylase (GAD) antibody was found to be high. Immunotherapy including intravenous immunoglobulin and methyl-prednisolone was started with a good clinical response. During the course, tumour screenings were negative. It has been a year since the immunotherapy has started. He is seizure free for the last six months on clobasam and methyl-prednisolone therapy. AE and DRESS syndrome are two different rarely seen autoimmune processes. We wanted to discuss the clinical significance of co-existence of both diseases in our case.

P115 - 2015

Preliminary data of national Romanian program of immunomodulatory treatment in children with multiple sclerosis

Sandu C, Dica A, Butoianu N, Iliescu C, Tarta-Arsene O, Cardas R, Craiu D, Burloiu C. *Pediatric Neurology Department, Al. Obregia Clinical Hospital, Bucharest, Romania – carmensandu_u6@yahoo.com*

Introduction: Multiple Sclerosis (MS) is an immune mediated inflammatory disease occurring most commonly in young adults but is also diagnosed in children and adolescents. The majority of children with MS present a relapsing-remitting form and the frequency of relapses is thought to correlate with disability on long term. There are recent studies considering initiation of early immunomodulatory therapy for reducing relapse rates and disease progression. **Material and methods:** A National Health Program of immunomodulatory treatment in children with MS has been setup since 2010 and 15 adolescent patients have been included. All patients have been evaluated and diagnosed in our clinic using revised Mc Donald criteria. Age group varied between 13 and 17 years of age and females were predominant (9 adolescent girls). On inclusion, clinically isolated syndrome (CIS) was present in 8 patients and 7 patients exhibited relapsing remitting forms. The average duration from onset of disease until initiation of treatment was 17, 15 months. 10 patients received Interferon β 1a and 5 patients received Interferon β 1b. Clinical features at onset of disease varied among patients. The EDSS score on inclusion was below 3 for all. There were 8 patients with 1 relapse before the initiation of treatment and 5 patients with relapses in the first year of treatment (only 10 patients with 1 year of treatment). The EDSS score on inclusion was below 3 for all patients. EDSS score was assessed for all patients after one year of treatment. Minor side effects were reported in most children at the initiation of treatment but no child discontinued treatment because of side effects. **Conclusions:** Further follow up will be needed and liaison with Adult Neurology Services in order to assess long term effectiveness and safety.

P116 - 1994

Subacute sclerosing panencephalitis presenting as schizophrenia and alpha coma pattern

Kartal A, Nese Citak Kurt A, Gürkas E, Aydin K, Serdaroğlu A. *Department of Child Neurology, Inonu University Faculty of Medicine, Malatya, Turkey – kartalays@gmail.com*

Introduction: Subacute sclerosing panencephalitis (SSPE) is a progressive neurodegenerative disorder of the central nervous system caused by a persistent defective measles virus. The disease is characterized by cognitive deterioration, behavioural disturbances and myoclonic jerks. The diagnosis of SSPE is based on specific electroencephalographic abnormalities and elevated measles immunoglobulin G (IgG) in the cerebrospinal fluid. SSPE can have atypical electroencephalographic features at the onset. We describe the case of a 14 year old girl who presented with atypical clinical and electrographic features which is manifested 3 months of the diagnosis and treatment of a psychiatric disorder. **Case:** A 14-year-old girl was presented at the Pediatric Neurology Department with a four month history of deterioration in school performance, and behavioral changes mainly manifested by insomnia, visual, auditory hallucinations. She was evaluated by a psychiatrist and schizophrenia was considered. She treated with antipsychotic drugs, without any noticeable improvement her neurologic status for 3 months. Then she was referred to our department due to progressive cognitive deterioration and unsteady gait. There were no history of any myoclonic jerks and seizure. The patient was hospitalized to investigate the etiology of progressive cognitive deterioration. Initial electrogram showed diffuse background slowing, which evolved into frontally dominant alpha frequency waves without reactivity, suggestive of “alpha coma”. On the 3rd day of admission, generalized myoclonic jerks were developed and the alpha coma pattern was replaced by a characteristic intermittent background slowing along with presence of periodic paroxysmal sharp and slow wave discharges which did not disappear with diazepam infusion. SSPE was suspected, and CSF analysis was performed for measles. The cerebrospinal fluid measles immunoglobulin G titer was $>1:1000$. SSPE diagnosis is based on the clinical symptoms and EEG findings and isoprinosine therapy was started. In conclusion, SSPE can present initially with psychiatric symptoms and physicians, should be aware of this rare possibility.

P117 - 1943

Response to rituximab in children with opsoclonus-myoclonus syndrome resistant to conventional treatments

Mirabelli-Badenier M, Fornarino S, Pisciotta L, Spinale B, Boeri L, Battaglia FM, Conte M, Battaglia T, Veneselli E, De Grandis E. *DINOEMI Department-University of Genoa, Child Neurology and Psychiatry Unit, Istituto G. Gaslini, Genoa, Italy – marisol.mirabelli@gmail.com*

Background: Immunosuppressive agents have been variably used over the years to treat childhood Opsoclonus-Myoclonus Syndrome (OMS). However, despite therapy, 70% of children have a chronic/relapsing clinical course with multiple neurological and developmental sequelae. Recently, multinational tasks forces proposed escalating treatments scheduling steroids pulses, intravenous immunoglobulins (IVIg), cyclophosphamide and rituximab, a CD20 monoclonal antibody. **Objectives:** to assess safety and efficacy of treatment with rituximab in resistant long-standing OMS forms as well as at earlier stages of disease. **Material and methods:** We report the long-term follow-up (range 1–4 years) after rituximab treatment of 5 OMS patients. Of these, 4 children showed chronic-relapsing course resistant to conventional therapies (steroids, ACTH and IVIg), while 1 child received early rituximab treatment after no benefit was reached with 7 steroid pulses. In all patients treatment response was recorded

on the basis of an international score (the “OMS Severity Scale”) and the long-term outcome was assessed by cognitive and neurological examination. **Results:** all patients underwent rapid and neurological improvement following rituximab administration; furthermore, no acute or late side effects were recorded during treatment. However, rituximab did not modify the cognitive impairment already present in long-standing forms. **Conclusions:** Our experience shows that rituximab represents a promising treatment for OMS and suggests that prompt treatment may be able to modify the clinical course of the disease. Rituximab, as a part of an escalating treatment strategy at earlier stages of disease, could protect against the irreversible cognitive and developmental deficits. Larger, controlled therapeutic trials are needed to confirm our results.

P118 - 1929

Herpes simplex encephalitis: a diagnostic dilemma

Voets S, Levy J, De Meirleir L. *CHU Saint Pierre, Brussels, Belgium – serge.voets@skynet.be*

A 6 month-old boy presented at the emergency room with a first episode of febrile generalized seizures. Consciousness was not altered. At the emergency ward (day 1) cerebrospinal fluid (CSF) exam was normal. The blood counts showed a mild infection. On day 3 after onset an EEG showed a lateralizing activity with generalized background slowing. A second CSF sample contained an elevated leukocyte count with predominance of neutrophils, pleocytosis and red blood cells but Herpes Simplex Virus (HSV)-DNA by polymerase chain reaction or other viral and bacterial cultures were still undetectable. HSV serology in blood was negative. Based on the EEG and suspecting Herpes Simplex Encephalitis (HSE) acyclovir treatment was started. On day 4 the MRI showed important unilateral multicystic encephalomalacia in the right occipital lobe with expansion to temporal and parietal lobes. Clinically general physical and neurological symptoms improved. During hospitalisation (day 8) the patient had again fever on a nosocomial infection, but in the septic screening a third CSF exam was performed. All viral and bacterial cultures were negative, but HSV-DNA by polymerase chain reaction was positive and confirmed the previous clinical diagnosis of HSE. Based on clinical findings, electroencephalographic changes and diagnostic imaging the patient was treated for 21 days. In conclusion, even when the CSF findings are normal, an HSV-encephalitis should still be considered and treated based on the clinical, electroencephalographic changes and possible diagnostic imaging.

P119 - 1890

Retrospective study to identify the viruses causing infections associated with febrile seizures

Voets S, DeBacker P, Franck E, Levy J. *CHU Saint Pierre, Brussels, Belgium – serge.voets@stpierre-bru.be*

Every winter many infants and children are admitted to the emergency room for an acute seizure with fever, and the parent's anxiety and remark – “Why? Thought my child was dying!” – returns. We reassure the parents and treat the child, but most of the time we can't clearly answer on the question of the parents. Febrile seizures are defined as seizures occurring in infancy or childhood, associated with fever but without evidence of intracranial infection, a previous afebrile seizure or other definable cause. It is usually accepted that that 2 to 5% of children will experience 1 or more febrile convulsions. The risk of febrile seizure is associated with many factors, including family history, and recent studies have identified gene loci associated with febrile seizures on chromosome 5, 8 and 19. These seizures are also age-dependent with the median age of first presentation

between 17 and 24 months, and even gender typed – more frequently in boys than in girls. With the diagnostic techniques, the importance of viral infections as the cause of the illnesses has been increasingly appreciated. However no recent study has comprehensively studied the viral etiology of the febrile episodes associated with febrile seizures. So we reviewed for this study all patients, admitted at the emergency room for febrile seizures from January till December 2012, to determine the causal virus of infection in the population of children found. And based on this information, we evaluated the specificity of certain viruses in the mechanism of the seizure: intensity of fever, height of body temperature, possible pathology in developing more complex type febrile seizures then simple febrile seizures and to design certain EEG patterns following causal virus in febrile seizures.

P120 - 1812

Amiodarone-associated lumbosacral radiculoneuropathy and rhabdomyolysis in a child

Kurian MA, Dejeu E, Gauthey M, Soroken C, Tissot-Daguette C, Truffert A, Korff C. *Pediatric Neurology, University Hospital, Geneva, Switzerland – mary.kurian@hcuge.ch*

Amiodarone toxicity has been reported in adults as a mixed polyneuropathy, vacuolar myopathy or both, in most cases after several months of treatment. We report the clinical, neurophysiologic findings and outcome of acute polyradiculoneuropathy and rhabdomyolysis in a child treated with amiodarone for atrial fibrillation. **Case report:** 14 year old girl of Senegalese origin, with severe mitral and tricuspid insufficiency and atrial fibrillation treated with amiodarone, introduced a week before surgery, presented on the fourth postoperative day, an abrupt onset of bilateral lower extremity tingling, numbness, pain and moderately severe asymmetric lower limb weakness. On examination, there was distal symmetric loss of sensibility of all modalities and absence of deep tendon reflexes in both lower limbs. Cerebrospinal fluid examination did not reveal albumino-cytological dissociation. MRI of the lumbosacral region was normal. Electroneurography showed evidence of an axonal-myelinic predominantly motor lumbosacral polyneuroradiculopathy. Serum creatine kinase levels were markedly elevated (10'206 U/l, normal values: 33–187). She had a poor nutritional state (weight 29 kg).

P121 - 1764

Hypercytokines in cerebrospinal fluid from patients with encephalitis

Chang YT, Chin ZN, Kuo HT, Chuang TY, Lin WD, Tsai CH, Chou IC. *Division of Pediatrics Neurology, Children's Medical Center, China Medical University Hospital, Taichung, Taiwan – iching@mail.cmuh.org.tw*

Objectives: Without evidence of culture proved pathogens, the mechanism of encephalitis remains unclear. Hypercytokines in the brain, with subsequent brain edema and degenerative changes in the neural cell that may lead to poor prognosis. Here, we assessed the differences of cerebrospinal fluid (CSF) cytokine changes in patients with encephalitis between different outcomes. **Material and methods:** Cytokine was analyzed using the Bio-Plex Cytokine Assay System (Bio-Rad Laboratories, Inc., San Diego, CA, USA). Interleukin (IL)-1, IL-2, IL-4, IL-6, IL-7, IL-8, IL-10, IL-12, IL-13, IL-17, granulocyte colony-stimulating factor, granulocyte macrophage colony-stimulating factor and monocyte chemoattractant protein-1 (MCP-1), interferon, macrophage inflammatory protein-1-alpha and tumor necrosis factor were measured in 8 serial CSFs taken from 6 patients with encephalitis. **Results:** The outcome was poor in one patient and good in five patients. Hypercytokines in CSF were noted in IL-6, IL-8, and MCP-1, which were 3810 pg/ml, 4475 pg/ml, and 1213 pg/ml,

respectively. Extremely high level (three to four times above the average) was noted in patients with poor prognosis. Such high level cytokines persisted in serial taping with 24-hour intervals. **Conclusion:** These finding suggesting that the accumulation of cytokines progresses in the central nervous system and results in a “cytokine storm” in the brain may lead to poor prognosis. However, the sample sized was small. Further study of prognostic value of CSF cytokines changes in encephalitis will be enrolled.

P122 - 1750

Unusual clinical cases that mimic acute disseminated encephalomyelitis (ADEM)

Duman O, Yurekli VA, Gencpinar P, Karaali K, Gumus H, Okuyaz C, Hazar V, Haspolat S. *Department of Child Neurology, Faculty of Medicine, Akdeniz University, Antalya, Turkey – pinargencpinar@yahoo.com.tr*

Introduction: Acute disseminated encephalomyelitis (ADEM) is an immune-mediated inflammatory demyelinating disorder of the central nervous system. Though most often observed as a single episode, relapsing or recurrent forms are also present. It can occur at any age, but it is predominantly a childhood disease. The diagnosis of ADEM is sometimes difficult, and depends on the exclusion of several other disorders. Herein, we reported six rare cases in whom clinical and radiological findings mimicked ADEM. **Cases:** Demographic characteristics, clinical and laboratory results of the patients were noted. Three of the patients (50%) had antecedent infections. Initial symptoms of the patients were as follows fever (50%), altered consciousness level (33.3%) and convulsions (16.7%). Upon neurologic examination, 83.3% of the patients were found to have long tract signs, 50% ataxia, 50% altered consciousness level and 33.3% hemiparesis. The final diagnoses were established by spinal MRI, by muscle biopsy and mitochondrial analysis, with clinical and laboratory findings, by bone marrow and spleen aspiration material examination and by brain biopsy from the lesional area in the cases. Final diagnoses were neuroblastoma, MELAS, CADASIL, Histiocytic sarcoma and Hemophagocytic syndrome. **Conclusion:** There is no simple test to secure diagnosis of ADEM, and its clinical presentation is polymorphic. Diagnosis depends on a synthesis of history, laboratory tests, neurological findings, treatment outcomes, and exclusion of other diseases. Our case series has demonstrated the difficulties in diagnosing ADEM and has provided samples of extremely rare disorders that radiologically and clinically mimic ADEM.

P123 - 1742

Extensive multifocal demyelinating encephalomyelitis with spectacular response to intravenous immunoglobulins

Verhelst H, Maes M, Meersschaut V, Verloo P, Van Coster R. *Department of Pediatrics, Division of Pediatric Neurology and Metabolism, Ghent University Hospital, Ghent, Belgium – helene.verhelst@ugent.be*

In a few trials in adult patients with multiple sclerosis (MS) was shown earlier that the administration of intravenous immunoglobulins may be a safe and effective alternative for treatment of acute MS exacerbation, especially when steroids are contraindicated. In children, only a small number of case reports showed beneficial effect of intravenous immunoglobulins in refractory cases of acute demyelination. We report on a pediatric patient with steroid resistant extensive multifocal demyelinating encephalomyelitis who showed a spectacular positive response to the administration of intravenous immunoglobulins. Propositus was a previously healthy 9-year-old boy who presented with unilateral progressive loss of vision followed by symptoms of encephalopathy (headache, vomiting), motor dysfunction and myelopathy (urinary incontinence). Three weeks

earlier, he had signs of gastro-enteritis. Ophthalmological examination revealed unilateral optic neuritis. MRI of the brain and spinal cord showed multiple, small, well-defined juxtacortical lesions in cerebrum and cerebellum, in the capsula interna, pons, medulla oblongata and spinal cord. Some of the lesions showed gadolinium enhancement. The differential diagnosis was between acute disseminated encephalomyelitis (ADEM), MS or neuromyelitis optica. Steroid pulse therapy was started. Shortly thereafter, headache and vomiting resolved and visual accuracy improved but motor problems and urinary incontinence worsened, and propositus became wheelchair bounded. Repeat MRI showed a marked increase in volume of existing lesions and an increase of the number of lesions. At that moment, an opportunistic infection was suspected although an infectious agent could not be demonstrated. Brain biopsy was performed revealing demyelination with infiltration of numerous lymphocytes and only limited signs of vasculitis consistent with the diagnosis of ADEM or MS. Therapy with intravenous immunoglobulins was started, 1g/kg/day for two days, with a remarkably positive effect. Symptoms started to improve after four days and completely resolved after one month. Also, subsequent MRI controls showed continued improvement of the lesions.

P124 - 1723

Acute neurological disease associated with *Mycoplasma pneumoniae* infection

Aguilera-Albesa S, Zarikian-Denis S, Moreno-Galarraga I, Yoldi-Petri ME, Durá-Travé T, Herranz-Aguirre M, Ocío-Ocío I, Díez-Bayona V, Molina-Garicano J. *Paediatric Neurology, Navarra Hospital, Spain – saquilea@navarra.es*

Objective: To describe the clinical characteristics, neuroimaging findings and outcome of 8 children with acute neurological disease associated with *Mycoplasma pneumoniae* (MP) infection. **Material and methods:** A retrospective review of 0–15 year-old patients with acute neurological manifestations, associated to positive serology in serum for MP. MP antibody titres over 1/160 were considered positive. **Results:** Mean age was 7 years (5–12), 4 boys. They were diagnosed with: idiopathic intracranial hypertension (IH, cases 1, 2, 3); febrile epileptic status in a previously healthy 6-year boy (case 4); meningoencephalitis (case 5); opsoclonus-ataxic syndrome after MP infection with occult neuroblastoma found after investigations (case 6); transverse myelitis (case 7); unilateral facial palsy (case 8). Five patients presented with previous respiratory infection. All showed positive MP antibody titres at neurological diagnosis (range 1/320–1/20480). In cases 1–7 lumbar puncture revealed 0–640 predominantly polymorphonuclear cells. PCR for MP in CSF was normal in 3/3. CNS MRI showed transient abnormal findings in 4/7: white matter right temporal T2 hyperintensity (case 3); ADEM-like pattern with basal ganglia T2+FLAIR asymmetric hyperintensities (case 4); selective symmetric basal ganglia hyperintensities (case 5); and transverse myelitis (case 7). EEG showed transient left frontotemporal slow-waves in cases 4–5. All patients received clarithromycin. Corticosteroids were used in cases 3, 5, 6, 7 and immunoglobulins in cases 5, 6 with significant clinical and neuroimaging improvement in all cases. Case 3 suffered a clinical relapse of IH with MP 1/640 titres one year after being asymptomatic with negative MP. In case 6 paravertebral neuroblastoma was removed but she required prolonged immunosuppressive treatment. **Discussion:** Acute neurological disease associated with MP is usually monophasic but also could be recurrent. MP may acts as a trigger for underlying pathology. Respiratory infection symptoms are not always present, and CSF studies can be normal. A causal relationship between MP and acute neurological manifestations remains to be elucidated.

P125 - 1700

MRI pattern recognition for congenital CMV

Aleksanyan A, Yepiskoposian M. Arabkir Joint Medical Center, Yerevan, Armenia – anidoc@mail.ru

Introduction: This report describes a case in which MRI pictures lead to diagnosis of Congenital CMV. **Case presentation:** 2 months old infant was hospitalized because of diffuse skin lesions. He is 1st child from 1st pregnancy, child was born at term, with low birth weight. He had microcephaly, severe spasticity, high tendon reflexes, restriction of hip abduction and he was underweight. Bilateral sensorineural hearing loss was revealed by audiometry and hepatic cyst was found by ultrasonography. MRI was done and diffuse white matter changes, bilateral temporal cysts, abnormal gyration, intraventricular septae were found in it. It was suspected CMV and then it was confirmed by PCR in dry blood of Guthrie card taken for screening purposes. **Conclusion:** The presence of the described MRI findings is an indication for CMV investigation. And MRI with such changes can be pattern recognition for Congenital CMV.

P126 - 1693

Paediatric sciatic neuropathy presenting as painful leg: a case report and review of literature

Iqbal M, Prasad M, Babiker M, Ritey C. Sheffield Childrens Hospital, Sheffield, UK – drmehtabch@yahoo.com

Introduction: Mononeuropathies in general are very uncommon in childhood. Sciatic neuropathy (SN) is probably underappreciated in childhood and likely to represent nearly one quarter of childhood mononeuropathies. **Method:** We present a 7 old girl who presented with painful right lower limb and abnormal gait. Detailed investigation revealed transient eosinophilia, abnormal neurophysiology and MRI suggestive of isolated sciatic neuropathy. **Results:** She has responded very well to physiotherapy and has made a complete motor recovery although she is left with an area of abnormal sensation affecting the lateral border of her right leg and the dorsum of her foot. **Discussion:** Differential diagnoses for paediatric SN will be discussed including compressive neuropathies in children and various hyper-eosinophilia syndromes. Compressive neuropathies in childhood are very rare and compression of the sciatic nerve is the second most common group after peroneal nerve lesion.

P127 - 1650

Severe PANDAS-like course: a case report

Cindro Heberle L, Pavlović M, Neubauer D, Al Tawari A. Al Sabah Hospital, Pediatric Department, Kuwait – heberlelada@hotmail.com

Objective: clinical spectrum of autoimmune disorders following infection with group A beta-hemolytic streptococcus may extend beyond Sydenham chorea and PANDAS. We report a boy with life-threatening course improved after immunotherapy. **Case presentation:** 11 years old boy with 1 year long history of facial tics developed fever with throat infection progressing to lethargy and epileptic status stopped by anticonvulsants but severe agitation, fidgeting and frequent tics were observed afterwards, soon to be followed by another epileptic status and central apneas requiring intubation and intensive care for several days. Virology work up and CSF study were normal, high titers of ASOT (3200 IU/ml) were found. EEG detected slow background activity, on MRI brain subtle thalamic changes were seen. Treated by antibiotics, immunoglobulins, methyl-prednisolone and antiepileptics the child gradually improved but cognitive impairment (IQ 68), depressive behavior, tics and occasional focal seizures have remained. **Conclusions:** we believe that the boy had an extremely

severe form of PANDAS-like condition finally leading to residual epilepsy, cognitive deficits and depression.

P128 - 1627

Overview of pediatric peripheral facial nerve paralysis: analysis of 40 patients

Ozkale Y, Erol I, Saygi S, Yilmaz I. Baskent University Faculty of Medicine, Department of Pediatrics, Adana Teaching and Medical Research Center, Turkey – ilknur_erol@yahoo.com

Objectives: Peripheral facial nerve paralysis (PFNP) in children might be alarming sign of serious disease such as malignancy, systemic disease, congenital anomalies, trauma, infection, middle ear surgery and hypertension. It may also be caused due to immunization and toxic factors or Bell's palsy. Therefore, careful investigation and differential diagnosis are essential in children. **Material and methods:** The cases of 40 consecutive children, and adolescents who diagnosed as PFNP at Baskent University Adana Hospital Pediatrics and Pediatric Neurology Unit between January 2010 and January 2013 were retrospectively evaluated. **Results:** There were 15 boys and 25 girls, age range, 2 months to 17 years (with a median age, 6.5 ± 4.51 years). All of the patients had acquired, first episode and unilateral PFNP. As regards the etiology of PFNP in children, we determined the most common cause was Bell's palsy (26 cases, 65%), followed by infection (11 cases, 37.5%), tumor lesion (1 case, 2.5%), suspected chemotherapy toxicity (1 case 2.5%). In the infectious group; 5 patients with PFNP had otitis media from clinical examination. Seven children had serological evidence of specific triggers: Borellia Burgdorferi (3); herpes simplex virus (3), mycoplasma (1). Thirty one patients with facial nerve paralysis were treated with oral steroids. We also didn't reveal a significant difference in the outcome of facial nerve paralysis between treated and not treated groups. We noted that younger patients had generally poor outcome than older patients with regardless of disease etiology. **Conclusion:** PFNP has been reported in many countries from America and Europe, however, knowledge about its clinical features, microbiology, neuroimaging, and treatment in Turkey is incomplete. Present study demonstrated that Bell's palsy, infection and trauma were the most most common etiologies of PFNP in Southern coast of Anatolia (Mediterranean region).

P129 - 1592

Isolated sphenoid sinusitis masquerading migraine

Jeong-Ho L, Suh ES. Department of Pediatrics, College of Medicine, Soonchunhyang University Hospital, Seoul, Korea – essuh@schmc.ac.kr

Objective: Sinusitis is a well-known cause of headache, with an incidence of around 9% among children and adolescents. But, isolated sphenoid sinusitis is a rare disease and its symptoms are often non-specific and confusing. So the diagnosis can be difficult to differentiate from migraine headache. But there are few reports of isolated sphenoid sinusitis and headaches in children. **Results:** Case 1: A 10-year-old boy was referred for evaluation of migraine headaches. Headache with diplopia started 6 months ago. His headaches were located at both parietal area associated with photophobia, lasting 1–2 hours. Events were occurred nearly every day, occasionally relieved by sleep. He was afebrile without evidence of nasal congestion or facial tenderness over his sinuses. His neurologic and ophthalmologic examinations were normal. The brain magnetic resonance (MRI) showed isolated Right sphenoid sinusitis. After oral antibiotic treatment for 3 weeks, his symptoms were relieved and follow up MRI showed improved sinusitis. Case 2: A 8-year-old female presented with a 2 weeks history of severe headache with dizziness, nausea. Her mother has the migraine history. She denied any nasal symptoms or fever. The headaches were described as both sided, constant

and throbbing, exacerbated with head movement, lasting 1 hour. Her neurologic examination was normal and no tenderness on sinuses area. MRI was requested to rule out intracranial pathology and revealed isolated sphenoid sinusitis. After one month oral medication, her headaches were relieved. **Conclusion:** Two children who presented for suspected migraine headaches had isolated sphenoid sinusitis.

P130 - 1577

A case of brain abscess arising from sinusitis

Lee BL. *Department of Pediatrics, Pusan Paik Hospital, Inje University College of Medicine, Busan, Korea – bototii@hanmail.net*

Introduction: Brain abscess is regarded as a significant intracranial complication of bacterial sinusitis. We report a case of cerebritis proceeded by acute sinusitis which progressed into a large abscess in spite of adequate empirical antibiotic therapy and sinus drainage. **Cases:** A 13-year-old girl was admitted to our hospital with pyrexia and headache. She had past history of chronic sinusitis. On examination, she had neck stiffness, but there was no focal neurologic deficit. Laboratory findings revealed a neutrophilia. Computed tomography of the brain identified a sphenoid sinusitis, but there was no other abnormal finding. A spinal tap showed normal cerebrospinal fluid. Empirical antibiotic therapy with cefotaxime was initiated. However, fever and headache were aggravated. Brain magnetic resonance imaging (MRI) performed on five days after admission revealed cerebritis of right frontal lobe, small abscess formation (<1 cm) in connection with anterior skull base wall and ethmoid and sphenoid sinusitis. Vancomycin and metronidazole were empirically added, and functional endoscopic sinus surgery (FESS) was done for sinus drainage. Bacterial culture from drainage presented *Staphylococcus aureus*. However, in spite of appropriate antibiotic therapy and FESS, her fever and headache appeared again after two weeks. Follow-up MRI showed enlarged rim enhancing lesion in right frontal lobe with central cystic necrosis (about 4.4×2.5 cm). A prompt neurosurgical bur hole aspiration was performed. Postoperatively, her symptoms were improved and intravenous antibiotics were continued for 6 weeks. MRI performed four weeks after operation showed a nearly improving state of abscess. No recurrence was noted during the 6-month follow-up period, and she remained free of neurologic deficit. **Conclusion:** Intracranial complication secondary to sinusitis can be progressed to be potentially life threatening despite the appropriate use of broad-spectrum antibiotics. Therefore, a high degree of suspicion, along with serial neuroimaging and prompt neurosurgical intervention, is required.

P131 - 1553

Acute cerebellitis presenting with sudden onset headache accompanied by elevated CSF IgG index

Lee KY. *Department of Pediatrics, Ulsan University Hospital, University of Ulsan College of Medicine, Korea – pdsnoopy@naver.com*

Acute cerebellitis, a rare inflammatory syndrome of the cerebellum, is one of the important causes of acute cerebellar dysfunction in childhood. Although it typically presents with cerebellar dysfunction such as ataxia, non-localizing symptoms such as headache can be much more prominent than cerebellar symptoms because of increased intracranial pressure as a result of cerebellar swelling. The cerebrospinal fluid (CSF) IgG index is most often tested clinically in the diagnosis of multiple sclerosis. However, it is not specific to multiple sclerosis, and can be elevated in a variety of neurologic diseases, including bacterial and viral central nervous system infections. A 7-year-old boy with acute cerebellitis presenting with sudden onset headache and only subtle cerebellar dysfunction demonstrated an elevated CSF

IgG index (1.1) and was oligoclonal band-negative. A two-month follow-up magnetic resonance imaging revealed cerebellar atrophy and remaining subtle signal changes in the cerebellum, albeit the patient showed no neurologic deficit.

P132 - 1525

Initial and hospital-acquired hyponatremia in children with CNS infection

Lee YJ, Yeon GM, Nam SO, Kim YM. *Department of Pediatrics, Pusan National University Children's Hospital, Yangsan-si, Korea – jimmyeye@hanmail.net*

Purpose: The aim of this study was to compare the effect of the different etiologies in the children with CNS infection on the incidence of initial vs hospital-acquired hyponatremia (IH vs HAH) (plasma sodium concentration, PNa <135 mmol/L). **Methods:** Children who treated for CNS infection and required the administration of intravenous fluid between 2011 and 2012 were evaluated retrospectively. The children were classified into 4 groups: group A of aseptic meningitis, group B of viral meningoencephalitis, group C of bacterial meningitis, and group D of tuberculous meningitis. All patients had measured the initial PNa and were retested serially. By the sodium concentration of fluid, children were divided into 2 groups: group I of the under 0.45% saline in dextrose, and group II of more than 0.45% saline. **Results:** We identified 248 children (185 in group A, 33 in group B, 27 in group C, and 3 in group D). The mean age was younger in children of group C (3.5±5.3 years) ($p=0.0124$) than in those of group A (5.7±3.9 years) or group B (6.3±5.5 years). IH and HAH was found in 13.3% (33/248) and 10.1% (25/248) of all patients, respectively. The incidence of IH was significantly higher in group C (8/27, 29.6%) ($p=0.0082$) than in group A (17/185, 9.2%) or group B (7/33, 21.2%). HAH was more frequent in group B (9/33, 27.3%) ($p=0.0004$) and in group D (2/3, 66.7%) ($p=0.0011$) than in group A (9/185, 4.9%) ($p<0.0001$) or in group C (5/27, 18.5%) ($p=0.1229$). Of the patients in group I, 27.6% (8/29) developed more common HAH compared with 7.8% (17/219) in group II ($p=0.0009$). Any hyponatremia was not noted in 82.2% (180/219) in group II during the period of hospitalization ($p<0.0001$). **Conclusion:** Hyponatremia was common in children with CNS infection, and the incidence showed distinct differences among the different etiologies. The administration of more than 0.45% saline could help in reducing the incidence of HAH in children with CNS infection.

P133 - 1513

Clinical application of viral CSF PCR studies: a retrospective 11-year experience

Kleines M, Scheithauer S, Schiefer J, Häusler M. *Department of Infection Control and Infectious Diseases, University Hospital RWTH Aachen, Germany – haeusler@rwth-aachen.de*

Background: The PCR is the method of choice to detect viral activity in the central nervous system (CNS). Positive findings, however, do not prove an impact on the neurological problem. Here, knowledge on large patient groups may facilitate data interpretation. **Methods:** A retrospective analysis of CSF PCR data concerning 514 pediatric and 2904 adult samples, focusing on Epstein-Barr virus (EBV), cytomegalovirus (CMV), herpes simplex virus (HSV), enteroviruses (ENV), human herpesvirus type 6 (HHV-6) and varicella zoster virus (VZV). **Results:** EBV was detected in 1.63%, VZV in 1.3%, HSV in 0.4%, ENV in 0.4%, CMV in 0.2% and HHV-6 in 0.2% of the patients studied, respectively. Detection rates were higher among very young and among older patients. HSV, VZV and ENV were dominant in typical infectious CNS diseases, EBV in further inflammatory diseases (bacterial CNS infections, multiple sclerosis, HIV infection) and in diseases not typically attributed to infections. HSV and VZV were frequent

in further immunosuppressive conditions. As for repeated PCR studies, negative results followed by positive results, indicative of viral reactivation, were found in 6/147 EBV studies and in 1/217 HSV studies. Positive results, finally followed by negative results were typical for HSV, VZV and ENV infections. The maximum duration of positive CSF PCR findings was 15 days for HSV and 12 days for VZV infections, respectively. **Conclusion:** Whereas HSV, VZV and ENV infections characterize patients with typical infectious CNS diseases, EBV and HHV-6 tend to reactivate in patients with further neurological diseases. For the latter situations, a clinical impact of the viral infection remains to be proven. In HSV infection repeated testing may be necessary to establish the diagnosis. Despite antiviral treatment, viral clearance from VZV or HSV can occur with delay which supports the need for repeated CSF PCR testing.

P134 - 1512

Clinical outcome and prognostic factors of acute necrotizing encephalopathy

Lee CG, Lee KH. Seoul, Korea – leechagon@hanmail.net

Acute necrotizing encephalopathy (ANE) is a fulminant disease of the brain characterized by bilateral thalamic lesions, which is prevalent among children in East Asia. ANE usually occurs following an antecedent infection, usually a viral illness such as influenza or parainfluenza. ANE shows various neurologic symptoms characterized by rapid deterioration of consciousness, seizure and brainstem dysfunction. Prognosis is usually poor with a high mortality rate and neurologic sequelae. This study was aimed to delineate the clinical characteristics and prognostic factors of ANE. We retrospectively analyzed clinical data of pediatric patients who were diagnosed with ANE at Samsung Medical Center from December 1998 to March 2011. Ten patients were identified. The mortality rate was 40%, and only 30% patients survived without neurological handicap. The extent and definite signal change of the brainstem on brain magnetic resonance imaging were only significantly correlated with mortality ($P = 0.04$). In conclusion, the broad and extensive brainstem involvement suggested a fulminant course of the ANE. Early diagnosis of ANE before brainstem involvement through careful identification of symptoms of brain dysfunction may be the best way to achieve better neurologic outcome.

P135 - 1511

Subacute sclerosing panencephalitis: a multinational survey

Häusler M, Yis U, Pacheva I, Yazar C, Altunbasak S, Korinthenberg R, Vintan M, Jovic-Jakubi B, Craiu D, Iliescu C, Hartmann H, Altunbasak S, Tarta-Arsene O, Lukban M, Takashi I, Anlar B. Department of Pediatrics, University Hospital RWTH Aachen, Germany – haeusler@rwth-aachen.de

Objectives: Subacute sclerosing panencephalitis (SSPE) is a chronic infection of the central nervous system with a mutated measles virus (MV). Its prevalence is likely to increase as vaccination rates decrease in Northern Europe. Clinical knowledge, however, is limited. **Material and methods:** A multicentric survey, summarizing clinical, diagnostic and treatment experience of 23 hospitals, based on experience derived from treating more than 500 patients with SSPE. **Results:** SSPE should be considered in all patients presenting with otherwise unexplained neurological symptoms. In most patients the diagnosis can be established by the combined finding of typical clinical symptoms (repetitive myoclonic jerks) and a strong intrathecal synthesis of antibodies to MV. Whereas therapeutic use of antiviral (amantadine, ribavirin) and immunomodulatory drugs (isoprinosine, interferon alpha), and of immunoglobulins has been reported, the efficacy of these drugs is not well studied. For part, this can be explained by the

fact that no common and detailed outcome measures, focusing on neurological and psychosocial aspects, have been established. Clobazam and carbamazepine are most frequently used to control typical myoclonic jerks. **Conclusions:** Collaborative studies, based on common clinical and laboratory standards are urgently needed to improve outcome of patients with SSPE.

P136 - 1502

Tic disorder as a presenting feature of Hashimoto's encephalopathy

Saygi S, Ozkale Y, Erol I. Baskent University Faculty of Medicine, Division Of Child Neurology, Adana, Turkey – semra_saygi@yahoo.com

Introduction: Hashimoto's encephalopathy (HE) also called steroid-responsive encephalopathy is a rare disorder in children and characterized by high titers of anti-thyroid peroxidase antibodies. The clinical features of HE are heterogeneous, and a high degree of suspicion is necessary for its diagnosis. The presenting clinical features of HE are fluctuating encephalopathy, cognitive impairment, and behavioral changes. **Case report:** A 12-year-old boy presented with motor tics in the form of involuntarily head nodding and upper limb shaking movements, without any past or present vocal tics, for 3 years. His past medical history was significant with diagnosis of pediatric autoimmune neuropsychiatric disorders associated with streptococcal throat infections (PANDAS) due to his history of recurrent tonsillitis and the presence of a mild elevation of anti-streptolysin O (ASO). Since the serologic evaluation of the anti-streptolysin O titer was 354 IU/ml, and considering the clinical history, the patient was also diagnosed as PANDAS. He received treatment with benzylpenicillin and pimozide with some initial improvement. Two years after admission, the patient's symptoms had worsened and he had become forgetful. Because of our previous experience of HE in a patient with unexplained psychiatric findings, an analysis of anti-thyroid antibody levels was performed. We found that both anti-thyroid peroxidase antibodies and anti-thyroglobulin antibodies levels were elevated. And Thyroid ultrasound and scintigraphy showed thyroiditis. A diagnosis of HE was suspected and therapy with prednisone 1 mg/kg daily was initiated. At the time of writing, the patient is on steroids but symptom free following therapy initiation. Prednisone is now being tapered. **Conclusions:** To our knowledge, this case study is the first to report tic disorder due to HE, as well as its course of treatment. We suggest that children who present with tic disorder should be further investigated with anti-thyroid antibody assays to exclude the presence of HE.

P137 - 1499

Acute disseminated encephalomyelitis in children and adolescents: a single center case series

Erol I, Ozkale Y, Alkan O. Baskent University Faculty of Medicine, Department of Pediatrics, Neurology Division, Adana Teaching and Medical Research Center, Turkey – ilknur_erol@yahoo.com

Introduction: Acute disseminated encephalomyelitis (ADEM) is an immune-mediated disease that produces multiple inflammatory lesions in the brain and spinal cord, particularly in the white matter. **Patients and methods:** We retrospectively evaluated 15 consecutive cases of ADEM in children and adolescents from a single institution in Adana, Turkey, between June 2008 and June 2012 (9 boys and 6 girls; age range, 0.5 years to 16 years; median age, 3.5 ± 4.40 years). **Results:** The cases occurred in a seasonal distribution with 73.3% (11 of 15) presenting in winter or spring. The majority of patients (13/15, 86.7%) had a history of acute febrile illness 2 to 40 days before presentation and 5 children had serological evidence of specific triggers: mycoplasma (2), influenza A (H1N1) (1), or Epstein-Barr virus (2). The most common

presenting symptoms were gait disturbance (12/15, 80%), altered consciousness (10/15, 66.7%), fever (7/15, 46.7%), headache (4/15, 26.7%), seizures (4/15, 26.7%), meningismus (4/15, 26.7%), and vomiting (3/15, 20.4%). Four of the patients exhibited isolated cerebral lesions whereas the other 11 showed additional involvement of the brainstem, spinal cord, and (or) cerebellum as revealed by magnetic resonance imaging. All children were treated with a standard protocol of three to five day IV administration of methylprednisolone and IV immunoglobulin for patients who continued to deteriorate. Follow-up evaluation ranged from 0.6 to 4 years (median, 1.8 ± 1.11 years). In 13 patients, all neurological signs and symptoms resolved after treatment. Only one patient was left with severe neurologic sequelae and the remaining child had recurrent attacks and was ultimately diagnosed with MS. **Conclusion:** Acute disseminated encephalomyelitis should be considered in children presenting with multifocal neurologic abnormalities and encephalopathy. Early treatment with immunomodulators agents is likely to result in a favourable outcome or even full recovery.

P138 - 2039

A taste of molten gold!

Hussain S, Desurkar A. *Sheffield Childrens Hospital, Sheffield, UK – shanawaz@doctors.org.uk*

Introduction: We present a 3 month old who was ventilated for respiratory deterioration in the midst of bronchiolitis season in the UK. He was subsequently found to be hypotonic with profound weakness and subsequently diagnosed with infantile botulism based on the history and microbiological confirmation. **Case description:** A 3 month old baby boy was seen at his local paediatric unit for poor feeding. He subsequently developed an oxygen requirement with worsening gases. He was ventilated and an initial CT head was reported as normal. He was transferred to the paediatric intensive care unit for further management. Whilst ventilated, despite being off sedation, he was noted to be markedly hypotonic, with no spontaneous eye opening, depressed deep tendon reflexes and no gag. A full septic screen and neuro metabolic screen were normal. An MRI revealed no structural abnormalities and an EEG was not diagnostic of any underlying abnormality. On direct questioning by the neurology team, parents confirmed they had given honey in the days leading up to his initial presentation. A clinical suspicion of infantile botulism was made and stool samples confirmed the presence of botulism neurotoxin B. He was treated with botulinum immunoglobulin (Baby BIG) on day 6 of his admission and had marked improvement in movement within 24hrs of administration. He was extubated on day 10. He was seen 1 month after discharge and had no neurological residual deficit on assessment. **Discussion:** Infantile botulism is a rare but treatable causes of acute paresis in infants. To date only 13 cases of infantile botulism had been reported in the UK. Rapid diagnosis based on clinical history and microbiological testing of stools is imperative so that it can be treated promptly with botulinum immunoglobulin. Prompt treatment has shown to reduce the mean duration of ventilation from 4.4 to 1.8 weeks.

P139 - 1715

Hematopoietic stem cell transplantation in severe refractory autoimmune diseases of central nervous system in pediatric patients

Kirgizov KI, Volkova EJ, Piliya SV, Maschan AA, Kuzenkova LM, Skorobogatova EV, Bembeeva RC. *The Russian Children's Research Hospital, The Federal Research Center of Pediatric Hematology, Oncology and Immunology, Moscow, Russia - kirgiz - off@yandex.ru*

Treatment of severe refractory CNS autoimmune diseases is sig-

nificant problem now. Hematopoietic stem cells transplantation (HSCT) can be effective treatment option in pediatric multiple sclerosis (MS) and neuromyelitis optica (NMO). We aimed to evaluate the effectiveness of autologous HSCT for severe refractory pediatric MS and allogeneic HSCT for severe refractory NMO. **Patients and methods:** This survey includes 9 patients with MS and 1 patient with NMO under 18 y.o. All patients had the confirmed diagnosis of severe refractory MS and NMO with high inflammatory activity on the background of corticosteroids, interferons, IVIGs and plasmapheresis. Patient with NMO received Cyclophosphamide and Rituximab additionally without the response. Disease duration - 2–4 years. Mean EDSS of MS patients enrolled to the study - 6.16 ± 0.2 points. Patient with NMO showed the spastic tetraplegia, vis=OD=OS=0 (amaurosis). **Procedures:** Peripheral blood stem cell (PBSC) mobilization for MS patients: Cyclophosphamide 60 mg/kg, G-CSF on day +7 from Cyclophosphamide. Preparation: Cyclophosphamide 200 mg/kg and ATGAM 160 mg/kg. PBSC reinfusion - day 0. G-CSF stimulation from day +5. NMO patient: preparation - Treosulfan 42 gr./sq.m. + Fludarabine 150 mg/sq.m. + Rituximab 375 mg/sq.m. followed by allogeneic bone marrow infusion. **Results:** MS patients showed fast improvement during early post-transplant period. Maximal EDSS improvement - 5.5 points, mean - 2.7 ± 0.1 points, observation period 2–40 months. Only one patient relapsed after 12 months. Patients received in-time HSCT showed the better response. NMO patient significantly improved the neurological presentation on day +150: chromatic sensitivity, walks without assistance (strength in extremities - 3.5–4 points). **Conclusion:** HSCT is the effective way of autoimmune inflammation reduction and successful approach for treatment of severe refractory pediatric MS and NMO. In-time HSCT can significantly minimize the disability level and improve the outcome of these diseases. In-time transplanted patients have the better possibility to improve neurological functions.

P140 - 1712

Behçet's disease: neurological presentation in two patients

Aduc T. *Neurologist Private practice, South Africa – andrent@mweb.co.za*

I present two patients at varying stages of their disease. The older one had presented with previous history of joint pain, recurrent lung disease and mouth ulcers. More recently he presents with complex partial seizures. The younger patient, 4 years old, presented with meningo- encephalitis, associated with demyelination, only responsive to high dose methyl prednisone, followed 3 weeks later with optic neuritis, causing loss of vision. At the second presentation, he was suspected of having Behçet's, and tested positive for the B51 antigen. The onset of neurological symptoms in Behçet's, investigation, management and prognosis will be briefly reviewed and discussed.

P141 - 2140

Clinical symptoms, investigations, treatment and outcome of children with Cerebral involvement in hemolytic uremic syndrome

Kaur B, Kirkham F. *Department of Paediatric Neurology, University Hospital Southampton NHS Foundation Trust, UK – docbalvinder@gmail.com*

Background: Neurologic involvement is the most serious complication of diarrhea associated haemolytic uraemic syndrome (D+HUS) and is associated with significant mortality. Spreading of microvascular thrombosis caused by combined effects of lipopolysaccharide, cytokine, enhanced shear stress, and verotoxin appears to play a major role in the development of central nervous dysfunction. **Methods:** We report a retrospective series of

patients with neurologic involvement that occurred in the course of D+HUS. **Results:** In total 34 patients were admitted with HUS between July 2004 and August 2012, out of which 7 had atypical HUS. 3/34 (8.8%) had cerebral involvement. All 3 had E.Coli 157 related HUS. All were females aged 1, 4 and 6 years. Symptoms at presentation included bloody diarrhoea and decreased urine output (3/3) and generalised seizure (1/3). 2 out of 3 patients developed right sided hemiplegia, within 10 days of admission. EEG was suggestive of encephalopathy in all 3 out of which two had generalised and one had asymmetric slowing. Neuroimaging (MRI brain) showed ischemic changes in bilateral thalami (2/3), cortical signal abnormality with diffusion restriction and local swelling affecting frontal operculum, insular cortex, left parietal lobe, diffusion restriction left hippocampus and right putamen (1/3), abnormal signal within peritrigonal white matter (1/3), small foci of subdural hemorrhage in right frontal lobe and shallow subdural hematoma beneath left tentorial leaf. 2/3 patients received Eculizumab, a monoclonal antibody directed against complement protein, C5. There were no deaths. One patient had no abnormal neurology at discharge. Right hemiparesis has improved significantly in one patient and is persisting in one, who is currently having rehabilitation in the form of physiotherapy and occupational therapy. **Discussion:** Although death may be uncommon, cerebral HUS continues to cause significant neurological morbidity.

P142 - 1632

Guillain-Barré syndrome in Japanese children: a retrospective analysis of clinical manifestations, epidemiology, and electrophysiological studies

Fujii K, Takeshita K, Takagi A, Mizuochi H, Suyama M, Uchikawa H. *Department of Pediatrics, Chiba University Graduate School of Medicine, Japan* – kfujii@faculty.chiba-u.jp

Objectives: Guillain-Barré syndrome (GBS) is characterized by muscle weakness and loss of tendon reflex due to immunological mechanism. Clinical pictures of GBS is different between Western countries and Asian one, and especially in children, details of GBS including clinical features, epidemiology, and electrophysiological studies has not been well described. In this study, we performed extensive retrospective studies to elucidate these issues. **Material and methods:** We retrospectively surveyed pediatric GBS patients for 20 years from children hospitals in which child neurologist could diagnose GBS with serological and electrophysiological methods. We then investigated their clinical manifestations, epidemiology, electrophysiological studies, applied therapies, and neurological outcome. **Results:** We enrolled 70 patients with GBS in this study. The mean age was 7.3 (1–15), male: female ratio was 6: 4. Most prevalent manifestations were muscle weakness (85%), parenthesis (38%), cranial nerve disorders (40%), and respiratory failure (13%). The time to the peak of symptoms was 9.4 days (1–38). We confirmed antecedent infection in 72% patients, and anti- ganglioside antibodies in 45%, including GM1, GD1a, GD1b, GT1a, and GQ1b ones. Electrophysiological studies revealed acute motor axonopathy (45%), acute inflammatory demyelinating polyneuropathy (39%), and Miller-Fisher syndrome (16%). The GBS patients were treated with intravenous immunoglobulin (45%), prednisolone (6%), plasma exchange (4%), and nothing (14%). Neurological outcomes at 1 year later revealed preferable results as Huges functional grade 0 (82%), 1 (15%), and 2 (3%). Epidemiology studies showed that the incidence of GBS has been decreased during these 20 years. **Conclusion:** This study demonstrated clinical pictures of pediatric GBS in Japan, including that AMAN dominancy, less than half detection of anti- ganglioside antibodies, and achievement of complete recovery with adequate treatment. Epidemiological results were intriguing to know the recent decreasing incidence of GBS in these 20 years.

Learning disorders – intellectual disability

P143 - 1988

Effectiveness of a sports training at school in children at risk of developmental coordination disorders

Hsairi I, Farhat F, Ayadi I, Ellouz E, Ben Romdahne L, Ben Othmen H, Kammoun F, Triki C. *Department of child neurology, Hédi Chaker Hospital, Sfax, Tunisia* – inesguid@yahoo.fr

Introduction: Developmental coordination disorders (DCD) is defined as a condition where motor ability is below that expected for age and cognitive ability, but is not attributable to any diagnosed sensory or neurological problems. The aim of this study was to evaluate the effectiveness of a sports training of children with DCD. **Patients and methods:** We conduct a prospective longitudinal study in three public schools in the region of Sfax. We evaluate 32 children, aged from 7 to 9 years selected from 320 students, reported as having difficulties during physical activity by a sports teacher. These 32 children had a neurological examination, the EDEI-AR and M-ABC battery. All the children scored below the 15th percentile in the MABC with a normal neurological examination and IQ greater than 70 were considered at risk for DCD. These children were reassessed after a sports training. **Results:** Among the 32 selected children with difficulties in physical activity, 18 were considered as at risk for DCD. After sports training, a significant increase in total score of M-ABC ($p < 0.0001$) was observed in all children. Only 4 children have kept a score below the 15th percentile in the M-ABC and were sent to the occupational therapist. **Conclusion:** Our study proves the effectiveness of an intensive sports training in children with risk of DCD. In countries with a lack of professional and specialized unit care as in Tunisia, this can be an alternative. Only children with remaining difficulties after this training will be sent to specialized professionals.

P144 - 1925

Longitudinal neurodevelopmental evolution in children with severe non-progressive encephalopathy

Antonini U, Soldini E, D'Apuzzo V, Brunner R, Ramelli GP. *Institute Provvida Madre, Balerna, Switzerland* – gianpaolo.ramelli@eoc.ch

Aim: The aim of this study was to evaluate the longitudinal neurodevelopmental evolution in children with severe non-progressive encephalopathy. **Methods:** Between 1984 and 2005, 17 patients diagnosed with severe non-progressive encephalopathy under the care of the Institute Provvida Madre underwent neurodevelopmental evaluation on an annual basis for at least 5 consecutive years using the Munich Functional Developmental Diagnostics test. The severity of each patient's encephalopathy was assessed using the Capacity Profile (CAP). Longitudinal development trends were assessed by means of linear regression analysis, while the degree of discontinuity of the development trajectories was quantified using the Mean Absolute Deviation from Perfect Linear Development (MADPLD). **Results:** We found that patients with severe non-progressive encephalopathy showed, on average, a linear maturation of 1.5 to 2.5 months per year, irrespective of the neurodevelopmental area considered. Nevertheless, we also discovered that the development trajectories could be discontinuous. Indeed, a given child can show no development at all for many years and then suddenly encounter a "development jump", especially in the active language and autonomy areas. However, the long-term development linearity hypothesis seemed to hold true in our study. **Conclusions:** The main findings of this study are important for physicians to form prognoses, counsel effectively and appropriately target therapeutic interventions. In this perspective, there is a strong need to

collect long-term repeated follow-up data concerning this group of infants in order to reinforce the findings presented. In fact, these results should be considered as a starting point for further research because they are based on a limited number of patients and more data are needed to confirm the findings.

P145 - 1904

Effect of risk factors on clinical and electrophysiological findings in ADHD

Kartal A, Aksoy E, Deda G. *Department of Child Neurology, Inonu University Faculty of Medicine, Malatya, Turkey – kartalays@gmail.com*

Objectives: Attention deficit hyperactivity disorder (ADHD) is one of the most commonly seen developmental disorders in childhood. Its etiology however is not well known even though bio-psycho-social reasons have been thought to play a big role. In this retrospective study, the risk factors of ADHD are identified in patients diagnosed with ADHD in childhood; and the aim of the study was to analyse the relationship between clinical symptoms and risk factors to which they were exposed to and their effects on the electrophysiological findings. **Material and methods:** In this study, the records of 310 patients between 6–15 years of age diagnosed as ADHD who were followed up between January 2007 to May 2012 at Ankara University Medical School Pediatric Neurology and Psychiatry departments were studied retrospectively. Out of 310 patients only 140 met the study criteria and were included in the study. The exclusion criteria were as follows; IQ levels below 80, patients with chronic diseases, patients with pervasive developmental disorders or psychotic disorders and syndromic patients. **Results:** The mean age of the subjects was 9.25 ± 2.02 , 119 (85%) were boys, and 21 (13.6%) girls. Epileptiform abnormalities in EEG were found in 32 (22.9%) patients, discharges were mostly in the centrotemporal, parietooccipital, and frontal area. A previous history of epileptic seizures was reported in 20 (14.3%) patients. ADHD-inattentive type was the most common subtype of ADHD. **Conclusion:** In our study, asphyxia was found to have an effect on the incidence of epilepsy, and gestational age, asphyxia were found to have an effect on the incidence of epileptiform activity.

P146 - 1892

The complex causes of progressive intellectual and neurological deterioration in UK children. Findings of a prospective epidemiological study after almost 16 years of surveillance

Verity C. *Cambridge, United Kingdom – christopher.verity@addenbrookes.nhs.uk*

Objectives: To identify all children in the United Kingdom (UK) with progressive intellectual and neurological deterioration (PIND) and determine the underlying diagnoses. **Material and methods:** Surveillance commenced in May 1997 using the British Paediatric Surveillance Unit (BPSU) to identify UK children with PIND. Anonymised clinical information about notified cases, obtained by telephone questionnaire or hospital visit, is independently reviewed by an Expert Group. **Results:** By April 2013 UK paediatricians had notified 3397 children who were thought to meet the criteria for PIND. Among them were 6 with probable or definite variant Creutzfeldt-Jakob Disease (vCJD). There were 1450 PIND children with other confirmed diagnoses and in these children there were 175 known neurodegenerative conditions, illustrating the complexity of classifying children with PIND. In the diagnosed cases the six commonest groups were - leukoencephalopathies (n=257), neuronal ceroid lipofuscinoses (NCL) (n=188), mitochondrial cytopathies (n=184), gangliosidoses (n=136), mucopolysaccharidoses (MPS) (n=117) and peroxisomal disorders (n=87). Within groups the commonest diagnoses were - leukoencephalopathies: metachromatic leucodys-

trophy (n=73), NCLs: late infantile NCL (n=94), mitochondrial cytopathies: Leigh syndrome (n=20), gangliosidoses: GM2 (n=102), mucopolysaccharidoses: type III Sanfilippo (n=82), peroxisomal disorders: adrenoleukodystrophy (n=67). The distribution of disorders varied with chronological age; relatively large numbers of PIND cases were found where there were high consanguinity rates. **Conclusions:** This long term study provides unique epidemiological data about the distribution of neurodegenerative diseases causing PIND in UK children, providing a model for similar studies. Individual conditions causing PIND are rare but collectively provide a significant challenge to carers and doctors. Information from our study should be invaluable when considering the differential diagnosis in children with worsening neurological symptoms and signs. Acknowledgements Thanks to UK paediatricians who report cases, to the PIND Expert Group and to the BPSU. Department of Health (DH) grant 121/6443: views expressed are not necessarily those of the DH.

P147 - 1885

Fine motor milestones and expressive language infants born through cesarean section between 37 weeks + 1 day–38 weeks + 6 days gestational age, during the first 2 years of life

Toma AI, Cuzino IA, Cozinov A, Olteanu R. *Life Memorial Hospital, Bucharest, Romania – tomaotiadi@yahoo.com*

Objective: to observe if there are differences from the point of view of the neuro-developmental milestones between the early term newborns (37–38 weeks+6 days gestational age) and neonates born at 40 weeks gestational age through cesarean section. **Methods:** 50 neonates born through elective cesarean section at 37 weeks + 1 day–38 weeks + 6 days (early term newborns) were compared with 50 neonates born through cesarean section at more than 39 weeks gestational age. A neurological examination was performed at 40 weeks corrected age for all the children. There were excluded from the group newborns born through emergency cesarean section, those with respiratory distress, perinatal asphyxia, sepsis and known metabolic diseases and congenital malformations. Then, at 6 months, 12 months and 24 months both neurological examinations and Bayley III tests were performed. The scores at different subsets of the test (cognitive, fine and gross motor, expressive and receptive language) were compared between the groups. **Results:** There was no difference between the groups at 6, 12 and 24 months at the cognitive, gross motor and receptive language subsets of the test. From the point of view of the fine motor subset, there was a significant difference between the two groups at 6 (mean score of 15 versus 18 ($p < 0.002$)) and 12 months (mean score of 30 versus 26 ($p < 0.03$)), but not at 24 months. Also, from the point of view of the expressive language there was a significant difference between the groups at 12 months (mean score of 15 versus 11 ($p < 0.01$)), but not at 24 months. **Conclusions:** The children born through elective cesarean section after 37 weeks but before 39 weeks gestational age, present with a transitory delay in acquisition of the fine motor and expressive language milestones during the first year of life, but recover the delay before attaining the age of 2 years.

P148 - 1835

Chromosomal microarrays testing in children and adolescents with autism spectrum disorder or cognitive impairment associated or not with congenital anomalies: Experience of a tertiary hospital

Rocha R, Sampaio M, Castro A, Flor de Lima F, Rodrigues M, Gonçalves V, Dória S, Fernandes S, Leão M. *Pediatric Neurology Unit - Department of Pediatrics, Centro Hospitalar S. João, Porto, Portugal – rubenrocha@gmail.com*

Objective: Recent guidelines and publications have recom-

mended that chromosomal microarray should replace G-banded karyotyping for the evaluation of children with autism spectrum disorders, developmental delay/intellectual impairment, and/or multiple congenital anomalies. The purpose of this study is to report our experience with this technique in our Hospital. **Material and methods:** We performed a retrospective study based on medical records review of all children who presented to our Outpatient Clinics of Neurogenetics and Pediatric Neurology with developmental delay/intellectual impairment, autism spectrum disorders and/or non-syndromic multiple congenital anomalies that underwent chromosomal microarray testing. **Results:** One hundred and twenty-four records were reviewed, 67 (54%) were males, with a mean age of 12 years old (1–26 years). Eighty three (67%) had developmental delay, 36 (29%) autism spectrum disorders and 66 (53%) dysmorphic features. We found pathological findings in 40 (32%) cases, possible pathological findings (considering the clinical and molecular findings) in 10 (8%) and results of unknown significance in 31 (25%) cases. The remaining 43 (35%) were normal. **Conclusions:** In our population the diagnostic yield of this technique was 32%. Our results are in agreement with the results that served as the basis for the consensus established in 2010 (9.6 and 35%).

P149 - 1825

How ADHD symptoms can be modulated by immediate environment modifications?

Baijot S, Deconinck N, Slama H, Söderlund G, Dan B, Colin C. *Centre de Recherche Cognition et Neurosciences (CRCN), Université Libre de Bruxelles (ULB), Belgium; Neurologie pédiatrique, HUDERF, Bruxelles, Belgium – sbaijot@ulb.ac.be*

Objective: Recent research has found that adapted noise can be beneficial for the nervous system (Moss et al., 2004). Noise benefits have been validated for several cognitive tasks like arithmetic, visual signals detection. In ADHD, an adapted level of noise has been suggested to compensate for the hypofunction of dopamine transmission (Solanto, 2002). For instance, it has been found that noise during an episodic memory task improved ADHD children's performance (Sikström & Söderlund, 2007). The objective of this ongoing study is to assess the potential benefits of noise, in ADHD compared to typically developing children (TDC), using both behavioral and neurophysiological measures (ERPs) during a neuropsychological task. **Method:** Nine ADHD children (mean age = 9; SD = 1) and 16 TDC (mean age = 9.1; SD = 1.3) performed a visual Cued Go/Nogo (adapted from Smith et Johnstone, 2006) across two conditions (noise and no-noise exposure). ADHD children stopped medication 24 hours before testing. ANOVAs were performed on Go (correct responses) and false alarms associated with impulsivity. **Results:** ADHD children committed more false alarms than TDC ($p=0.05$). A significant interaction Group \times Noise ($p=0.009$) indicated a difference between groups in the no-noise condition ($p=0.01$) but no difference when ADHD listened to the noise ($p=0.96$). In addition, ADHD children had less Go responses than TDC ($p=0.004$). A marginal interaction Group \times Noise ($p=0.08$) indicated a difference between groups in the no-noise condition ($p=.005$) but no difference when ADHD listened to the noise ($p=0.18$). **Conclusion:** Our first preliminary results are congruent with our hypothesis. ADHD children did benefit from noise during executive task. They improved their performance as regards to both correct responses and false alarms. Group differences disappeared during white noise exposure, mainly due to ADHD group improvements rather than impairments by the control group.

P150 - 1818

Neurofibromatosis type 1: the complex interplay of cognition and attention deficit

Lidzba K, Granström S, Krägeloh-Mann I, Mautner V-F. *Department of Pediatric Neurology and Developmental Medicine, University Children's Hospital, Tübingen, Germany – karen.lidzba@med.uni-tuebingen.de*

Introduction: Attention Deficit with or without Hyperactivity (AD(H)D) is a common comorbidity of Neurofibromatosis Typ 1 (NF 1). While NF 1 is associated with problems in cognitive development, comorbid AD(H)D represents an additional risk factor. In this study, we tested the hypothesis that permanent medication with Methylphenidate can rescue cognitive problems in children with NF 1 and comorbid AD(H)D. **Patients and methods:** We retrospectively analysed data of a clinical sample of patients with NF 1 with or without comorbid AD(H)D, who underwent standardized neuropsychological diagnostics twice (age range: T1 6–14 years; T2 7–16 years; mean interval 49.09 months). 16 children without AD(H)D were compared to 14 unmedicated children with AD(H)D and to 13 medicated children with AD(H)D. Effects of medication and attention on cognitive outcome (full-scale IQ) were tested by repeated measures analysis of covariance (rmANCOVA). **Results:** We found a significant interaction between time and group, i.e., medicated children with NF 1 improved significantly in full-scale IQ from T1 to T2 (IQT1 = 80.38, IQT2 = 98.38, Cidiff: -25.59 to -10.40 , $p<0.0001$), this effect was not evident for the other groups. The interaction remained marginally significant when adding attention improvement as covariate. **Conclusion:** Children and adolescents with NF 1 and comorbid AD(H)D may profit from MPH medication with respect to general cognition. As improvements in attention do not seem to be a strong source of this effect, this could be a specific feature of NF 1. Future prospective studies have to evaluate the mechanisms behind it.

P151 - 1803

Autism spectrum disorders and food selectivity in children: risk for nutritional deficiencies?

De Bie J, Olivie H, Rayé I, Ortibus E. *KULeuven, Belgium – els.ortibus@uzleuven.be*

Objectives: Food selectivity is frequently mentioned by parents of children with Autism Spectrum Disorder (ASD). Studies have shown that children with ASD eat less varied than typically developing children (TD), but the influence of this selectivity on their nutritional status is unclear. Literature suggests that sensory processing difficulties are an important contributing factor for this behaviour. **Material and methods:** In 18 children with ASD (mean age 59 ± 15 months), we evaluated the presence of eating problems. We defined a child as a selective eater when, on a 5 point Likert scale, parents scored selective intake as at least 4 compared to TD. We used several questionnaires investigating eating behaviour: parent mealtime actions, food frequency and sensory sensitivity and stimulus processing. A 3 day food record was used to calculate energy and nutrient intake. **Results:** Twelve of the 18 children were selective eaters, starting at a young age. Despite this selectivity, 2 children were overweight, while the majority was normal, with only 3 children being underweight. All children had a lower intake of fibers and vitamin D. Micronutrient deficiencies were equal in both groups, with the most frequent being vitamin B2 (15/16), vitamin C (14/16), vitamin A (13/16), vitamin B1 (12/16) and calcium (12/16). Selective eaters refused an average of 47 products of a 90 items food frequency questionnaire, compared to 21 items in the non-selective group. Also, selective eaters had more oral sensory sensitivity and processing problems. **Conclusions:** Children with ASD and food selectivity frequently have an abnormal oral sensory sensitivity and stimulus processing and eat less varied, without

having more nutritional deficiencies. The use of a food frequency questionnaire is valuable to assess the selectivity problems in these children. Screening from early life is indicated.

P152 - 1772

The economic burden in children with developmental delay: a nationwide population-based case-control study

Chang YT, Mu CH, Chin ZN, Chou IC, Tsai CH, Kuo HT. *Division of Pediatric Neurology, China Medical University Hospital, Taiwan, Province of China – d6582@mail.cmuh.org.tw*

Objectives: Socioeconomic status, a variable combining income, education, and occupation, is correlated with a variety of social health outcomes including school dropout rates, early parenthood, delinquency, and mental illness. Therefore, we enrolled this study to view the economic burden in children with developmental delay. **Material and methods:** We selected younger than 6 years-old children with developmental delay from NHI database. Those children were defined three criteria: 1. children with any diagnosed code for developmental delays; 2. children with diagnosed code continual more than two years; 3. children with criteria and received with assessments. We counted the cost for assessments and intervention for each year and assessed the risk of development delays and associated factors in children. **Results:** The cost for care in children with developmental delays increased with year increasing for each criterion. Boys, children with age at 2–3 years-old, children had hospitalized, children spent more medial cost, children with prematurity and cerebral palsy had high risk of developmental delays. Children with chromosome anomaly, cerebral palsy and prematurity spent more 950.4, 692.1 and 554.3 US dollars then those children without disease conclusions: Children with developmental delay increases economic burden in 5 years of following, especially in children with cerebral palsy and prematurity. The increasing costs may have negative influence in their outcomes. It is imperative that clinical decision-makers and budgetary and service planners recognize the overall economic impact of each condition in their service planning, as well as the potential contribution of clinical and sociodemographic factors to economic outcomes. More pertinently, in our opinion, our mean cost and utility estimates and their associated distributions can act as data inputs for cost-effectiveness models of preventive or treatment interventions for childhood with developmental delay.

P153 - 1714

Neurodevelopmental problems in children with optic nerve hypoplasia

Dahl S, Wickstrom R, Ek U, Fahnehjelm KT. *Department of Women's and Children's Health, Karolinska Institutet, Stockholm, Sweden – sara.dahl@karolinska.se*

Background: Optic nerve hypoplasia (ONH) is a common cause of visual impairment in children and adolescents. Although there are studies indicating frequent neurological and behavioural problems in this group, the prevalence of such problems is not fully elucidated. **Objectives:** We studied the prevalence of neurological and behavioural problems among children and adolescents with ONH with the hypothesis that these problems are frequently seen and that bilateral ONH is associated with a higher risk. **Material and methods:** A population-based cross-sectional study of patients below 20 years of age who had been diagnosed with ONH and were living in the county of Stockholm in December 2009 was performed. Following an ophthalmological classification a structured neurological assessment was made. **Results:** Neurological assessment was made in 51 patients (27 with bilateral and 24 with unilateral ONH). Neurological impairments were seen in 24/51 patients (47%) and were more common

among bilateral ONH patients ($p < 0.001$). In bilateral ONH 18/27 (67%) had impairments in gross motor function and 15/26 (58%) in fine motor function. In contrast, among patients with unilateral ONH only 4 (17%) had impairments in gross motor function and one (4%) in fine motor function. Also, 13 (48%) of the patients with bilateral ONH were diagnosed with a developmental delay and 4 (15%) with an autism spectrum disorder, but none in the unilateral group. **Conclusions:** This study demonstrates that neurological and behavioural problems are common among children with ONH, and particularly so among those with a bilateral disease. Screening for such deficits is therefore of great importance, regardless of the severity of ophthalmological disease.

P154 - 1683

Effects of methylphenidate on default-mode network/task-positive network synchronization in children with attention deficit hyperactivity

Querne L, Fall S, Le Moing A-G, Delignières A, Simonnot A, Berquin P. *Service de Neuropédiatrie & GRAMFC U1105, CHU Amiens, France – patrick.berquin@u-picardie.fr*

Background: A failure of the anti-phase synchronization between the default-mode network (DMN) and the task-positive network (TPN) may be involved in one of the main manifestations of attention deficit hyperactivity disorder (ADHD): moment-to-moment variability. Although methylphenidate reduces response time (RT) variability during tasks and increases DMN deactivation, it is not clear whether methylphenidate affects TPN/DMN synchronization. The present study investigated temporal aspects of hemodynamic activity in order to test the hypothesis whereby methylphenidate may improve TPN/DMN synchronization in children with ADHD. **Methods:** Eleven drug-naïve ADHD children and 11 typically developing (TD) children performed a flanker task during magnetic resonance imaging. The ADHD group was scanned twice, before initiation of methylphenidate and one month afterwards with methylphenidate (extended-release formulation). The blood-oxygen-level-dependent signal was analyzed by independent component analysis. Components involving the DMN were sought. **Results:** As expected, TD group showed anti-phase synchronization between the DMN and TPN during the flanker task. Prior to initiation of medication, the ADHD group showed synchronous activity in posterior regions of the DMN only. This component was positively correlated with RT variability during the flanker task. Methylphenidate partially restored anti-phase synchronization in the TPN/DMN complex, reduced RT variability during the task and abolished the correlation between RT variability and DMN activity. **Conclusions:** Our results suggest that a failure of the TPN/DMN synchronization is involved in the moment-to-moment variability displayed by children with ADHD. Methylphenidate initiated TPN/DMN synchronization, which in turn appeared to reduce moment-to-moment variability during goal-directed tasks.

P155 - 1648

DTI study of medication-free children with Tourette syndrome

Debes NM, Jeppesen SS, Simonsen H, Hansen AE, Rostrup E, Larsson H, Skov L. *Paediatric Department, Herlev University Hospital, Denmark – nanettemol@hotmail.com*

Background: The pathophysiology of Tourette syndrome (TS) is not yet fully understood. There is considerable evidence that cortico-striato-thalamo-cortical (CSTC) pathways are involved in the generation of tics. Diffusion tensor imaging (DTI) is a sensitive marker for water molecules diffusion. It can reveal changes in the tissue architecture and connectivity in the brain, especially in the white matter. Several DTI studies have been performed in children with TS, but the results are widespread. These inconsis-

tencies may be ascribed to different methodological approaches and inclusion of heterogeneous groups of TS patients (with or without comorbidities and/or medication). **Objective:** The main objective of this study was to investigate changes in grey and white matter in a clinically well described, medication-free cohort of children with TS. **Material and methods:** We included 24 medication-free children with TS (13 children with TS-only and 11 children with TS+comorbidity) and 18 healthy controls. We investigated grey and white matter density using a region of interest (ROI) based method, a tract-based-spatial-statistic (TBSS) analysis of the white matter skeleton, and voxel based morphometry (VBM) to analyse grey matter. Sex, age and scanner drift were included as covariates. **Results:** When comparing the three groups (TS-only, TS+comorbidity, and healthy controls), no statistically significant differences were found when using the three described methods. When lowering the statistical level several tendencies were found, namely an increase of Apparent Diffusion Coefficient and radial diffusivity in frontal areas, and a decrease in grey matter density in the frontal medial cortex in children with TS when compared to healthy controls. **Conclusion:** No statistically significant differences were found between healthy controls, children with TS-only, and children with TS+comorbidity in any of the three used methods (ROI, TBSS, VBM).

P156 - 1637

Breastfeeding may protect from developing attention deficit and hyperactivity disorder

Mimouni-Bloch A, Kachevanskaya A, Mimouni FB, Shuper A, Raveh E, Linder N. *Loewenstein Rehabilitation Hospital, Raanana, Israel and Sackler Medical School, Tel Aviv University, Tel Aviv, Israel – aviva100@bezeqint.net*

Introduction: Breastfeeding has a positive influence on physical and mental development. Attention deficit and hyperactivity disorder (ADHD) is the most common neurodevelopmental disorder with major social, familial and academic influence. The present study aimed to evaluate a possible association between breastfeeding and ADHD. **Patients and methods:** In this retrospective study, children diagnosed at Schneider's Children Medical Center with ADHD between 2008 and 2009 were compared to two control groups. A first control group consisted of siblings of children diagnosed with ADHD, and who had no ADHD themselves. The second control group consisted of children that consulted the otolaryngology clinic and had no ADHD. A constructed questionnaire about demographic, medical, perinatal, feeding history during the first year of life and a validated adult ADHD screening questionnaire were given to both parents in each group. **Results:** Breast feeding (exclusively or combined with formula) was significantly associated with a lower risk for ADHD. In children later diagnosed as ADHD, 43% were breastfed at three months of age compared to 69% in the sibling group and 73% in the control non-related group ($P < 0.002$). **Conclusions:** Breastfeeding during the first months of life is associated with a lower risk of ADHD. We speculate that breastfeeding may have a protective effect from developing ADHD later in childhood.

P157 - 1537

Spectrum of neurodevelopmental disabilities in a cohort of children in Hungary

Gergev Gy, Máté A, Sztriha L. *2nd Department of Paediatrics, Semmelweis University, Budapest and Department of Paediatrics, University of Szeged, Szeged, Hungary – sztriha.laszlo@med.u-szeged.hu*

Objectives: Neurodevelopmental disabilities are a group of heterogeneous disorders associated with disturbance in develop-

mental progress in one or more domains. Our aims were to survey the profile of neurodevelopmental disability subtypes and aetiological yield of investigations in a cohort of patients in Hungary. **Material and methods:** A retrospective survey of patients referred to our paediatric neurology clinic between 1 January 2006 and 31 December 2011 was carried out. Examinations, investigations and neuropsychological testing of the intellectual abilities followed protocols recommended in the literature. **Results:** A total of 241 children (131 boys) were included in the study. Neurodevelopmental disabilities occurred without known prenatal, perinatal, and/or neonatal adverse events in 167 patients (69.29%), while the history revealed prenatal, perinatal and/or neonatal adverse events in 74 children (30.71%). Genetic syndromes were found in 12.03%, intellectual disability in association with dysmorphic features not recognized as specific syndromes in 9.54%, intellectual disability without recognized aetiology or dysmorphic features in 18.67%, brain malformations in 14.52%, inborn errors of metabolism in 2.49%, leukoencephalopathies in 1.66% and epileptic syndromes in 1.66%. Neuromuscular disorders were diagnosed in 4.98%. Developmental language impairment as a single domain disorder was found in 3.73%. Cerebral palsy occurred after preterm delivery in 14.94%, while it was found after delivery at term in 8.30%. Neurodevelopmental disability without cerebral palsy followed prenatal, perinatal, and/or neonatal adverse events in 7.47%. Overall the aetiology was found in 66.39% of the patients and a specific genetic cause (chromosomal numerical/structural abnormalities, or single gene defects) was identified in 21.16%. **Conclusions:** Classification of patients with neurodevelopmental disabilities into special categories is mandatory in order to clarify the aetiology. The majority of children in this series had aetiology of known or still unknown genetic origin. Recognition of the pathogenesis and special features of even more disorders has preventive and therapeutic implications.

P158 - 1518

Early markers of malneurodevelopment of orphans

Palchik A, Evstafeyeva I. *Department of Psychoneurology of Pediatric Medical State University, St. Petersburg, Russia – xander57@mail.ru*

Objective: Objective of this study is to detect early signs of unfavourable neurodevelopment of orphans. **Material and methods:** In specialized psychoneurological orphanage we observed 100 babies from 37 weeks PMA to 1.5–2 years old (52 boys, 48 girls) exposed to intrauterine HIV-infection. Pregnancy and delivery optimality were estimated according to F. Kainer et al. (1997). All children underwent routine somatoneurological examination and standard ultrasonography. Neurodevelopment dynamics was estimated with Motor Quotient (MQ), Developmental Quotient (DQ) up to 2 years old, and with 30-point scale by L.T. Zhurba et al. (1981) up to 1 year old. Standardized videotaped recordings of general movements (GMs) were obtained (H.F.R. Prechtl, 1997). **Results:** Early outcomes in the examined children were classified as follows: 2 children were diagnosed with cerebral palsy (CP) (1 of them had spastic diplegia; the other one – atonic-astatic form); 13 children – with neurodevelopment delay ($DQ < 0.75$; $MQ < 0.7$); infantile autism in 1 child, paraautistic development in 4 children, attention deficit hyperactivity disorder in 4 children. Among children with CP we noted significantly low pregnancy optimality-score ($\chi^2 = 5.00$; $p = 0.0254$), more frequent moderate and severe neonatal cerebral distress ($\chi^2 = 9.96$; $p = 0.0016$) as compared to the children declared healthy by 2 years old. Children with autism or paraautistic development were born to the mothers who admitted more frequent alcohol abuse during present pregnancy ($\chi^2 = 11.97$; $p = 0.0005$), they showed steady deviations of qualitative and quantitative fidgety parameters ($\chi^2 = 5.11$ – 5.78 ; $p = 0.0162$ – 0.0238), lower scores of MQ and DQ after the age of 1 year old ($\chi^2 = 4.14$ – 25.04 ; $p = 0.0419$ – 0.0001). **Conclusion:** Unfavourable prog-

nosis (CP development, mental retardation, motor delays, autism, paraautistic development) is predetermined by disturbances of endogenously generated movements during “major neurological transformation” period (48–60 weeks of PMA).

P159 - 1686

A child with developmental delay and tall stature

Verma A, Sharma S, Bhakri B, Aneja S. *Department of Pediatrics, Lady Hardinge Medical College and associated Kalawati Saran Children Hospital, New Delhi, India – verma.anupama@gmail.com*

Background: We present a 15 month old female who presented with developmental delay, who was diagnosed with Soto's Syndrome. **Methodology:** A 15 month old female child born of non consanguineous marriage presented with myoclonic jerky movement since 1 year. Antenatal and family history is negative. The child's birth weight was 3kg and cried immediately after birth. Global developmental delay was present since birth. On examination child had headcircumference 51.5cm, weight 11.5kg, height 93cm. Child had enlarged head with frontal bossing. Neurological examination was normal & no organomegaly was present. In view of above presentation bone age evaluation, EEG, MRI brain, gene mutation study was done. **Results:** Bone age done at 15 months shows age corresponding to 24 months and height age of 26 months. EEG study was normal. MRI showed features suggestive of confluent periventricular deep white matter hyperintensities on T2W and flair sequences in bilateral frontoparietal and peritrigonal occipital lobes with abnormal restricted diffusion and thinning of corpus collasum suggestive of periventricular leukomalacia. Mutation of NSD1 gene was present suggestive of Soto's syndrome. **Conclusion:** Thus the final diagnosis of Soto's syndrome was made. Antiepileptic was started. Parents were counselled and advised for follow up.

P160 - 1672

Assessing children with disabilities: WHO ICF-CY classification and Rasch analysis

Illum NO, Gradel KO, Laulund LW, Bergstein KR, Szomlajski N, Johansen MN. *H.C. Andersen Children's Hospital, Denmark – niels.illum@rsyd.dk*

Purpose and background: Assessing disabilities in children is difficult. In year 2007 WHO launched the International Classification of Functioning, Disability and Health, Child and Youth Version (ICF-CY). It is a uni-versal coding system for better communicating disabilities and disorders in and across health sectors and to register impact of interventions on functioning in daily living. We analysed aspects of ICF-CY. Results will contribute to decision on implementing in the Danish Health System. **Design:** A field research interview study was conducted. **Methods:** Families to 367 children with spina bifida, spinal muscular atrophies, muscular disorders, cerebral palsy, blindness, deafness, mental retardation and brain damage following treatment for brain tumours were contacted and selected ICF-CY codes on body functions, activities and participation, environment and personal issues were rated. Most important variables Assessing disabilities in each child was carried out employing the 5-point Likert scale for each code. Mean scores, variances, corrected individual code-total correlations and inter code-correlations together with Cronbach's alpha were employed. Further, Rasch analysis was used to measure integrity of each code, child-to-code relationships and the formation of a common disability variable. **Results:** Families to 332 children (90.5%) participated. Coding body functions using 47 representative codes and 57 on activities and participation showed inter-code correlations of 0.50 and 0.63, thus measuring a common construct. Reliability was high with Cronbach's alpha of 0.98. Rasch analysis reduced codes from 47 to 33 and from

57 to 39 respectively. Ordering of codes and children across disabilities was sound clinically. Data were stable across age and gender. **Conclusion:** Rasch analysis resulted in a common disability construct giving each child a unique disability measure and independent on codes used. The construct was based on properly functioning ICF-CY codes and 5-point qualitative Likert scale scoring.

Miscellaneous

P161 - 2086

Aetiology, comorbidities and causes of death in 133 patients with polyhandicap treated in two dedicated hospitals

Billette de Villemeur T, Rousseau MC, Motawaj M, Mathieu S, Grimont E, Brisse C. *Fédération du polyhandicap, APHP, Paris, France – thierry.billette@orange.fr*

Aim of the study: We retrospectively studied causes of death in children and adults with severe polyhandicap (PLH) treated between 2006 and 2012 in two dedicated hospitals. Their polyhandicap associated motor disorder, profound intellectual deficiency, limited mobility and extreme restriction of autonomy. **Method:** For each patient with PLH who died, the following data were collected: aetiology, duration of hospitalization, sex, age, place and cause of death and the following co-morbidities: chronic respiratory failure, pulmonary infections (when more than 3 a year), urinary infections (at least 1 a year), epilepsy, severe scoliosis (more than 50 degrees), chronic digestive disorders, behavioural disorders. **Results:** There were 133 children and adults who died during these 7 years; 67% were male; 53% were under 18. The average duration of hospital stay was 10 years (1 month – 43 years). 79.7% had chronic respiratory failure, 72.2% had episodic iterative pulmonary infections, 21.8% had chronic urinary infections, 60.2% had important scoliosis, 66.9% had drug-resistant epilepsy, 78.9% had digestive disorders and 6.8% had behavioural disorders. Main aetiologies of PLH were: perinatal anoxia (26), encephalopathy of unknown aetiology (19), epileptic encephalopathy (15), lysosomal disease (16), central nervous system malformations (6), genetic (6), postnatal infection (5), polymalformative syndrome (3). Progressive encephalopathies represented 27% of aetiologies. The average age at death was 21 (3–52). Death occurred in 60% in hospital, in 31% in intensive care unit, in 6% at home and in 3% in nursing homes. The causes of death were: pulmonary infections (63.2%), sudden death (18%), epileptic seizures (6.8%) and unknown (12%). **Discussion:** The main comorbidity and the main cause of death among patients with polyhandicap was respiratory failure. 66.9% of the patients had epilepsy. Patients presented numerous co-morbidities which justify prevention.

P162 - 2057

Clinical and radiologic features of schizencephaly in children

Myrzaliyeva B, Lepessova M. *Almaty State institute of advanced medical education, Almaty, Kazakhstan – myrzaliyeva@gmail.com*

Background: Schizencephaly is an uncommon disorder of neuronal migration characterized by a cerebrospinal fluid-filled cleft, which is lined by gray matter. The cleft extends across the entire cerebral hemisphere, from the ventricular surface to the periphery of the brain. **Purpose:** The analysis of etiological factors, clinical presentation, neurodevelopment progress and seizures in children with schizencephaly. **Material and methods:** We examined 10 children (6 boys, 4 girls) at the age of 1 month to 3 years at the time of schizencephaly diagnosis. The neuroimaging (MRI) was performed in all of the patients. **Results:** Analysis of etiological factors showed leadership intrauterine cytomegalovirus infection. The active form of the infection was detected in 8 of

mothers during pregnancy. In two cases the etiology was not clear. We found bilateral open-lip schizencephaly in 5 and bilateral closed-lip in 2 patients; unilateral open-lip in 2 and unilateral closed-lip in 1 of them. In 8 patients the brain anomalies other than schizencephaly were found (lissencephaly - 1, absence of the septum pellucidum - 3, hydrocephalus - 4). Epileptic seizures are present in 5 patients; in 4 of them the epilepsy is drug resistant. Neurodevelopmental outcome was generally poor, 5 of patients having severe deficits, 3 of patients having moderate impairment, and 3 – mild impairment. Unilateral closed-lip schizencephaly was associated with the best neurodevelopmental outcome; in contrast, 5 of 5 children with bilateral open-lip clefts had severe disabilities. **Conclusion:** Schizencephaly is a severe brain malformation almost always leading to developmental delay and epilepsy. Children with closed-lip schizencephaly presented with hemiparesis or motor delay whereas patients with open-lip schizencephaly presented with hydrocephalus or seizures. Developmental delay and motor abnormalities correlates with the degree of anatomical abnormalities, especially when there are fissures bilateral. Seizures are relatively common and were classified as difficult to control.

P163 - 2048

A case report of recurrent isolated 3rd nerve palsy in a child

Aucharaz KS. Sheffield Children's Hospital, Sheffield, UK – ksaucharaz@hotmail.co.uk

Background: Idiopathic isolated unilateral recurrent 3rd nerve palsy is a very rare condition in children. **Methods:** We report of an interesting case of recurrent intermittent ptosis. A 7 year old boy was referred by family doctor with acute onset of left upper lid ptosis and diplopia. He was a very active boy and there was no history of easy fatigability or fever. His first episode of left eye ptosis was at 6 months of age following a viral illness for which he was reviewed by the paediatric neurologist and extensively investigated, all of which was reported to be normal. There was complete resolution of ptosis in two weeks time. Since then he has had further 4 episodes before this one, each of them involving his left eye with complete resolution in 5–10 days time. There was no history of any headache or involvement of any other cranial nerve in any of the previous episodes. There was no family history of myasthenia or heritable neuropathy. **Results:** Examination revealed a bright and alert child with isolated left 3rd nerve palsy with drooping of left upper eyelid. The pupils were 2 mm equally reacting to light, the direct and consensual light reflex was normal in both eyes. There was no other cranial nerve involvement and rest of the neurological examination was unremarkable. Ptosis again completely resolved spontaneously within 7 days. His investigations including brain MRI with contrast was normal. Myasthenia gravis antibodies, results awaited. **Conclusion:** Unilateral ptosis is a very rare condition in children with only brief mention in literature in anecdotal case reports. In the absence of any abnormal neurology and eye examination an MRI scan of the brain and orbit is warranted to rule out any intracranial or intra-orbital lesion. Awareness of this rare benign idiopathic condition is important for paediatricians.

P164 - 2014

History of child neurology in Moldova

Grefe A, Ciobanu M, Railean A, Railean G. Wake Forest University Baptist Medical Center, North Carolina, United States – agrefe@wakehealth.edu

The History of Child Neurology in the Republic of Moldova Child neurology is a young specialty. In the United States, it was recognized as a board-certified specialty only 44 years ago, although both neurologists and pediatricians have been making important

contributions to the neurologic health of children since the late 19th century. The history and development of child neurology in North America has been eloquently described by several eminent practitioners. Similar growth occurred in Western Europe with plenty of cross-fertilization across the Atlantic, especially after the World War I. At the same time, parallel developments occurred in Eastern Europe and the Soviet Union behind the almost impenetrable barrier of the Iron Curtain. With the dissolution of the Soviet Union, that political barrier has crumbled; however, historical, cultural and especially language barriers have kept most Westerners from learning much about the medical systems in the former Soviet Republics. One of these is the Republic of Moldova, a small land-locked country of some 3.5 million inhabitants, wedged between the Ukraine in the East and Romania to the West. For centuries this small but feisty country has played the role of a geopolitical football between the powers of the East and those of the West. Accordingly, its medical system, like that of the other former Soviet republics, has been subject to the major geopolitical upheavals of the 20th and early 21st century. In this essay we examine how child neurology evolved in Moldova during this turbulent period, how young child neurologists are trained, and what the future holds for child neurology in that country. We believe that the story of child neurology in Moldova and other former Soviet republics is not only intrinsically fascinating but holds lessons for the development of our specialty worldwide.

P165 - 1953

Hopkins' syndrome a rare complication of asthma

Crozier J, Espil-Taris C, Maincent K, Meyer P, Nogues M-C, Rivier F, Echenne B, Roubertie A. *Neuropédiatrie unit of Montpellier CHU, France* – crozier_jessica@hotmail.fr

Objectives: Neurologic complications of asthma are rare. Hopkins's syndrome is an acute flaccid paralysis due to lesion of anterior horn cells which occurs a few days after an asthma attack. **Material and methods:** We reported the observations of three children who presented Hopkins syndrome. The patients undergone brain and medullar magnetic resonance imaging (MRI), and electromyographic recording. Extensive infectious and immune investigations were performed. **Results:** Two patients were referred for asthma attack at the age of 5, the third patient was referred at 9; intensive care unit monitoring was mandatory for one of the youngest patient. Few days later, the patients developed acute flaccid motor paralysis of a limb (2 of the upper limb, 1 of the lower limb). Electromyographic recording was concordant with anterior horn neuron lesion with very low motive amplitude answer. Cerebro-spinal fluid (CSF) interferon alpha dosage was increased in one patient (>8 UI/ml). The MRI showed localized T2 hypersignal of injured anterior horn. Etiological assessment was otherwise normal. Two patients were treated with corticoid pulses and intravenous immunoglobulin: the first one (which has the lower limb palsy) had a complete recovery, the other patient only a partial one. The third patient benefited of corticosteroid treatment and intravenous immunoglobulin followed by six sessions of plasmapheresis; motor recuperation was poor. **Conclusion:** This syndrome's physiopathology is still debated, the elevation of Alfa interferon (>8 UI/ml) in CSF of one of our patients leads us to discuss a post-viral polio- like syndrome. An immune-allergic injury, by analogy with atopic myelitis, was also suggested by some authors. We have observed incomplete recovery in our patients as it is mainly reported in the other cases so far. In the current literature, the recovery seems to be independent of the injury location, of the asthma attack's severity, or of the treatment initiation's precocity.

P166 - 1881**Using ICF-CY to demonstrate clinical reasoning in pediatric physiotherapy: a systematic review**

Demyati H, Adair P, Schroder C. *University of Salford, Manchester, United Kingdom – hdemyati@yahoo.com*

A service providing in pediatric physiotherapy includes complex processes. Some of these processes are based on child growth and development, focusing on a family- centered approach, encouraging daily activities and routines and promoting outcomes that are meaningful to children and their families in daily life (Palisano, 2006; Furze et al., 2013; Atkinson and Nixon-Cave, 2011). The International Classification of Functioning, Disability and Health: Children and Youth (ICF-CY) is a framework that aims to describe and identify all of the components that influence children's health and activity levels. The ICF-CY model consists of interactive components of functional, environmental and personal factors that can help to enhance reasoning skills in pediatric physiotherapy (WHO 2007; Furze et al., 2013). Clinical reasoning is an integral part of a health professional's repertoire to refine decision-making and reasoning skills that are used in clinical practice (Higges et al., 2008), which is an interaction between the therapist, the child and the caregiver. Developing clinical reasoning is a growing area in pediatric physiotherapy and is a prominent subject for study in order to provide desirable outcomes and improve decision making in daily clinical practice (Higges et al., 2008). The objectives of this review are to identify the clinical reasoning skill or strategies being utilised in pediatric physiotherapy using the ICF-CY model and determine how these strategies can improve the judgment and decision-making of pediatric physiotherapists. The inclusion criteria are based of a literature search: All searches will be limited to research reported since 2002 because the ICF model release in 2001 by WHO. The articles should use ICF to determine clinical reasoning in paediatric physiotherapy. The ICF model was used as underlying structure in examination, evaluation, programme development and re-examination. The review will include infant/children/adolescents (0–18) years old with any disabling conditions that categorized by WHO, 2002.

P167 - 1872**Congenital heart disease in neurofibromatosis**

Schutte D, Schroer C, Halbertsma F, Stumpel C, ABok L. *Veldhoven, The Netherlands – l.bok@mmc.nl*

Neurofibromatosis type 1 is associated with many congenital and/or developmental abnormalities. The incidence rate of NF1 is 1 in 3500 newborns. NF1 is characterized by its cutaneous manifestations, café au lait spots, lentiginos, and neurofibromas with a variable clinical expression. Neurofibromin, NF1 protein product, is shown to be involved in the cardiovascular development in neurofibromin-deficient mouse. But the prevalence rate of cardiac abnormalities in NF1 is low (2.3%). Atrioventricular canal abnormalities, which represent 2% of the congenital cardiac abnormalities in children, are not reported in NF1, though some have reported left sided AV valve prolaps and/or regurgitation in combination with NF1. We present a patient who presented with a balanced incomplete Atrio-Ventriculo- Septal Defect (AVSD), including an ASD type 1 of 14 mm, and left sided AV valve regurgitation with suspicion of a mitral valve cleft. After 1 year she developed 6 café au lait spots, DNA investigation for neurofibromatosis showed a pathologic mutation c.5401C>T, p.Gln (exon 3*) in the NF1 gene. Further details will be presented. This unique observation widens the spectrum of possible cardiac abnormalities in NF1 and suggests a embryologic relationship between NF1, AV valve regurgitation and AVSD.

P168 - 1606**A retrospective analysis of paediatric patients with medically unexplained neurological symptoms: epidemiology, management and outcomes**

Vidouris M, Kamath Tallur K, Auckland K. *The University of Edinburgh, Cheshire, United Kingdom – s0906278@sms.ed.ac.uk*

Introduction: Although there is wide range of literature and research looking into the trends, diagnosis and appropriate management of medically unexplained neurological symptoms (MUNS) in the adult setting there is a lack of information regarding paediatric MUNS. Retrospective analysis of the demographics of these paediatric patients as well as the outcomes of their symptoms after various treatments will help in order to evaluate which aspects of care that were most successful and which were detrimental to the recovery of the child. This will allow a basis for a structured care plan for these patients to be made. **Method:** This is a retrospective analysis of patients attending the Neurology Department at a hospital from 2003 to 2012 and diagnosed with MUNS. **Results:** 35 patients were identified. The predominant symptoms were headaches (13) and visual disturbances (11). There were reports of impaired mobility 31.4% (11/35), effects on education 48.6% (17/35) and sleep disturbance 25.7% (9/35). 77.1% (27/35) were girls; they presented younger (median 11.7 years) than boys (median 12.5 years). Multiple, repeated investigations were carried out. No positive results were found. 4 MRIs showed incidental findings. Management included referral to mental health services 77.1% (27/35), pharmacological 51.4% (18/35) and non-pharmacological treatment 25.7% (9/35). 77.1% (27/35) improved in an average follow-up of 15.4 months. Those that fully recovered 60% (21/35) did so in an average of 10.1 months. 2 deteriorated and 6 remained the same. **Conclusion:** Paediatric MUNS is a little researched area. It involves a range of symptoms causing varying levels of impact on daily life. There are complex underlying psychosocial stressors precipitating these symptoms and a multidisciplinary approach is required by paediatricians, psychologists, parents and teachers to minimise the physical and psychological consequences of this condition.

P169 - 1578**3 year evaluation of community based interdisciplinary outpatient clinics**

Spiel G, Finsterwald M. *Pro mente: kinder jugend familie (NGO), Klagenfurt, Austria – georg.spiel@promente-kijufa.at*

Within the last years, evidence for effectiveness and efficiency of different offers in the area of healthcare are getting more and more important due to limited financial resources and legal issues. There is an increasing demand for quality assurance (QA), evaluations and quality development (QD) that matters for inpatient as well as outpatient institutions. QA is especially challenging for institutions assisting children/adolescents with neurological and/or mental health problems. In the following contribution a corresponding approach will be presented that aims to assess the quality of outpatient clinics for children/adolescents with neurological and/or mental health problems. The evaluation concept and evaluation results of two outpatient clinics will be reported that are both part of a NGO (located in Austria) that is specialized in supporting the development of those children/adolescents. In the sense of participatory evaluation (e.g. Cousins, & Whitmore, 1998), an evaluation team was formed in 2008 that developed an ecological feasible evaluation concept. A pre-post-follow-up design was chosen compromising self- estimations as well as estimations of others (parents, psychologists/therapists) and covers the main goals of the outpatient clinics: (1) positive changes according to the reduction of symptoms and (2) raising quality of life. Data collection started in January 2009. In the following contribution cross sectional and

longitudinal results according to the named evaluation goals will be reported for the first three years. This study comprises cross sectional data from 1792 children/adolescents (35% girls; 52% between 5 and 9 years) who completed the initial diagnostic phase and longitudinal data from 237 children/adolescents who finished at least one therapeutic intervention. The analysis showed significant positive effects for both evaluation goals. The derived implications for quality development will be discussed at the end of the contribution.

P170 - 1572

Mesenchymal stem cell application in cuprizone-induced demyelination

Korkusuz P, Hanalioglu S, Yorubulut M, Akar Soyacan I, Sara Y, Arslan ME. Ankara, Turkey – banlar@hacettepe.edu.tr

Objectives: Mesenchymal stem cells (MSC) have neuroprotective potential attributed to their production of trophic factors. Their therapeutic value is being assessed in experimental models of demyelinating diseases and multiple sclerosis. We intended to examine the effect of MSC in preventing experimental demyelination in mice. **Material and methods:** Demyelination: Adult C57/BL6 mice (n=6) were fed regular diet or diet containing cuprizone (SIGMA) for 6 weeks. MSC obtained from banked bone marrow of healthy donors were characterized according to differentiation potential and immunophenotyping. Mice were injected with MSC (2000 in 2 μ l) unlabeled or labeled with iron particles (Endorem, Guerbet) into the corpus callosum. Control mice were given medium only. **Histology:** One animal from each group who received iron-labeled MSC underwent MRI (3T). Other animals (n=3) were perfused 3 weeks later with 4% paraformaldehyde. The brain was fixed by immersion in paraformaldehyde, cryoprotected in 3% sucrose, gradually frozen and kept in liquid nitrogen until sectioning in 6–8 μ m-thick serial coronal sections (-2.3 to 1.8 mm from bregma). Sections were stained by luxol-fast blue/cresyl violet (LFB) and HE, images were captured via Leica DMR microscope, Leica DC500 digital camera (Wetzlar, Germany). Demyelination percentage was quantitated (Leica application suite software) in blinded manner. The ratio of pale (unmyelinated) versus total (pale and blue-stained myelinated fibers) surface of the corpus callosum. **Results:** Cuprizone-fed animals had less distinct signal in corpus callosum on MRI. Histologically, cuprizone with or without MSC caused patchy demyelination in the corpus callosum. Demyelinated% was 0.03 ± 0.03 in the control mouse, 0.17 ± 0.10 in the cuprizone-only and 0.13 ± 0.09 in the cuprizone+MSC-treated mice. **Conclusion:** These preliminary results suggesting a protective or remyelinating effect of MSC in toxin-induced demyelination are subject to further confirmation in larger experiments and different periods of toxin exposure.

P171 - 1509

Malnutrition in young adults with epilepsy and neurodisabilities

Cliffe C, Das KB, Mensah A. University of Bristol, United Kingdom – cc8363@bristol.ac.uk

Nutritional deficiencies are common in people with epilepsy and other chronic neurologic conditions. **Purpose:** 1. To explore the causes of nutritional problems in young adults prescribed nutritional supplements at a specialist centre. 2. To determine the effectiveness of supplements. 3. To investigate the extent of Vitamin D deficiency in this population. **Method:** Retrospective review of case notes over a 3 year period at Young Epilepsy, a specialist residential unit in U.K for young people with complex epilepsy and neurodisabilities. BMI was used as a marker of nutritional status to assess progress. Vitamin D levels were compared in the two groups: those with epilepsy versus those without epilepsy. **Results:** Twenty young adults were started on nutritional supple-

ments due to clinical indications. All had intellectual disabilities, 17 had epilepsy and 9 each had autism and behavioural problems. The cause for malnutrition was identified in 11 (55%). In four it was attributed to their eating habits, 3 had swallowing problems and in 2 each it was due to seizures or behavioural issues. 10/20 (50%) were on anticonvulsant drugs (Topiramate and Levetiracetam), which might have contributed to weight loss. There was significant improvement in their nutritional status following supplementation, with a mean BMI increase of 6.8% ($p = 0.003$). 34 subjects with epilepsy and 11 without epilepsy had vitamin D results available. 33/34 (97%) of those with epilepsy versus 7/11 (63.6%) of those without epilepsy had severe or borderline Vitamin D deficiency. **Conclusion:** Young adults with epilepsy and neurodisabilities are at high risk of nutritional deficiencies. The causes of malnutrition can be multifactorial in this population. Anticonvulsants are an important contributing factor. Supplementation significantly improved their nutritional status. Vitamin D deficiency is higher in those with epilepsy. Vulnerable subjects should be screened for Vit D deficiency and early supplementation should be considered.

P172 - 2136

Papilloedema as the only sign of a blocked ventriculoperitoneal shunt in an infant

Stallard L, Kaliaperumal C, Mandiwanza T, Leonard J, Caird J, Crimmins D. Department of General Paediatrics, Children's University Hospital, Temple Street, Dublin, Ireland – lorraine_stallard@hotmail.com

Background: Symptoms of a malfunctioning VP shunt can be subtle. Early recognition of shunt malfunction is important as the consequences of acutely raised intracranial pressure can be devastating. Common presenting features include headache, drowsiness and vomiting. We describe a case of a 12-month-old boy whose sole feature of shunt malfunction was papilloedema without any other symptoms of raised intracranial pressure. **Case:** A 12-month-old boy with VP shunt presented with papilloedema diagnosed at routine ophthalmology assessment. He was otherwise completely asymptomatic. Physical examination was unremarkable. CT brain showed moderate dilatation of the lateral and third ventricles. He underwent emergency shunt revision which showed proximal shunt blockage. Repeat CT brain 3 days post shunt revision demonstrated considerable reduction in ventricular size. Resolution of papilloedema was observed 6 weeks post surgery. He is being followed up with 3monthly rather than 6 monthly eye examination. **Discussion:** Shunt malfunction can sometimes be difficult to detect and the signs are often non specific. Although papilloedema is usually regarded as a late sign of raised intracranial pressure, in this case it was the only sign of shunt blockage. This highlights the importance of regular ophthalmology review in these patients. **Conclusion:** There is subgroup of children who do not manifest the classic signs and symptoms of shunt malfunction. In these children, only papilloedema without any other symptom is enough to warrant an urgent neurosurgical referral for further management. Ophthalmology follow-up may be necessary more frequently than yearly follow up.

P173 - 2131

Rhomboencephalosynapsis: clinical presentation of three cases

Souza DB, Leal MM, Siqueira ES. Pediatric Neurology, Secretary of Health Hospital Regional da Asa Sul, Brasília, Brazil – denizebomfim2006@gmail.com

Introduction: Rhomboencephalosynapsis is a malformation of the central nervous system (CNS), posterior fossa, characterized by the absence of the cerebellar vermis and fusion of the medial

cerebellar hemispheres, rare, it can occur in association with other congenital supra-tentorial. The etiologic factors are not yet well established and most reported cases are sporadic. **Objective:** The authors describe the presentation and the diagnosis is only possible with magnetic resonance imaging of the brain (MRI). **Case report:** Case 1 – Teen 14 years old female with no risk factors, progressed with developmental delay observed after three months, and neurologic examination revealed generalized hypotonia. Performed electromyography standard normal karyotype with G band corresponding to female, 46, XX, and MRI of the brain with rhomboencephalosynapsis. It evolves with learning difficulties and neurodevelopmental disorder. Case 2 – Boy 10 years admitted to the service to evolve with global developmental delay, delay in motor skills and speech acquisition. Neurological examination showed no major dysmorphia or motor deficit, but had severely compromised cognition. Performed with the NMR brain malformation, metaphase karyotype 46, XY, and research for Fragile X syndrome by PCR negative. Case 3 – Female infant, 14 months of life, with microcrania and craniosynostosis. Dysmorphic facial and hands. Controlled generalized seizures and global developmental delay. **Discussion:** Neuroradiological failed to clarify the pathogenesis of CNS abnormality, since embryogenesis occurs in cerebellar fourth week of pregnancy. There is possibility of environmental factors and genetic factors associated with this event and there are possible that is related to the fact that there is a spectrum defined for this entity. **Conclusion:** Rhomboencephalosynapsis is a cerebellar malformation, prevalence not known, and has variable clinical presentation.

P174 - 2114

Intracerebral calcifications in children with progressive neurological clinical picture: diagnostic difficulties through clinical cases

Barca D, Iliescu I, Dica A, Acsinte I, Pomeran C, Tarta-Arsene O, Budisteanu M, Craiu D. *Pediatric Neurology Department, Prof. Dr. Alexandru Obregia Psychiatry Hospital, Bucharest, Romania – diana_barca@yahoo.com*

Objective: Intracerebral calcifications (IC) are present in numerous disorders. They may be physiologic, stationary, without a clinical expression or secondary to infection, trauma, degeneration, neoplasia or to metabolic disorders, acquired or inherited. They affect mainly the basal ganglia, thalami, subcortical white matter and nucleus dentatus. The aim of the paper is to emphasize the importance of extensive investigations in children with a history of progressive neurologic deterioration and IC and also the difficulties in elucidating the diagnostic of severe cases, exemplifying with an Aicardi-Goutieres phenotype (AGS), a Cockayne syndrome and a case of pseudohypoparathyroidism type 1a. **Material and methods:** 3 cases from our clinic are presented, with their history, clinical and neurological examinations and extensive investigations. MC is a girl aged 9, first seen at 4 for progressive spastic tetraparesis with onset at 2, later a hypokinetic-rigid syndrome and also cognitive impairment. Her imaging showed progressive symmetrical calcifications affecting the basal ganglia, but also subcortical white matter and cerebellum. TD is a boy aged 14, admitted for motor and cognitive decline, post-natal growth failure and skin sensitivity to sunlight, progeric appearance. Brain imaging showed basal ganglia and cerebellar calcifications and white matter abnormalities. AP, a boy of 14 years, was admitted for progressive hemiparesis, dysmorphism and a history of epileptic seizures. He presented a history of severe hypocalcemia. The investigations showed high levels of parathormone, hypothyroidism and IC on MRI and CT, involving basal ganglia, but also disseminated diffusely. **Results:** For MC, after completion of investigations in Kremlin-Bicetre Hospital, the suspicion was AGS (though negative genetic testing), in TD case a diagnostic of Cockayne syndrome was formulated and for

AP the diagnostic was Albright osteodystrophy. **Conclusions:** It is important to be aware of the extensive range of etiologies of IC, requiring thorough evaluations, in order to establish the correct diagnostic and the management algorithm.

Mitochondrial disorders

P175 - 1963

Mitochondria DNA depletion syndrome presenting as an unusual case of myopathy with prolonged post-operative paralysis in a neonate

Thomas M, Canham N, Kinali M. *Neonatal Department, Chelsea and Westminster Hospital NHS Foundation Trust, London, United Kingdom – maria.kinali@chelwest.nhs.uk*

Background: we report a case of mtDNA depletion syndrome being unmasked by peri-operative muscle relaxation in a neonate. **Case report:** a male infant was born at 35 weeks gestation by Caesarean section. Parents were non-consanguineous. Antenatal scans showed absent right subclavian artery at 20 weeks and oligohydramnios at 29 weeks. He required no resuscitation at birth but became cyanosed during feeds. A nasogastric tube could not be passed into the stomach and a diagnosis of oesophageal atresia with trachea-oesophageal fistula was made. At surgery, the fistula was found behind the aberrant subclavian artery, making repair difficult. The infant was electively paralysed for five days post-operatively using vecuronium that stopped on day six. He remained paralysed until day 12, when he had small movements of his eyes and extremities. Cerebral ultrasound and aEEG were normal. EMG and nerve conduction studies showed moderately severe sensorimotor primary axonal polyneuropathy. At three weeks he required high frequency oscillatory ventilation (HFOV). MRI brain was not possible due to HFOV. On day 32 he deteriorated suddenly requiring CPR for 20 minutes. aEEG showed a burst suppression pattern, intensive care was withdrawn and the infant died. There was no paucity of anterior horn cells on post-mortem. Bloods (SMN1 & DMPK genes, CK, infant & maternal ACh receptor & anti-MuSK antibodies, very long chain fatty acids, acyl carnitine profile, plasma amino acids and array comparative genomic hybridisation) were normal. Muscle biopsy showed pale COX and SDH staining. Respiratory chain analysis revealed a marginal decrease in complex IV activity. Mitochondrial DNA (mtDNA) analysis was negative on blood but mtDNA depletion was low at 28% of the normal. Extensive genetic investigations were negative. **Conclusions:** Our case highlights the importance of rigorous ante and post-mortem investigation when the cause of a severe, neonatal myopathy is uncertain.

P176 - 2043

A ten year old girl with acute encephalopathy in the context of NARP syndrome

Triantafyllidou A, Katsarou E, Voudris C, Delis D, Mastroianni S. *1st Pediatric Clinic, "P.&A. Kyriakou" Childrens Hospital, Athens, Greece – aab@ath.forthnet.gr*

NARP syndrome, a clinically heterogeneous condition is characterized by a combination of sensory-motor neuropathy, cerebellar ataxia and night blindness and is caused by a mitochondrial DNA mutation. The onset of the disease is in the childhood and early adulthood and occasionally the course of the disease is interrupted by symptoms of acute encephalopathy. **Case report:** A ten year old girl appeared in acute hospital having acute ataxia, walking difficulty and headache. Rapidly these symptoms had been progressed to conscious level disturbances, with drowsiness, response only to painful stimuli, diminished deep tendon

reflexes, sialorrhea and hyperpnea. Personal history: leg-length discrepancy, bilateral pes cavus deformity, mild intellectual impairment. **Family history:** Her mother died at the age of 45 years, from acute encephalopathy of unknown origin and she also had pes cavus deformity and walking difficulty. First brain MRI: demyelinating lesions of the cerebellum and the basal ganglia consistent with any demyelinating/inflammatory disease. Brain MRI (six days after): progression of the lesions into the lenticular nuclei and the caudate nucleus with multiplication of the lesions of the white matter making the Leigh disease the most probable diagnosis. CSF examination, infection screening, CSF Immunoelectrophoresis: within normal. CSF lactic acid: elevated (twice). She received iv IVIG and pulses methylprednisolone with progressive amelioration of her clinical situation. The respiratory chain enzyme examination (skin fibroblast) revealed complex I borderline activity. The blood mitochondrial DNA sequencing revealed the MT8993 (T>C) mutation which is diagnostic of the NARP syndrome. Four years after the diagnosis she remains stable, in a satisfactory neurological condition, having a mild ataxic walking and dysarthria. **Conclusion:** Mitochondrial diseases could be a cause of acute encephalopathy. For this reason in any case with consistent clinical/family history and imaging findings a thorough laboratory investigation is indicated. The acute encephalopathy in the context of NARP syndrome could be reversible.

P177 - 2041

Acute metabolic decompensation after lead exposure in an infant with Leigh syndrome

Kara B, Maras H, Bato E, Yalcin EU, Yildizli E. *Kocaeli University Medical Faculty, Department of Pediatrics, Division of Child Neurology, Kocaeli, Turkey – bkuskudar@gmail.com*

Leigh syndrome is a progressive neurodegenerative disorder of infancy and childhood, with symmetric necrotizing lesions in the brainstem, basal ganglia, thalamus and spinal cord. Clinical findings, such as failure to thrive, muscle weakness, disorders of ocular movements, bulbar dysfunction and respiratory failure, start after a few months of normal development. Acute metabolic stress, for example, infections, vaccination, starvation, etc., may trigger the rapid deterioration of the patient with Leigh syndrome. Lead intoxication also is a known factor which damage mitochondrial function, but there is no reported case with Leigh syndrome triggered with lead exposure. 6-month-old boy was reported for refractory vomiting, weight loss and constipation. He had metabolic acidosis with normal anion gap and required high dose bicarbonate supplementation. Bicarbonate loss was renal tubular origin. Cranial magnetic resonance imaging showed bilateral symmetric hyperintense lesions on basal ganglia and mesencephalon at T2-weighted and FLAIR images, and lactate peak at magnetic resonance spectroscopy. Serum lactate and lactate/pyruvate levels were high. The diagnosis was Leigh syndrome. In the history of the patient, it was learned that, he had lead exposure three different times in ten days, due to a traditional practice. In this practice, melted lead pours into cold water over the head of the sick person in order to break an evil spell. Serum lead level was 7 µg/dl (N: <5 µg/dl), three weeks after the last exposure. Ankle radiography showed linear sclerotic band at the metaphyseal end of the tibia. Dimercaprol (BAL) chelation therapy was ordered due to symptomatic lead intoxication. Melting the lead is probably originated from shamanism. It is a common practice in some parts of the world, also in Turkey, so it can be an underestimated community health problem. Patients with unexplained acute or subacute refractory vomiting, weight loss and constipation should be screened for lead toxicity.

P178 - 2004

Leigh syndrome (LS) in 13 Tunisian patients

Ellouz E, Abid A, Abdelhedi J, Chamkha I, Ben Othmen H, Kammoun F, Fakhfakh F, Triki C. *Neuropediatric Department EPS Hedi Chaker, Sfax, Tunisia – ellouzemna@yahoo.fr*

Introduction: LS is the most common clinical phenotype of mitochondrial disorders in childhood. The diagnostic criteria include progressive neurological disease with psychomotor delay, symptoms of brainstem or basal ganglia disease and characteristic symmetric necrotic lesions in the basal ganglia or brainstem. We try to determine clinical, radiological and genetic features of LS in Tunisia. **Methods:** We reviewed the observations of patients with a clinical and radiologic presentation suggestive of LS; we determined the clinical and radiological features of these patients. Respiratory chain enzymes Study weren't performed. The molecular study was performed for some patients. **Results:** We collected 13 patients from 9 families. The mean age was 15 years; the mean age at onset was 2.1 years. Psychomotor delay was noted in 7 patients, gait difficulties and movement disorders were noted in 9, cerebellar ataxia in 5. Facial dysmorphism and hypertrichosis were noted in 3. Brain MRI showed involvement of putamen in 9 cases, caudate nucleus and pallidi in 3, brain stem in 5. Molecular study showed a novel missense mutation in the mitochondrial cytochrome C oxidase III gene in 2 patients, and a SURF1 mutation in 1. **Discussion and conclusion:** LS has a clinical and genetic heterogeneity. In our patients the symptoms of brain stem or basal ganglia disease associated with suggestive lesions on brain MRI leads to the diagnosis. LS is the consequence of different biochemical and genetic defects. A defect of cytochrome C oxidase is one of the most common biochemical abnormalities. This defect can be due to SURF1 mutations or mitochondrial DNA mutations. In our study this enzymatic defect is rare, in fact one patient had a SURF1 mutation and two others had a mutation in the mitochondrial cytochrome C oxidase III gene. Further genetic study were needed to determine molecular basis of Leigh syndrome in Tunisia.

P179 - 1798

Mitochondrial dysfunction in myotubular myopathy X-linked (MTM1) at the origin of a multivisceral disease

Le Moing AG, Delignières A, Simonnot A, Slama A, Biancalana V, Roméo B, Deroussen F, De Broca A, Berquin P. *Service de Neuropédiatrie & GRAMFC U1105, CHU, Amiens, France – LeMoing.Anne-Gaelle@chu-amiens.fr*

Background: X-linked congenital myopathy myotubular is an inherited neuromuscular disease. The incidence is estimated at 1/50000 male births. It is caused by a defect in the gene MTM1 responsible for the myotubularin protein production. **Case report:** We report the case of a child whose diagnosis of myotubular myopathy X-linked was brought to birth to the severe hypotonia and respiratory failure. The child presented a spontaneous rupture of a cavernous hemangioma of the liver at the age of 5 months. Histological muscle analysis revealed the presence of myotubules. Molecular diagnosis revealed a large deletion of the gene for myotubularin (MTM1). In addition, mitochondrial respiratory chain study was performed on muscle biopsy and fibroblasts. A complete mitochondrial deficiency has been demonstrated. The motor development is stable for this child at 12 months. The girdle muscular deficit is predominant. He's beginning to pronounce a few of words. When he was 10 months, gastrostomy and invasive ventilation by tracheotomy has been installed. **Discussion:** Myotubularin is an essential protein for the stability of the cytoskeleton of the skeletal muscles by interacting with another protein like desmin protein, responsible for other congenital myopathies. This desmin-myotubularin complex is an actor of mitochondrial homeostasis. This pathophysiology

explains probably the clinical severity of these children with multiorgan failure (respiratory, muscular, vascular, ...) and the risk of life-threatening events. The involvement of mitochondrial dysfunction in vascular membranes explains for these patients a higher risk of vascular diseases caused by arteriopathy like arteriovenous malformations.

P180 - 1827

NDFUS8-related Complex I Deficiency – “PEO-Plus” and mild Leigh syndrome

Della Marina A, Schara U, Pyle A, Möller-Hartmann C, Holinski-Feder E, Abicht A, Czermin B, Lochmüller H, Griffin H, Santibanez-Koref M, Chinnery PF, Horvath R. *Paediatric Neurologie, University of Essen, Germany* – adela.dellamarina@uk-essen.de

Background: At present only few reports describe the clinical phenotype of mutations in the mitochondrial complex I related gene NDUFS8. The reported patients showed mitochondrial encephalomyopathy with lactate acidosis and early death, only in one patient a milder phenotype was reported. **Patients and methods:** We describe the clinical phenotype of three children (2 brothers and 1 sister) from a consanguineous Afghan family with muscle hypotonia, cerebellar symptoms and “Progressive External Ophthalmoplegia (PEO) plus “Leigh” syndrome. The oldest, most severely affected brother, showed muscle and facial hypotonia since infancy with mild ptosis and ophthalmoplegia. At the age of 5 years cerebellar symptoms occurred and his muscle weakness deteriorated. His younger brother (12 y) showed milder symptoms and can currently still walk independently. Both brothers exhibited worsening of their symptoms during febrile infections; cognitive impairment was diagnosed in both. Their younger sister presented at 9 years of age with mild generalized muscle hypotonia, an unlimited walking distance and normal mental development. Muscle biopsy of the oldest brother showed non-specific variation of fibre size. Enzyme histochemistry for cytochrome C oxidase, NADH-CoQ-Oxidoreductase and succinate dehydrogenase revealed no abnormalities. Biochemical analysis of the respiratory chain enzymes in muscle showed a isolated reduction of complex I activity (NADH-CoQ-Oxidoreductase). The diagnosis of a mitochondrial disorder with complex I deficiency was diagnosed. Brain MRI findings of both brothers supported this diagnosis (abnormal signal in basal ganglia). Whole exome sequencing was performed and a homozygous mutation in NDUFS8 could be detected (c.160C>T, p.Arg54Trp) in all three affected siblings. **Conclusion:** An exact clinical description of patients carrying a mutation in mitochondrial complex I related genes diagnosed by whole exome analysis is necessary. It broadens the spectrum with a milder and later onset of symptoms in our patients. Because of the unusual phenotype it would not have been considered in this context.

P181 - 1833

Atypical infantile onset Alexander disease masquerading as a mitochondrial disorder diagnosed by whole exome sequencing

Nishri D, Blumkin L, Edvardson S. *Metabolic Neurogenetic Clinic, Wolfson Medical Center, Holon 58100, affiliated to Sackler School of Medicine, Tel-Aviv University, Tel-Aviv, Israel* – danini200@yahoo.com

Introduction: There are many similarities, both clinical and radiological, between mitochondrial leuko-encephalopathies and Alexander disease, an astroglipathy. Clinically, both can manifest with myriad of symptoms and signs, arising from the neonatal period to adulthood. Radiologically both may demonstrate white matter changes, signal abnormalities of basal ganglia or thalami, brainstem abnormalities and contrast enhancement of white matter structures. Magnetic resonance spectroscopy may reveal elevation of the “classic” mitochondrial marker lactate in

the abnormal white matter of Alexander disease making the distinction even more challenging. We present a case of a child considered to have an infantile onset mitochondrial disorder, due to combination of neurological symptoms and signs (developmental regression, failure to thrive, episodic deterioration, abnormal eye movements, pyramidal and cerebellar signs), urinary excretion of 3-methyl-glutaconic acid and imaging findings (extensive white matter changes and cerebellar atrophy). Head circumference was normal. **Method:** Whole exome sequence analysis. **Results:** The child was found to harbor the mutation R416W, one of the most prevalent mutations in glial fibrillary acidic protein that causes Alexander disease. **Conclusions:** Alexander disease should be considered in the differential diagnosis of an infant presenting in the first year of life with a clinical picture suggesting a neuro-metabolic disorder, even when no macrocephaly is present. Next generation genetic sequencing is a useful aid in unraveling the molecular etiology of leuko-encephalopathies.

P182 - 1614

Mitochondrial Complex I deficiency due to a mutation in the NDUFV1 gene: a case report

Arslan M, Aydın HI, Vurucu S, Ünay B, Gül D, Akın R. *Department of Pediatric Neurology, Gülhane Military Medical School, Ankara, Turkey* – mutluayarslan@yahoo.com

Complex I deficiency is the most frequent oxidative phosphorylation system (OXPHOS) disorder in children but only a few mutations have been reported in each of its subunits. We present clinical, radiological and molecular findings of a fifteen-year old female diagnosed with complex I deficiency due to NDUFV1 mutation. The patient had a history of psychomotor retardation, epilepsy, diabetes mellitus and she showed increased irritability, generalized spasticity, diffusely brisk reflexes, extensor plantar response bilaterally and truncal ataxia. Brain magnetic resonance imaging (MRI) showed rarefied and cystic cerebral white matter lesions. There were also signal abnormalities in the posterior limb of the internal capsule, bilateral pyramids in the brainstem, middle and inferior cerebellar peduncles and cervical spinal cord and upper part of the thoracic spinal cord. There were no signal abnormalities in the basal nuclei, thalami, and lower part of the spinal cord. Brain MR spectroscopy (MRS) demonstrated elevated lactate in the abnormal white matter. Molecular analysis of NDUFV1 gene revealed homozygosity for c.1022 C>T (p.A341V). The patient was started on co-enzyme Q10, carnitine, creatin, biotin, vitamin E and vitamin B complex supplementation. Our case demonstrates that the clinical expression of complex I deficiency is heterogenous and defining the clinical and genetical features of more cases with complex I deficiency may provide new insights for the disease.

Movement disorders

P183 - 2117

Dystonia with diurnal variability in Lesch-Nyhan variant syndrome

Buzatu M, Coppens S, Vilain C, Ceballos-Picot I, Van Bogaert P. *CHU Charleroi, Departement of Pediatrics, Université Libre de Bruxelles, Brussels, Belgium* – b_marguta@yahoo.fr

Lesch-Nyhan Syndrome is an inborn error of purine metabolism caused by deficiency of the enzyme hypoxanthine-guanine phosphoribosyl-transferase (HPRT) with transmission X linked-recessive. The classic form includes overproduction of uric acid with lithiasis and gout, severe generalised dystonia, mental retardation and self-injurious behaviour. A partial deficiency of HPRT induces an attenuated phenotype in which some features

of classic presentation are attenuated or absent. We describe two brothers with attenuated form of Lesch-Nyhan syndrome. The diagnostic was delayed by atypical presentation. Dystonia with diurnal fluctuations and mild psychomotor delay was the initial clinical presentation and the etiological work-up was focused in the causes of fluctuating dystonia. No self-injurious behaviour was present and uric acid level was normal at presentation. Attenuated variant of Lesch-Nyhan Syndrome should be considered in the differential diagnosis of dystonia with diurnal fluctuation. Activity of the HPRT should be measured in unexplained early onset dystonia, even in the absence of hyperuricemia.

P184 - 2022

The brain-lung-thyroid syndrome as a rare cause of chorea: case report of a novel mutation in the thyroid transcription factor-1 (TTF-1) gene

Wouters L, De Bruyn G, De Waele L, Jansen K, Francois I, Reynaert N, Buyse G, Lagae L, Goemans N. *UZ Leuven, Belgium – leen.wouters@uzleuven.be*

A 7 year-old boy came first to medical attention at the age of 2 years with signs of delayed motor development and hyperlaxity of joints. His mother was known with hypothyroidism and hyperlaxity, his maternal grandmother with hyperlaxity. His perinatal history was unremarkable for pulmonary problems. During his first year of life he suffered recurrent airway infections. Creatine kinase and electromyography were normal. The boy was treated with ankle foot orthoses and a positive developmental evolution was noted at further neuropsychiatric follow up. Gradually the hyperlaxity became less prominent, however, an aberrant, clumsy gait and choreoathetotic movements affecting upper and lower limbs and trunk became striking. Brain magnetic resonance imaging and neurometabolic investigations showed no abnormalities. At the age of 6 years he was diagnosed with subclinical hypothyroidism for which treatment with oral L-thyroxine was indicated. These clinical and laboratory findings, together with the absence of neuroradiological and neurometabolic abnormalities, were suggestive of the brain-lung-thyroid syndrome. This syndrome is caused by a mutation in the TTF-1 gene, linked to chromosome 14q, encoding a transcription factor essential for morphogenesis of basal ganglia, lungs and thyroid. The phenotype is variable, ranging from isolated benign hereditary chorea to the complete triad of hypothyroidism, pulmonary disease and neurological problems. Sequencing of the coding sequence of TTF-1 in this patient revealed the presence of a single nucleotide deletion (c.131delG) leading to a premature stop codon. Although this mutation has not been described to date, its nature strongly pleads for its pathogenic role. The patient's family is being genetically studied. As previous reports show a beneficial effect of dopamine agonists with improvement of gait and choreoathetotic movements, we recently assayed a treatment with Levodopa.

P185 - 1981

Excellent response to ketogenic diet (modified Atkins diet) in a case of alternating hemiplegia of childhood

Roubergue A, Philibert B, Gautier A, Kuster A, Markowicz K, Billette de Villemeur T, Vuillaumier-Barrot S, Nicole S, Roze E, Doummar D. *AP-HP, Service de Neuropédiatrie, Hôpital Armand Trousseau, Paris, France – an_schlum@yahoo.fr*

Background: Alternating Hemiplegia of Childhood (AHC) associates early onset of plegic and tonic/dystonic attacks and permanent movement disorders with mental retardation. AHC is caused by heterozygous mutations in ATP1A3 encoding the neuron-specific Na⁺/K⁺-ATPase α 3 subunit. Treatment outcome is poor. To our knowledge, there are no reports on the response

to Ketogenic diet/modified Atkins diet (KD/MAD) in AHC. Yet KD/MAD is effective in treating paroxysmal movement disorders due to GLUT1 deficiency syndrome. **Objectives:** To evaluate response to KD/MAD in a child with AHC. **Case report** A 2 ½ year-old girl presented with tonic/dystonic (2/month) and plegic attacks (2 to 4/month) with onset at age 8 months and age 2 years respectively. Attacks were mostly triggered by exercise and emotions. They were associated with mild mental retardation and very mild permanent movement disorders. The child was issued from a family with an atypical AHC. Paroxysmal exercise-induced dystonia was the prominent symptom in the mother, maternal uncle and grandmother. Treatment with KD/MAD was considered because the paroxysmal exercise-induced dystonia and the plegic attacks were similar to those of GLUT1 deficiency syndrome. MAD was chosen because it was easier to manage than KD. The 4 symptomatic familial members were ultimately shown to harbour the ATP1A3 p.Asp923Asn mutation (Roubergue et al 2013). **Results:** MAD resulted in complete disappearance of the plegic/dystonic attacks (with one year of follow-up) and in improvement of the speech disorder. Mild mental and language delay persisted. **Discussion/Conclusion:** MAD showed a complete prophylactic effect on the attacks of AHC in our patient. This contrasts with the only partial effect shown by the drugs usually administered in AHC (flunarizine, etc.). Our results suggest a new therapeutic approach in AHC. It also suggests that KD/MAD act on paroxysmal movement disorders independently of their aetiology.

P186 - 1857

Alternating hemiplegia of childhood in Denmark: clinical manifestations and ATP1A3 mutation status

Hoei-Hansen CE, Dali C, Lyngbye TJB, Duno M, Uldall P. *Department of Pediatrics, University Hospital Hillerød, Denmark – chh@dadlnet.dk*

Alternating hemiplegia of childhood (AHC) is a rare neurodevelopmental disorder characterized by early-onset recurrent distinctive hemiplegic episodes commonly accompanied by other paroxysmal features and developmental impairment. De novo mutations in ATP1A3 were recently identified as a genetic cause of AHC. To describe the entire Danish cohort of paediatric AHC patients we approached neuropsychiatrists nationwide. All currently acknowledged Danish patients ≤ 16 years with AHC were genetically tested and seen by the same child neurologist (PU). Ten patients; seven girls and three boys were identified. Mean present age was 10.0 years (range 1–16). Mean age at presentation was 7.4 months (range 1–18 months). Sequencing of ATP1A3 in all ten patients revealed a pathogenic mutation in seven. Two females with moderate psychomotor impairment were heterozygous for the known p.G947R mutation, whereas one severely retarded boy was heterozygous for the common p.E815K mutation. The prevalent p.D801N mutation was identified in two moderate to severely retarded children. Interestingly, in a set of monozygotic male twins a novel p.D801E mutation was identified, underscoring that the asparagine at position 801 is a mutation hotspot. Three girls aged 5 to 13 years did not reveal any ATP1A3 mutations. They were rather mildly clinically affected and displayed a normal or near-normal psychomotor development. In this first study of AHC in the Danish pediatric population we have found that the patients harboured a wide range of psychomotor difficulties. Patients with no mutation detected tended to be less severely affected. Prevalence was approximately 1 per 100,000 children.

P187 - 2088**A case of debilitating fluctuating myotonia due to autosomal dominant mutation in SCN4A gene**

Gnidovec Strazisar B, Writzl K, Leonardis L. *Department of Child, Adolescent and Developmental Neurology, University Children's Hospital Ljubljana, Slovenia – barbara.gnidovec@mf.uni-lj.si*

Objective: Myotonia fluctuans is an autosomal-dominantly inherited nondystrophic myotonic disorder due to the mutation in SCN4A gene. It is cold insensitive, dramatically fluctuating and is profoundly worsened by potassium ingestion. We describe a case of debilitating movement-induced myotonia in a boy who inherited an autosomal dominant mutation in SCN4A gene from his mother who only had periods of fluctuating myotonia during her two pregnancies. **Case report:** 3-years-old boy presented to child neurologist after his mother was diagnosed with myotonia fluctuans during her second pregnancy. He had daily episodes of myotonia involving mainly the eyelids and limb muscles resulting in frequent falls. Episodes of stiffness were brief and were often provoked by exercise. Myotonia usually occurred shortly after the initiation of the movement giving patient great difficulties walking on the stairs or running where he had to stop after several steps due to muscle stiffness that resolved completely after short period of rest. Cold had no influence on myotonia and muscle paralysis was never observed. Patient had generalized muscle hypertrophy with good muscle strength and percussion and hand grip myotonia. EMG was performed only in his mother where it showed prominent myotonic bursts. Genetic testing in mother revealed a heterozygous missense mutation c.3917 G>T in exon 22 of SCN4A gene resulting in a gly1306-to-val substitution in domain α of Nav1.4 skeletal muscle sodium channel and was later confirmed also in her son. **Conclusion:** Myotonic disorders due to autosomal dominant mutation in SCN4A gene represent a spectrum of diseases with diverse clinical features its severity even in the same family.

P188 - 1949**Investigation and diagnosis in children presenting with chorea**

Le Prevost NC, Kirkham F. *University Hospital Southampton, United Kingdom*

Aims: There are few prospective studies worldwide looking at investigation and final diagnosis in children presenting with chorea. Although many will have post-streptococcal (Sydenham's) chorea, a few will have diagnoses such as systemic lupus erythematosus (SLE) that must not be missed if we are to prevent later complications. Our index case was labelled as Sydenham's and subsequently presented with idiopathic intracranial hypertension and then a large middle cerebral artery territory stroke, when the diagnosis of SLE was made. **Methods:** We audited all children under 19 years presenting to a tertiary paediatric neurology centre in the UK since 2005 with chorea. Using our electronic letter database we identified 54 children who had the word "chorea" in a letter. Twenty-three were excluded as the reference was e.g. "does not have chorea". Six were excluded as their diagnosis had been made and investigated elsewhere, 7 were excluded as they presented prior to 2005 when the electronic pathology records started and 4 were excluded as they had a pre-existing diagnosis to account for their chorea. We then looked at which investigations had been undertaken in each child, and their final diagnosis. **Results:** We found that of 14 children presenting with chorea, 11 had ASOT or anti-DNAseB sent, of which 8 were positive; although two of these also had SLE. Of the others, one had anti-NMDA receptor antibodies, and there was 1 additional case of SLE. Three children had no investigations sent for SLE. Three children were labelled as Sydenham's Chorea although there was no lab evidence of streptococcal infection, and one had no definite diagnosis. **Conclusions:** SLE was

the diagnosis in about a fifth of the children in this series presenting with acute chorea. Laboratory screening for SLE should be undertaken in parallel with ASOT, and Sydenham's chorea should be a diagnosis of exclusion.

P189 - 1939**Gratifying movements, a benign cause of paroxysmal movements**

Buyck C, Aerssens P, Werckx W. *Hasselt, Belgium – wwerckx@hotmail.com*

Case report: A 16 month old girl was referred for evaluation of abnormal movements since the age of 5 months. She had recurrent, paroxysmal, rhythmic pelvic movements with contractions of both legs. Her parents remarked associated grunting, facial flushing, grimacing and irregular breathing. An episode could last till 10 minutes, but stopped immediately when the girl was distracted. The parents showed a home video of several episodes occurring while the child was sitting in a chair, fixed between her legs. Physical and neurologic examination were normal. The girl showed a normal development. **Discussion:** Gratifying movements or self-stimulation attacks are "attacks" during which children make movements that give them a pleasant feeling. They rub their legs against something or against each other by means of rhythmic movements, become rubicund and turn into themselves. Thence these "attacks" are sometimes confused with epileptic seizures. A good history and video recording of the attack can be enlightening. These attacks may occur during the first years of life and are totally innocent. They usually disappear by the age of four years. The attacks are a part of the discovery of the own body and don't have to be treated, nor punished. Once the diagnosis of gratifying movements is made, a history of sexual abuse and perineal irritation should be ruled out. **Conclusion:** In evaluating movement disorders home video records might be crucial in establishing the right diagnoses and avoiding extensive, unnecessary diagnostic testing. A key feature in gratifying movements is that it is voluntarily and can cease with distraction.

P190 - 1938**Twist of the headache (video)**

Vaessen S, Leroy P, Dubru JM, Misson JP. *CHR Citadelle, Liège, Belgium – sdnaessen@hotmail.com*

We report the case of a two years old boy who presented movement disorders of the neck and headache. Those movements appear a few days after a little fall. The boy presents a tilt of the neck and headache with, sometimes when he is standing, an ataxia. The episode takes a few seconds, sometimes a few minutes. When it ends he says "it's ok" and continues his activities. It seems to be more significant after eating. A Sandifer syndrome is suspected, even if there is no reflux and the age is already two. A treatment by omeprazole, domperidone and gaviscon is tried. No improvement is observed. Dystonia is also suggested. Finally, benign paroxysmal torticollis is evoked. A treatment by carbamazepine is tried but worsens the movements. Finally, all treatments are stopped. Of course, all exams were done to exclude epilepsy, tumor, or neurologic disorder. MRI was normal. EEG during episode is normal too. Neurologic and general examinations were normal. Benign paroxysmal torticollis belongs to childhood periodic syndromes like benign paroxysmal vertigo, abdominal migraine, and cyclic vomiting syndrome. Usually, benign paroxysmal torticollis occurs in the first months of life and disappears at about five years. It is sometimes associated with vomiting, ataxia, headache, sweating, pallor or irritability. Recently some genes are identified in childhood periodic syndromes. The same genes are also found in adult migraine.

P191 - 1924**Diagnosis of myoclonus dystonia (DYT11) in two unrelated toddlers**

Hackenberg AM, Wille D, Laccone FA, Plecko B. *Department of Pediatric Neurology, University Children's Hospital, Zürich, Switzerland – annette.hackenberg@kispi.uzh.ch*

Myoclonus dystonia is a rare but characteristic movement disorder. Onset usually occurs at a mean age of 6 years, but can vary from infancy into late adulthood. Myoclonus is the presenting symptom in most cases. It can be mistaken as benign myoclonic epilepsy, tic or tremor. We report on two unrelated girls with early disease manifestation and a positive family history. Patient 1 is a 2 year old girl who presented with anxiety and jerky movements predominantly of the upper limbs which impeded independent food intake. Family history revealed an adult half-sister with motor problems from the age of 4 years with a fluctuating course and aggravation on emotional stress and at least 3 further affected family members. On examination the otherwise healthy child exhibited action triggered myoclonus of both arms with mild signs of dystonia. Patient 2 is an 18 months old girl with a history of febrile seizures at the age of 2 and 15 months respectively. At the age of 13 months she had a transient episode of abnormal posture of her head and left arm over 5 days that resolved spontaneously. Her cranial MRI was normal. EEG revealed generalized epileptiform discharges. She developed frequent episodes of head tremor and tremor and dystonic posturing of the left arm from the age of 16 months. Family history revealed a hypermotoric movement disorder of the paternal grandmother and her sister. On exam she too had typical action myoclonus. Both girls fulfilled the clinical criteria for definite myoclonus dystonia. Diagnosis was confirmed by detection of mutations in the epsilon-sarcoglycan gene (DYT11, SGCE gene) and paternal transmission. Febrile seizures in patient 2 are probably not causally related. Symptomatic therapy is available but in many cases disappointing.

P192 - 1919**Specific patterns of movement abnormalities in infancy – a risk factor? A 7-year follow-up study**

Sadovskaya J, Blokhin B. *Moscow, Russia – j.sadovskaya@mail.ru*

The purpose is to attempt to identify interrelation between specific patterns of movement abnormalities (SPMA) during the first year of life and sensory processing disorders at toddlers. **Material:** A sample of 248 full term children was studied at 0 the 12 months of age regarding their neurodevelopment. These infants were seen in the follow up clinic at 1, 3, 6, 9, 12, 15 months of age. At long-term detailed neurological examination of infants were revealed SPMA which had the unknown predictive importance. Short Sensory Profile (SSP) was performed to all toddlers at 3 and 5 y.o. None had a current or previous clinical or DSM-IV-TR diagnosis of autistic disorder or pervasive developmental disorder-not otherwise specified. Set of independent variables was: birth conditions, socioeconomic, environmental. Analyses were performed using statistical methods. Katamnesis was 7 years. **Results:** Patients were divided into 2 groups: the 1st – children with SPMA to 1 years of life (57 patients (23%)); 2nd – typically developing children (191 patients (77%)). A 2-nd group of typically developing children was also recruited as a comparison to the 1st group. We carried to SPMA unusual body movement, or body position, asymmetric patterns and non-epileptic transient motor actions. Of 50 children with SPMA 22% showed a definite difference and 66% a probable difference in sensory processing on the total score of the SSP. Neurological studies have identified differences on SSP in children of 1st and 2nd groups ($p < 0.05$). **Conclusion:** The correlation between the SSP and specific patterns of movement abnormalities in infancy was significant. Our

research has demonstrated that children with SPMA during 1 years of age distinguish from those who are developing typically on SSP. SPMA may predict difficulties of sensory processing so that they are risk factors.

P193 - 1897**Single-center register of early onset ataxias (EOA)**

Brankovic-Sreckovic V, Milic Rasic V, Popara J, Zekavica A, Todorovic S. *Clinic for Child Neurology and Psychiatry, Belgrade, Serbia – vesna.brankovic.npk@gmail.com*

Introduction: Despite significant progress in understanding pathogenesis and molecular genetics of early onset hereditary ataxia, many questions are still unanswered, including therapeutic approaches. **Objectives:** To make a clinical registry of patients with EOA in order to select them based on clinical and radiological parameters, for further genetic and epidemiological studies. **Methods:** We did a retrospective study searching for diagnosis G11 in the database from January 2002 to January 2013 in a single center in Belgrade, Serbia. Inclusion criteria were: ataxia as a prominent feature, congenital/early onset, and an absence of other known underlining disease. The parameters of interest were: the age of the onset, accompanying features, disease progression (quantified by SARA), genetic confirmations and MRI characteristics. **Results:** Within the 11 yr period, we selected 71 children with diagnosis G11; in 52 (73.2%) medical history was available for the study and they fulfill inclusion criteria. Congenital onset was registered in 16 (30.8%), FA in 16, and other HA in 19 (36.5%) pt. The mean age of disease onset was 5 ± 4.7 yr (FA 8 ± 3.2 ; other HA 7.1 ± 4.4). Positive family history had 16 pt (3 FA, 6 other HA, 7 CA), and genetic confirmation 20 (38.5%) pt- 15 FDRA, 3 ANO10, 1 SACS and 1 SCA2 mutation. Disease progression was significantly greater in the group of FA ($p = 0.007$) compared to the other subgroups. Pathological finding on brain MRI had 30 pt (2 FA, 12 other HA, 16 CA) and 15pt had a normal MRI (8 FA, 6 other HA, 1 CA). **Conclusion:** Despite bias our study shows that FA, as an entity, was the most frequently and straightforwardly diagnosed among early onset ataxias. Patients with CA and other HA show more heterogeneity and need additional selection criteria. We stress the importance of having national registry of EOA patients.

P194 - 1878**Benign non-epileptic paroxysmal disorders: a study of 106 newborns and infants**

Hostnik T, Hrastovec A, Paro Panjan D, Neubauer D. *Department of Child, Adolescent & Developmental Neurology University Children's Hospital Ljubljana, Slovenia – david.neubauer@mfn.uni-lj.si*

Background: Wide range of paroxysmal non-epileptic motor events (PNME) appear in newborns and infants. In our previous study we concluded that syndromes with benign myoclonus (benign neonatal sleep myoclonus (BNSM), benign sleep myoclonus of infancy (BSMI) and benign myoclonus of early infancy (BMEI)), are three times more frequent than West syndrome. **Aim:** To analyze clinical characteristics of infants with the diagnoses of BMEI, BNSM and BSMI. **Methods:** Retrospective analysis of clinical presentations, laboratory values, neuroimaging and neurophysiological assessments was performed in 30 children with BNSM, 39 with BSMI and 37 with BMEI. **Results:** Among infants with the diagnoses of BNSM and BSMI the motor paroxysms were occurring during sleep, in majority (55.1%) as generalized, symmetric, synchronous, repetitive jerks. The commonest presentation of BMEI was shuddering/shivering, presenting in 29 and/or myoclonus, presenting in 20 children during wakefulness. At first neurological assessment 29 infants had mild and one moderate neurodevelopmental impairment. Nonspecific changes of laboratory values were seen in results of 22. Neuroimaging

showed mild abnormalities in 20 infants. Ictal EEG recording of one child and interictal EEG recordings of nine children were nonspecifically changed. Three children with the diagnosis of BNSM were initially treated with anti-epileptic drugs (AED). 38% of children were examined on follow-up. The length of follow-up ranged from one to 101 months (average 14.25 months, median 5 months). One girl, initially diagnosed as having BNSM, was eventually found to have myoclonic-astatic epilepsy. **Conclusions:** BNSM, BSMI and BMEI are benign, paroxysmal syndromes occurring during first two years of life. Diverse spectrum of motor phenomena is included in the diagnosis of BMEI, as well as in BNSM and BSMI. Laboratory values, neuroimaging and neurophysiological assessments are normal or nonspecifically changed. Interictal or ictal EEG shows no signs of epileptic activity. The outcome is favorable.

P195 - 1860

Status dystonicus in children: report of eight cases

Magalhães C, Rocha S, Vieira JP, Figueiroa S, Calado E, Robalo C, Temudo T. *Serviço de Neuropediatria do Departamento da Criança e Adolescente do Centro Hospitalar do Porto, Portugal* - c - magalhaes@netcabo.pt

Introduction: Among the neurologic emergencies in children, movement disorders emergencies are very infrequent and there are few reports on the subject. They include diseases presenting as parkinsonism, myoclonus, coreia and dystonia. Status dystonicus, a rare clinical entity, is characterized by increasingly frequent and severe dystonia, which obliges to urgent hospital admission for treatment. The risk of respiratory, renal and metabolic complications is high, with important morbidity and mortality. Management includes medical and often surgical procedures. **Objectives:** To report eight cases of status dystonicus, describing clinical manifestations, treatment strategies and outcome. **Methods:** Retrospective analysis of clinical records of patients with status dystonicus admitted in two neuropediatric centers. **Results:** We present eight cases of children admitted with status dystonicus, four boys and four girls, with ages between two and thirteen years old. The etiology, was classified as heredo-degenerative in four cases - three children had PKAN (pantothenate kinase-associated neurodegeneration) and one Huntington disease; three had secondary dystonia: two encephalitis (probably autoimmune) and one generalized dystonia still under investigation, probably due to an immunologic disorder; one had idiopathic generalized dystonia. Status dystonicus was the presenting feature of the underlying disease in two of them. A precipitating factor was identified in three patients. Treatment included systemic drugs in all patients, intrathecal baclofen in three and deep brain stimulation in four cases. Two patients died. **Conclusions:** The small size of our series does not allow us to compare the results with other series. However, we think that the rarity of this entity justify the description and report of small series of patients in order to contribute to a better knowledge and development of more accurate treatment strategies of status dystonicus.

P196 - 1828

A girl with abnormal head shaking

Jain P, Sharma S, Aneja S. *Lady Hardinge Medical College and Associated Kalawati Saran Children's Hospital, New Delhi, India* - puneet_mpa@yahoo.com

Objectives: Absence seizures associated with myoclonic phenomena have been associated with typical absence seizures, myoclonic absence seizures, eyelid myoclonia and perioral myoclonia with absences. We describe a young girl with episodes of head shaking precipitated by hyperventilation. **Methods:** The

clinical details of a girl diagnosed with neck myoclonia with absence seizures were reviewed and reported. **Results:** A previously normal, 9-years old girl, presented with recurrent episodes of abnormal head shaking for past 5 months. Each episode was brief lasting for 15–20 seconds with abrupt onset and termination. It was associated with vacant stare and shaking of the head. There was no eyelid fluttering or lip smacking. The frequency of these episodes gradually increased to 25/day. The systemic examination was unremarkable. Hyperventilation precipitated these episodes. Her neuroimaging was normal. The ictal-EEG revealed 3-Hz spike-and-wave discharge. The clinical presentation was consistent with neck myoclonia with absence seizures. She had partial response to valproate monotherapy. Now, she is seizure free for 6 months on valproate and clonazepam. **Conclusions:** The absence epilepsies may be a heterogeneous group of epilepsy syndromes. Identification of specific clinical features may help to delineate separate clinical entities. This case may further support the existence of newly described entity of neck myoclonia with absence seizures.

P197 - 1806

Denial mechanisms cause delay of diagnosis in families with hereditary Huntington's disease

Thiels Ch, Saft C, Hoffmann R, Luecke T. *University Hospital for Children, Department of Neuropediatrics, Bochum, Germany* - charlotte.thiels@rub.de

Introduction: Huntington disease (HD, MIM 143100, chrom 4p16.3) is hereditary in an autosomal dominant fashion. The likelihood of developing HD for offspring of afflicted individuals therefore is 50%. This high level of disease risk poses an enormous emotional burden and frequently leads to denial and delayed diagnosis. Nevertheless, presymptomatic targeted genetic analysis is prohibited because of "Gene-Diagnostic-Laws". **Cases:** 1: Grandfather, paternal great uncle, and father HD patients. Patient exhibited motoric disabilities at 1.5 y/a; abnormalities were more pronounced by 3.5 y/a (muscle hypotonia, gait disturbances). Expanded gene (9 y/a): 80 CAG repeats. At 12 y/a, pronounced gait abnormalities, rigidity, cognitive decline, and dystrophy; therapy: Pramipexole and Seroquel. 2: Father HD patient; patient born prematurity 35 weeks; At 9 y/a progressive problems in fine and gross motor skills, cognitive decline. 13 y/a: hypomimia, slowing in finger tapping, dysarthria, tremor. Mother attributed problems to the prematurity. Expanded gene: 73 CAG repeats. Therapy (17 y/a): Pramipexole, Seroquel, Valproate, Lithium, Venlafaxin. 3: Father HD patient, death by suicide; the elder sister HD patient (onset at 15 y/a). Decrease in school performance and depressed mood prompted the school to encourage medical consultation. 13 y/a: depressive, discrete tremor and slowing in finger tapping. Expanded gene: 48 CAG repeats. Therapy: psychotherapy, stabilization of performance in school. Cognitive performance was compromised because of the emotional burden associated with the hereditary nature of HD. 15 y/a: no pharmaceutical treatment. 4: Father HD patient. Patient prematurity 37 weeks. As toddler progressive motoric and speech problems, stumbling, learning disability. Expanded gene (9 y/a): 81 CAG repeats; therapy (17 y/a): Pramipexol. **Conclusion:** Expansion of the mutation especially in paternal transmissions with earlier onset in the following generation should be considered. Patients clearly benefit from symptomatic therapy. In cases of hereditary risk for Huntington disease it may be advisable to conduct gene analysis for HD early to improve the quality of life.

P198 - 1805

Paroxysmal dyskinesias in children

Garrido C, Damásio J, Temudo T, Carrilho I. *Serviço de Neuropediatria Centro Hospitalar Porto, Portugal – cgarridopt@gmail.com*

Introduction: Paroxysmal dyskinesias are relatively rare and heterogeneous movement disorders, characterized mainly by recurrent and brief episodes of dystonia or chorea. Three forms are clearly recognized and distinguished by the attacks trigger, frequency and duration: kinesigenic, nonkinesigenic and exercise-induced. In pediatric age, paroxysmal torticollis is included in this group of diseases. **Objectives:** Our aim was the clinical characterization of children with paroxysmal dyskinesias followed in a tertiary neuropediatric centre in the last 10 years. **Material and methods:** Retrospective clinical chart analysis of children with a diagnosis of paroxysmal dyskinesia and more than two years follow up. We excluded children with benign paroxysmal torticollis because they have a distinct clinical presentation and pathogenesis. **Results:** Of the initial 41 cases, we eliminated 22 benign paroxysmal torticollis and 3 with an insufficient follow-up. We included sixteen children, with a disease onset between 2 months and 14 years (median of 12 months). The movement pattern was dystonic in the vast majority of the cases; only 3 children had choreic phenomena. The distribution was segmental in seven, hemidystonia in six and generalized in three. We found 10 nonkinesigenic dyskinesias: seven secondary (one MoyaMoya disease, one pyruvate dehydrogenase deficiency, one leucinoses, two alternating hemiplegia of childhood, one GLUT1 deficiency syndrome and one mastocytosis), one probably symptomatic and two primary. The four cases of kinesigenic dyskinesias were primary. Two children presented exercise-induced paroxysmal dyskinesia, one of them had a pyruvate dehydrogenase deficiency and the other was probably symptomatic. **Conclusions:** In our series, the large number of symptomatic paroxysmal dyskinesias, outlines the need for a systematic workup, in the pediatric age, to exclude the presence of other disorders, namely inborn metabolic errors.

P199 - 1785

Six cases of Dopa-responsive dystonia with GCH1 mutations

Ryu HW, Kim HM, Lim BC, Hwang H, Chae JH, Choi J-E, Hwang YS, Kim KJ. *Department of Pediatrics, Seoul National University Children's Hospital, Korea – ryuhyewon@hanmail.net*

Objectives: Dopa-responsive dystonia (DRD) is childhood-onset focal dystonia characterized by diurnal fluctuation and dramatic response to low dose of levodopa. Most common cause of DRD is mutation in GCH1 gene that encodes guanosine triphosphate cyclohydrolase 1. We aimed to investigate the clinical and genetic features of patients confirmed to have GCH1 mutation. **Patients and methods:** We performed GCH1 analysis by direct sequencing for the pediatric patients with focal dystonia and diurnal variation. We analyzed the characteristics in 6 patients with mutation in GCH1 gene. **Results:** The mean age of onset was 7.7 ± 3.7 years (range from 5 to 10). Among them, 3 cases were misdiagnosed with cerebral palsy or equinovarus and underwent surgery before a visit to neurology clinic. Among the six mutations, five were new (c.175dup, c.240_252del13, c.626_c.626+1insTG, c.245_262del18, c.257C>A), and one has been described previously (c.631_632delAT). They were successfully improved with low dose levodopa trial. **Conclusion:** Our findings expanded the mutational spectrum of GCH1 gene by the identification of five novel mutations. In children with focal dystonia with diurnal fluctuation, DRD should be considered and levodopa trial and GCH1 analysis should be made to avoid unwanted surgery.

P200 - 1735

Acute ataxia revealing PDH deficiency in a 22-month old boy

Delmelle F, Vincent MF, Lissens W, De Meirleir L, Nassogne MC. *Université Catholique de Louvain, Cliniques Universitaires Saint-Luc, Bruxelles, Belgium – francoise.delmelle@uclouvain.be*

Introduction: Pyruvate dehydrogenase complex (PDHC) deficiency is an inborn error of metabolism that occurs most commonly due to mutations in the X-linked E1 α subunit gene (PDHA1). In hemizygous males, neonatal lactic acidosis and Leigh encephalopathy are the most frequent clinical presentations. Intermittent ataxia has been also rarely reported. We report a new case of acute ataxia in a 22-month-old boy revealing PDHE1 α deficiency. **Clinical case:** This 22 month-old boy was addressed to the emergency room for a gait disorder. He's the first child of non-consanguineous Armenian parents. His medical history is uneventful. Parents described a child falling for two days and having trouble of standing. There was no infectious context. Clinical examination showed a mild ataxia with a decreased strength in the lower limb. The child falls after a few steps. The force is normal in the upper limbs. Tendon reflexes were absent. EMG and toxicological investigations were not contributory. Brain MRI showed a discrete high signal of the thalami on the diffusion sequence. CSF lactate was increased up to 4.6 mmol/l. Blood lactate, pyruvate and alanine concentrations were raised with a normal lactate/pyruvate ratio. Diagnosis was confirmed by demonstration of a hemizygous mutation in c.262C>T; p.Arg88Cys on the PDHA1 gene. The clinical condition of the boy improved within one month. This patient is currently treated with Thiamine. **Discussion and conclusion:** This case illustrates the fact that PDH deficiency should be considered in patients with unexplained intermittent and/or recurrent acute ataxia. An increase of CSF lactate may suggest the diagnosis. Long-term prognosis and outcome remain uncertain.

P201 - 1718

Twins with remarkable stereotypical hand movements

Van Ingelghem I, Hellinckx J, Wojciechowski M, Matthijs G, Ceuterick-de Groote C, Ceulemans B. *AZ Klina Brasschaat, UZ Antwerp, Belgium – ingrid.vanengelghem@me.com*

Introduction: The neuronal ceroid lipofuscinoses (NCL; CLN) are a clinically and genetically heterogeneous group of neurodegenerative disorders characterized by the intracellular accumulation of autofluorescent lipopigment storage material. It is often a long search before the diagnosis can be made. **Case report:** We describe the case history of a monozygote female twins, normal at birth and with progressive microcephaly, psychomotor regression and absent of social contact from the age of 10 months. Both parents were consanguineous and had already a 2-year old daughter developed normally. The pregnancy and perinatal period of both girls was without any problems and also during the first months the development was normal. At the age of 12 months they showed loss of social contact and remarkable stereotypical hand movements. On clinical examination there was a declining head circumference which lead to the start of an extensive genetic search for Rett syndrome. We found a missense mutation in MECP2gen, not known in the international Rett database. The mutation was absent in the father, present in the mother, but maternal X-inactivity showed 95% skewing, supporting the hypothesis that it was a pathogenic mutation. Further genetic search in the maternal family was negative. At the age of 2 both girl could barely sit, there was a restlessness in arms en legs, hyperreflexia and evolution to spasticity combined with total loss of visual contact. The girls were very irritable and sleep was disrupted. On further examination, skin biopsy was abnormal with intracellular accumulation of lipopigment storage material. The pattern was described as granular osmiophilic deposits, pathog-

nomonic for NCL 1. **Discussion:** NCL 1 must be included in the differential diagnosis of children with Rett-like symptoms.

P202 - 1696

A case of unusual lower limb movement disorder in association with Klippel-Trenaunay syndrome (KTS)

Joseph S, Yeo TH. *The Fraser of Allander Neurosciences Research Group, The Royal Hospital for Sick Children, Yorkhill, Glasgow, United Kingdom – ShukoNagasawa@doctors.org.uk*

Introduction: KTS is a rare sporadic congenital disease. The diagnostic criteria are: (1) congenital vascular malformation (capillary, venous, arteriovenous and lymphatic) and (2) disturbed hyper- or hypotrophic growth of bone or soft tissue [1]. It is a multi-system disorder [2] with cutaneous, visceral organ and nervous system (rarely) involvement reported [3]. These include; hemi-megaencephaly, cervical intra-medullary and brain stem cavernomas [4,5,6], carpal tunnel syndrome [7,8] and sciatic neuropathy [9,10]. We describe a previously unreported case of movement disorder localized to the affected limb. **Case:** The patient is an 11-year-old female with an extensive cutaneous haemangioma over her right leg. She has hemi-hypertrophy of leg, recurrent cellulitis and severe chronic leg pain. The later has been unresponsive to carbamazepine and gabapentin. She developed new onset myokymia localised over the gastrocnemius muscle, persisting at rest, with new ankle clonus. The lower limb reflexes were symmetrical and neither sensory impairment nor motor weakness was present. The involuntary movements responded well to clonazepam. **Results:** Brain and Spinal MRI scans were normal. MRI of the leg showed an extensive complex vascular malformation. The vascular malformation infiltrated the muscle, especially at the posterior compartment of the calf. There was atrophy of the involved muscle especially at the medial head of the gastrocnemius. There was no evidence of focal impingement on the neurovascular bundle. **Conclusion:** We describe an unusual constellation of localised involuntary movements in association with KTS. We believe the myokymia is secondary to vascular infiltration and atrophy of the gastrocnemius muscle. We also postulate that she developed a peripheral myoclonus. Peripheral myoclonus is focal, involves denervated muscles and is often rhythmic. It can follow periods of pain affecting a denervated area and may overlap or accompany myokymia [10.] The ankle myoclonus, due to its location, mimicked clonus secondary to spinal or cortical level lesions.

P203 - 1670

Ataxia rating scales are age-dependent in healthy children

Brandsma R, Spits AH, Kuiper MJ, Lunsing RJ, Kremer HPH, Burger H, Sival DA. *Beatrix Children's Hospital, University Medical Center Groningen, University of Groningen, Department of Neurology, The Netherlands – d.a.sival@umcg.nl*

Introduction: Early Onset Ataxia (EOA) involves a heterogeneous group of diseases and the course and underlying aetiology is still unknown. To clarify the phenotypic spectrum, European adult and pediatric Ataxia Interest Groups strive to assemble one longitudinal EOA-database, with application of identical quantitative ataxia rating scales in children and adults. However, age-related maturation of the nervous system may impose an influence upon the quantification of fine motor skills and coordination. In young children, this could implicate that ataxia rating scales are confounded by age. **Objectives:** To determine age dependency of ataxia rating scales in children. **Methods:** Three independent neuro-pediatric observers cross-sectionally scored a set of ataxia rating scales in a group of 52 healthy children aged 4 to 16 years. The investigated scales involved the “International Cooperative Ataxia Rating Scale” (ICARS), the

“Scale for Assessment and Rating of Ataxia” (SARA), the “Brief Ataxia Rating Scale” (BARS) and a PEG-board test. We investigated the inter-relatedness between individual ataxia scales, age and gender dependency, inter- and intra- observer agreement and test-retest reliability. **Results:** Spearman rank correlations revealed strong correlations between ICARS, SARA BARS and PEG-board test (all $p < .001$). ICARS-, SARA-, BARS- and PEG- board test outcomes were age-dependent until 12, 6, 8 and 10 years of age, respectively. Intra-class correlation coefficients (ICC's) varied between moderate to almost perfect [inter-observer agreement: 0.85, 0.72 and 0.69; intra-observer agreement: 0.92, 0.94 and 0.70; and test-retest reliability: 0.95, 0.50 and 0.71; for ICARS, SARA and BARS, respectively]. Inter-observer variability decreased after the sixth year of life. **Conclusion:** In children, ataxia rating scales are reliably applicable on the condition that outcomes are interpreted against the child's age. By pediatric validation of SARA, the “European Pediatric Ataxia and Cerebellar Study Group” aims to provide age dependent norm values.

P204 - 1658

Ataxia, headshaking and hyperactive behavior in prenatally diagnosed rhombencephalosynapsis

Vargiami E, Hourmouzi D, Psarra N, Kyriazi M, Dragoumi P, Ververi A, Bellou A, Zafeiriou DI. *1st Department of Pediatrics, Aristotle University of Thessaloniki, Greece – jeff@med.auth.gr*

Rhombencephalosynapsis is a midline brain malformation characterized by missing cerebellar vermis with apparent fusion of the cerebellar hemispheres. It can be seen in isolation or together with other central nervous system and extracranial nervous system malformations. We report of a 21 month-old male with prenatally diagnosed rhombencephalosynapsis (fetal ultrasound and MRI), whose diagnosis was confirmed with a repeated brain MRI at the age of 7 months. He manifested at the first months of life with generalized hypotonia, delay in head control and other major motor milestones, hence he was referred for physical therapy at the age of 7.5 months. After initiation of physical therapy, independent sitting was achieved at 9 months, crawling at 13 months and independent walking at the age of 17 months. However, cerebellar ataxia became prominent with limited righting reactions and difficulties preserving eye contact with target while walking. Moreover, hyperactive, impulsive and sometimes pervasive behavior with short attention span, as well as headshaking episodes, especially under stress, became evident. Today, his GMFM score is 81.2%, while his Sensory Profile indicates either low registration and/or sensory seeking in auditory, visual, vestibular and proprioceptive sensory processing. Regarding the rest of his development, he is not yet talking, demonstrates poor eye contact and visual tracking and receives speech and occupational therapy. Brainstem and visual auditory evoked potentials, EEG, fundoscopy, abdomen and heart ultrasound and band karyotyping yielded normal results. Rhombencephalosynapsis represents a rare cerebellar dysplasia that addresses specific developmental issues and a movement disorder comprising ataxia, hyperactivity, poor visual tracking and headshaking episodes.

P205 - 1655

Autosomal dominant guanine triphosphate cyclohydrolase deficiency (GTPCH; Segawa's disease)

Zafeiriou DI, Vargiami E, Batzios S, Dragoumi P, Verbeek MM, Kamsteeg EJ, Blau N, Wevers R. *1st Department of Pediatrics, Aristotle University of Thessaloniki, Greece – jeff@med.auth.gr*

Autosomal dominant guanine triphosphate cyclohydrolase deficiency (GTPCH; Segawa's disease) is a disorder of monoamine metabolism and specifically of BH4 synthesis, which presents with fluctuating dystonia in childhood. An 11 year-old girl was

admitted to the Neurology Outpatient Department for inward gait since the last 2 weeks. Pregnancy and birth were uneventful, as was her whole development up to that timepoint, with normal developmental milestones and school performance (currently attending the 5th Grade). The neurological examination was entirely normal, except from a right foot dystonia with internal rotation and mild supination, which was not always present at the same degree, but varied during the day, according to her parents. CSF neurotransmitter analysis demonstrated low HVA (133 nM; ref. 330–668), low 5-HIAA (58 nM; ref. 109–214) and low MPHG (28 nM; ref. 32–68), findings consistent with GTPCH deficiency (Segawa's disease). The diagnosis was confirmed by findings of borderline low GTPCH activity in cultured skin fibroblasts (1.9 pmol/mg; ref. 1.4–6.5) and a new mutation c44g>A (p.Gly150Arg) of the GTPCH gene. L-dopa substitution at low doses (10 mg/kg/BW), resulted in complete disappearance of the dystonia, within a week. The patient remains entirely normal after 5 years of follow-up, maintaining the same low L-dopa dose. Segawa's disease should be considered in any case of sudden onset limb dystonia occurring in childhood. A marked sustained response to L-dopa without any side effects, may be profoundly life altering at any age.

P206 - 1647

Paroxysmal kinesigenic dyskinesia, an uncommon movement disorder

Potoms M, Aerssens P, Werckx W. Hasselt, Belgium – marliespotoms@hotmail.com

Case report: A 11-year old girl was referred for evaluation of a 1-year history of abnormal movements in shoulders, head and limbs. Events consisted of brief attacks of abnormal movements and postures (dystonic and choreoathetoid). Dystonia could be provoked by unexpected movements, which resulted in excessive harassing at school. Consciousness was normal during all episodes. Clinical neurological examination was normal. Brain MRI and laboratory values were normal. Pimozide and psychologic counselling did not bring any improvement. With persistence of events, Carbamazepine was started with total disappearing of symptoms. **Discussion:** Paroxysmal kinesigenic dyskinesia (PKD) is characterized by brief episodes of involuntary movements that are precipitated by sudden voluntary movement of the body, primarily face and limbs, especially after a period of rest. Rare cases may be secondary to a lesion in the supplementary motor area. Electroencephalography is often required to exclude epilepsy, though clinical manifestations of PKD are uniquely different from seizures. Age of onset is usually in later childhood or adolescence. Prognostically, there is a tendency for symptoms to diminish with age. Many patients with PKD respond to treatment with anticonvulsants, particularly carbamazepine. Genetics and pathophysiology of PKD have recently been investigated. Increased spontaneous brain activity in the cortical-basal ganglia circuitry is a common pathophysiology in PKD. Proline-rich transmembrane protein 2 (PRRT2) gene has been identified as a causative gene of PKD. **Conclusion:** Most cases of PKD have a benign neurological course, tending to diminish in severity and frequency with age. The episodes are brief and respond well to anticonvulsant medication. Given the apparently benign nature of childhood PKD, and the potential adverse effects of anticonvulsants, it is critical to discuss with parents whether treatment may or may not be indicated. In this case treatment allowed the child to go back to school, which makes continuing of treatment currently essential.

P207 - 1613

Cognitive behavioral treatment of movement disorders in children

Khachapuridze N, Bakhtadze S, Geladze N. Tbilisi State Medical University, Georgia – sophiabakhtadze@yahoo.com

Objectives: Movement disorders include conditions in which there is anatomical and/or functional evidence of involvement of basal structures responsible for the control of movement. Tics are the most frequent movement disorder in children. They are involuntary, purposeless contractions of functionally related groups of skeletal muscles, involuntary noises or involuntary utterance of words. Drug therapy was considered as the most successful treatment approach for several years. In recent period clinicians attempt to use cognitive behavioral methods as drugs often fail to control tics. The aim of our study was to use non pharmacological treatment like EEG biofeedback – neurofeedback (NF) for the treatment of tics in children. **Methods:** We have examined previously non treated 23 children (15 boys, 8 girls) with simple tics (average age 10 years). All children with complex tics and with other comorbidities were excluded from the study. Tics frequency and severity were assessed by Yale Global Tic Severity Scale (YGTSS). Sensorimotor rhythm (SMR) training was used for NF therapy. 30 session of NF with duration of 30 minutes of each was conducted in every patient. Data was analyzed by SPSS 10.0 ANOVA was used to determine the effect of treatment on YGTSS parameters. **Results:** The ANOVA showed a significant effect of treatment on YGTSS measures ($F(1.37)=223.69$, $MSE=114.735$, $p<0.0001$). These evidences suggest that NF significantly improves the severity and frequency of tics. **Conclusions:** Thus efficiency of SMR training in children with tics is important as the drugs frequently used for the treatment have severe side effects, compliance problems and etc. Cognitive behavioral therapy is significant not only for reducing of tics but also for increasing self esteem and social skills as well.

P208 - 1790

EPNS SARA age validation trial: preliminary results

Lawerman TF, Baxter P, Brandsma R, Brankovic-Sreckovic V, Calabro GE, Catsman-Berrevoets CE, Craiu D, de Coe IFM, Gburek-Augustat J, Kammoun F, Kennedy C, Lunsing RJ, Mancini F, Mirabelli-Badenier M, Nemeth A, Steinlin M, Synofzik M, Triki Chahnez C, Valente EM, Sival DA. Department of Neurology, University Medical Center Groningen, University of Groningen, The Netherlands – d.a.sival@umcg.nl

Introduction: Early Onset Ataxia (EOA) is caused by a group of relatively rare and heterogeneous disorders, often with an autosomal recessive inheritance mode. To elucidate the phenotypic disease course, European Ataxia Interest Groups are preparing one longitudinal EOA database from child- to adulthood, in which ataxia progression is quantified by SARA (Scale for Assessment and Rating of Ataxia). Since pediatric coordination matures over time, the development of age-related normative values is a prerequisite before SARA is applicable in children. **Objectives:** For pediatric SARA, we aimed to assess age-related normative values and inter-observer agreement. **Methods:** Eighteen European pediatric neurologists (of 8 different countries) consented to participate in this study. For normative outcomes with a precision of 10%-20%, we are eventually aiming to include 150–600 healthy children (4–16 years; $m/f=1$). We expressed inter-observer agreement by intra-class correlation coefficients [ICC: <0.20 slight; 0.21–0.40 fair; 0.41–0.60 moderate; 0.61–0.80 substantial; >0.81 almost perfect]. **Preliminary results** (obtained in 36 Dutch children; 4–16 years): Nine observers from five countries revealed that SARA scores are age-dependent ($R^2=0.64$) and moderately-reliable (ICC 0.58). National assessors (speaking the child's language) revealed more speech-subscore fluctuations ($p<0.05$) than

international assessors. After exclusion of speech subscores, the ICC of international assessors improved slightly above the “substantial” level (0.61), whereas the ICC of national assessors remained substantial for both conditions (0.80). **Conclusions:** Preliminary results suggest that internationally obtained pediatric SARA scores are age-dependent and moderately to substantially reliably assessable. During further study progression we will aim to clarify the potentially confounding influence by language and to investigate the effect of word replacement by universal “non-sense” speech phrases.

Neonatology

P209 - 1497

Early diagnosis of hypoxic-ischemic central nervous system injury in newborn babies

Afonin AA, Papsheva AA, Loginova IG, Bobrova SG, Drukker NA. Rostov Scientific-Research Institute of Obstetrics and Pediatrics, Rostov-on-Don, Russia – miiap@yandex.ru

Objective: Detection of biochemical criteria of early (pre-clinical) diagnosis of perinatal central nervous system injury (PCNSI) in newborns. **Material and methods:** 38 full-term newborn babies born by women with complicated course of gestation and childbirth with the deferred clinical manifestation of brain damage were examined (onset of clinical symptoms of PCNSI was recognized in 1–2 months after the birth). Control group was comprised of 15 healthy children. Level of neuron specific enolase (NSE) and S-100 β protein in the serum of the umbilical blood was defined using immune-enzyme assay technique with CanAg Diagnostics Company kits (Sweden). Distribution-free method of statistics (Mann-Whitney test) and design method of receiver-operating characteristic (ROC) curves. **Results:** It is established that in children with deferred manifestation of neurologic symptoms the content of NSE and S-100 β protein in the serum of the umbilical blood was definitely higher than the control values. Statistic analysis with the help of the developed macro in the Excel medium using the method of design of ROC curves allowed to find cut off frequency: with NSE values equal to 11.26 ng/ml and more (accuracy of the method – 81.13%; sensitivity – 76.32%; specificity – 93.33%), and with S-100 β protein values – 487.1 ng/l and more (accuracy of the method – 98.11%; sensitivity – 100.00%; specificity – 93.33%) perinatal central nervous system injury is diagnosed at birth. **Conclusions:** The developed method of early diagnosis of PCNSI on the basis of content estimation of neuron injury markers and macroglia of brain (NSE and S-100 β protein, accordingly) in the serum of the umbilical blood in newborns from the perinatal risk group permits to detect brain damages at the pre-clinical stage of disease.

P210 - 2028

Motor and cognitive outcome of congenital unilateral cerebellar hemisphere hypoplasia: a prospective study of ten prenatal cases

Bénézit A, Rougeot C, Roy A, Delpouve J, Peyric E, Paulignan Y, Ville D, Cagneaux M, Guibaud L, des Portes V. National Centre of Reference for “Cerebellar Malformations”, Hôpital Femme Mère Enfant, Hospices Civils de Lyon, France – vincent.desportes@chu-lyon.fr

Objectives: Congenital unilateral cerebellar hypoplasia is a rare malformation with uncertain prognosis. When diagnosed during pregnancy, the risk of motor skills impairment and learning disability remains unclear. **Material and methods:** Between 2003 and 2010, fourteen women were referred to a regional prenatal diagnosis center for an isolated unilateral cerebellar hypoplasia. Ten decided to continue the pregnancy. Two hypoplasia were

related to FACE Syndrome. Other cases were due to ichémic-haemorrhagic defects. Five boys and five girls were followed, through a standardized clinical and cognitive assessment (Brunet Lézine, WPPSI-II, WISC-IV). A first data analysis was performed in 2012: mean age was 4 years 5 months [2 years to 8 years 7]. In order to better assess fine motor skills, three patients performed a kinematic task to reach, grasp and lift an object (optotrack system). **Results:** All patients walked before two years old. No patient had static cerebellar syndrome. One had a transient unilateral kinetic cerebellar syndrome, ipsilateral to the lesion. All school age children attended a normal school without help, except for one child. No one had disturbing behavior. One patient had mild visuocognitive dyspraxia. Expressive language was delayed in six patients but intellectual skills were in the normal ranges in all. Three patients had ADHD. Preliminary analysis of the kinematic task exhibited a mild motor programming deficit, with bad adaptation of the speed depending on the distance, and weak adjustment of the thumb-index pinch amplitude to the size of the object. **Conclusions:** In this small series, no major motor or cognitive impairment was noticed. Nevertheless, language delay, mild dyspraxia and attention deficit were observed. Moreover, fine motor programming impairment was elicited through a kinematic task. Further follow-up in a larger series is mandatory before definite conclusions.

P211 - 1968

Spatial patterning of oscillatory activities recorded by high-density electroencephalography in newborn infants

Pelc K, Cebolla AM, Dan J, Dewulf L, Johansson AB, Cheron G, Dan B. Neurology, Hopital Universitaire des enfants Reine Fabiola, ULB, Brussels, Belgium – bernard.dan@ulb.ac.be

Electroencephalography (EEG) has long been used as the par excellence non-invasive functional approach to brain physiology. Clinical use in neonate has increasingly incorporated various paradigms, including amplitude-integrated EEG monitoring. EEG has excellent temporal resolution but the spatial resolution is very poor compared to other neurophysiological techniques. This issue can be solved to a large extent by increasing spatial sampling by the use of high-density EEG, based on a high number of scalp electrodes. Improved spatial resolution allows source localization of current dipoles in a volume conductor model of the head. This provides a potentially useful model of intracerebral generator of the recorded potentials. Here we report the use of 64-channel EEGs obtained in a clinical setting in 15 newborn infants and compared it with standard neonatal EEG. We found dense spatial patterning of oscillatory EEG activities on high density EEG, which could not be consistently identified on standard EEG. Several sources were characterized, such as the fusiform gyrus for alpha band activity and the middle frontal gyrus for beta activity. We conclude that optimal neonatal EEG recording would require significantly more electrodes than numbers used in standard practice. We also highlight the use of oscillatory activity analysis for assessing neural integrity in the newborn child.

P212 - 1960

Spectral EEG analysis in young adults after perinatal mild-moderate hypoxic-ischaemic encephalopathy (HIE)

Bregant T, Lesar S, Neubauer D, Belic A. Department of Pediatric Neurology, University Children's Hospital, University Medical Centre Ljubljana, Slovenia

Objectives: In children with mild-moderate HIE learning disorder in the absence of overt neurological sequelae can be observed. The purpose was to evaluate cortical electrical activity in young adults with perinatal HIE by spectral EEG analysis and compare it

to the healthy, age matched controls. **Material and methods:** We studied an inception cohort of 13 young adults with mild (69.2%) to moderate HIE (30.8%): 5 girls (38.5%), 8 (61.5%) boys, born with mean GA of 36.3 ± 3.4 weeks and mean BW of 2640 ± 807 g, now mean age 22.1 ± 0.7 years, compared to healthy students: 5 girls (50.0%), 5 (50.0%) boys, mean age 23.2 ± 1.1 years. HIE in the perinatal period was confirmed clinically. Participants were examined and interviewed, follow-up EEG after sleep deprivation with spectral analysis was performed. **Results:** In HIE group, epilepsy evolved in 15.4% adolescents: one had focal, the other had focal and generalized seizures. Both were excluded from spectral EEG analysis. Spectral analysis was done in all with normal EEG: in 11 HIE adolescents (84.6%), who in 8 (72.7%) had local maximum at mean 10.0 ± 0.8 Hz, mean spectrum rebounds 82.3 ± 72.5 , while in 3 (27.3%) local maxima were absent. All 3 had learning problems. Learning problems were present in 2, who had local maximum at 9 and 11 Hz, one having 3 and one 221 rebounds, which made their spectral analysis curve outlier. In healthy student group, 7 (70.0%) had local maximum at mean 11.3 ± 1.7 Hz, mean spectrum rebounds 42.3 ± 40.7 , while in 3 (30.0%) local maxima were absent. These were good students, with no learning problems. **Conclusions:** Presence of local maximum in the alpha spectrum is observed in young people, who are successful in school, be healthy or after perinatal insult, suggesting that local maximum in the alpha spectrum is associated with school success.

P213 - 1934

Inter-observer agreement study of a new scoring system of neonatal EEG in term infant

Badiola R, Cipierre C, Nguyen S. *Child Neurology Unit, CHU Bordeaux, France – synguyen@chu-angers.fr*

Conventional EEG (cEEG) is recognized as the gold standard for the neurological assessment of cerebral injury in neonates suffering from anoxo-ischemic encephalopathy. cEEG evaluates the degree of cerebral injury and diagnoses seizure, often subtle or sub clinical at that age. However cEEG is technically challenging, the interpretation can appeared to be subjective and several classifications hardly understandable by clinicians have been proposed. The objective of this study was to test the reproducibility of a simplified scoring system of neonatal cEEG. **Methods:** Two child neurologists with different level of experience in EEG analyzed separately using a specific scoring system neonatal cEEGs selected in our EEG database. The score was based on EEG continuity and amplitude, on the presence or absence of physiological aspects, sharp waves, discharges, or seizures. Information regarding pregnancy and delivery and clinical status at birth were collected. A scoring value was established hour by hour and an average score was calculated every 12 hours interval during the 3 first days of life. A Kappa coefficient was used to assess agreement between observers. **Results:** The EEG recorded between 2008 and 2011 in 41 term babies with AIE were analyzed (mean duration of 20 hours of cEEG by patient) The scores ranged from 7 (normal) to 19 (very discontinuous tracing and seizures) and were well correlated to clinical examination at H12, H24 and H36. The kappa values were high 0.69 (0.47–0.90) at H12, moderate at H24, H36 and H72, and low at H96. **Conclusion:** Using a scoring sheet may ease the analysis of cEEG in neonates. Early recording, in the first 48 hours of life seems to be the more reliable.

P214 - 1831

Medical problems in adolescents with myelomeningocele

Tsolaki M-R. *The Queen Silvia Children's Hospital, Gothenburg, Sweden – mariarallou@yahoo.gr*

Aim: To describe the medical needs of adolescents with myelomeningocele (MMC) in a population born 1994–1997 and to

compare with two previous cohorts. **Background:** In Sweden the multidisciplinary care of children with MMC is organized within the habilitation organization, the tertiary care being supplied at regional centers. There is a lack of coordinated medical care for adults with MMC. A previous retrospective study investigated medical data on all adolescents with MMC born 1986–1989 and living in Sweden on July 1st 2004 (Cohort 1). A second Swedish cohort comprised all adolescents with MMC born 1990–1993 and living in Sweden on July 1st 2008 (Cohort 2). The present study describes the third Swedish cohort and compares it with the earlier ones. **Method:** In a retrospective study all adolescents with MMC or lipo MMC born in the years 1994 to 1997 and living in Sweden on July 1st 2012 were identified. A modified version of earlier inventories was used. **Results:** There is strong evidence for a decreasing trend in the prevalence of MMC in the three cohorts. The majority of the adolescents had hydrocephalus with a decreasing trend between the cohorts. About one third of the adolescents had undergone tethered cord release and about one third had scoliosis. The frequencies do not differ much between the cohorts. More than half of the adolescents had a severe motor impairment with a decreasing trend over the years. The majority used clean intermittent catheterization and more than half used incontinence pads. More than half of the adolescents used enemas for bowel emptying and about one third were using incontinence pads due to incomplete bowel control. **Conclusion:** Adolescents with MMC have several medical problems that may lead to serious, life threatening complications. Multidisciplinary, coordinated, life long follow up by specialists with knowledge on MMC is necessary.

P215 - 1820

Development and implementation of the German guideline for the diagnosis of fetal alcohol syndrome

Landgraf MN, Heinen F. *Department for Pediatric Neurology and Developmental Medicine, Dr. von Hauner Children's Hospital, Ludwig-Maximilians-University of Munich, Germany – mirjam.landgraf@med.uni-muenchen.de*

Background: Fetal alcohol syndrome (FAS) belongs to fetal alcohol spectrum disorders (FASD) and affects 0.02% to 0.8% of all annual births with a high number of undetected cases. FAS has severe lifelong consequences for the affected individual and his family. FAS also has significant implications for the social and health system. **Aim:** The aim of the German guideline is to provide objectively evaluated, evidence-based, clinically relevant and easily applicable diagnostic criteria for the full picture of FAS. **Methods:** A systematic literature review (2001 - 2011), as well as an analysis of international guidelines and a focused hand search were performed. A multidisciplinary guideline group (14 Professional Societies, patient support group "FASD Germany" and 15 additional experts) determined recommendations for the diagnosis of FAS based on the evidence-assessed literature. **Results:** The following criteria reached official consensus for the diagnosis of FAS: at least one deficit of growth, three defined facial characteristics and at least one functional or structural anomaly of the central nervous system. Confirmation of intrauterine alcohol exposure is not required for FAS diagnosis. **Conclusion:** The German guideline for the diagnosis of FAS is a first step towards unbiased evidence-based diagnosis of patients with fetal alcohol spectrum disorders. One mean of implementation is the pocket guide FAS that gives an overview of the diagnostic workup for everyday clinical work.

P216 - 1751

Long-term outcome of B19 maternal infection: arguments for careful developmental follow-up

Ortibus E, Naulaers G, Cossey V, De Catte L. *KULeuven, Faculty of Biomedical Sciences, Department of Development and Regeneration, Belgium – els.ortibus@uzleuven.be*

Objectives: Maternal parvovirus B19 infection is a potential hazard to the fetus and it results in a significant number of fetal deaths. Less is known about the longterm neurodevelopmental outcome of the survivors, although serious complications such as cortical malformations have been described. **Material and methods:** In the present study, 22 pregnancies complicated by B19 infection were carefully followed up: fetal and neonatal specimens were investigated by serological and/or virological assays and fetuses were clinically evaluated by ultrasound. Survivors were assessed with appropriate developmental measures for motor and cognitive development. **Results:** Of the 22 pregnancies, 8 ended in fetal (spontaneously or by termination of pregnancy) or neonatal death. Of the 14 survivors, 4 children were lost to follow up and 10 children (6 boys/4 girls) were followed until a mean age of 32 months (range 12 – 60 months). In these children, mean birthweight was 2680 g (range 2100 – 3460g) at a mean postmenstrual age of 38 weeks (range 37 – 40 weeks). In 4 of 8 survivors, fetal brain MRI was normal but in the other 4 it showed either cerebellar hypoplasia, asymmetric ventricles or periventricular hyperintensities. Five of the children were underweight and had small stature. Clinical neurological examination was normal in all. None of the children had epilepsy. However, cognitive evaluation was borderline in one and showed a moderate learning disability in another child. In the latter individual, motor assessment was borderline as well. In one other boy, an abnormal visuomotor examination was found. **Conclusions:** Children born following congenital parvovirus B19 infection, are prone to cerebral lesions and/or developmental delay. A routine follow up of these children, including neuroimaging and detailed neurodevelopmental assessment until school age is recommended.

P217 - 1694

Neonatal hiccups: to worry or not to worry?

Iqbal M, Prasad M, Mordekar S. *Sheffield Childrens Hospital, Sheffield, United Kingdom – drmehtabch@yahoo.com*

Objective: To present three cases who presented in neonatal life with hiccups who later were diagnosed with NKH. **Material:** Non Ketotic Hyperglycinemia (NKH) is a life threatening metabolic encephalopathy usually present in the neonatal period. Most infants appear normal at birth and remain asymptomatic for a brief period, seldom longer than 48 hours. They present with rapidly progressive neurological symptoms such as lethargy, poor feeding, seizures, high pitched cry and generalized hypotonia. Hiccups are frequently observed. Most patients lapse into coma and die within a few weeks. Survivors usually have severe psychomotor retardation, spasticity, microcephaly and uncontrolled seizures. **Case description:** We present three babies who presented in neonatal life with hiccups who later were diagnosed with NKH. Two babies presented on 2nd day of life with hypotonia, poor feeding and abnormal movements including jitteriness, hiccups and twitching. The third baby presented at 3 months of age with poor feeding, drowsiness and jerky movements. This was on a background of back arching episodes for which he was being treated with antireflux medications. All three cases needed extensive investigations before reaching the diagnosis including metabolic screen, LP, EEGs and CT/MRI. The first two babies needed intubation on their 2nd day of life because of apneas in whom later, the care was withdrawn after reaching the diagnosis of NKH because of poor prognosis. The third baby was discharged home on oral Dextromethorphan and Ketogenic

diet. **Discussion:** We discuss the importance of early recognition of symptoms and investigation needed to reach the diagnosis early as it helps in making decision to either carry on treatment or withdraw care because of poor prognosis. It also helps in genetic counselling and prenatal diagnosis can be offered at the subsequent pregnancies.

P218 - 1646

Frontonasal dysplasia and periventricular heterotopia: a very rare congenital malformation

Potoms M, Aerssens P, Termote B, Werckx W. *Hasselt, Belgium – marliespotoms@hotmail.com*

Case report: A female infant was born with facial dysmorphism with true ocular hypertelorism, broadening of the nasal root and absence of the septum of the nose. The left opening of the nose was not accessible. Further clinical examination was normal, there were no other visible malformations. Brain MRI revealed periventricular nodular heterotopia in the right parieto-occipital area. **Discussion:** FND is a developmental defect of the craniofacial region where mid-face does not develop normally. Most cases are sporadic and presently, it is not possible to assign a definitive genetic mode of inheritance to this condition. The proposed theory is that unknown factors arrest migration of olfactory epithelium into the nasal capsule during the third week of gestation. At birth presence of two or more of the following symptoms is considered positive for FND: a skin-covered gap in the bones of the forehead; hypertelorism; median cleft lip; median cleft nose; and/or any abnormal development of the center (median cleft) of the face. In most cases facial surgeries are required. These may include canthoplasty, orbitoplasty, surgical positioning of the eyebrows and rhinoplasty. Individuals diagnosed with frontonasal dysplasia usually are of average intelligence and can expect a normal life span. In literature there are 2 other cases of FND associated with periventricular nodular heterotopia. These patients have a bilateral periventricular nodular heterotopia, regional cortical dysplasia, mild mental retardation and frontonasal malformation. Genetic research into FND with and without brain anomalies is ongoing. **Conclusion:** FND is a very rare malformation. Further research into the genetic origin of this disorder is needed. Multistage craniofacial surgery is justified, and is generally performed from the age of 6–8 years. It can give satisfying cosmetic and functional results.

P219 - 1640

The math model for assessment of probability of successful treatment of preterm

Nurmagambetova B, Chuvakova T, Tortaeva G, Kamieva R, Dyisenbieva L, Temirbaeva G, Jaxybayeva A. *JSC “National Research Center for Maternal and Child Health”, Astana, Kazakhstan – altynshash@gmail.com*

Purpose: development of a mathematical model which can allow estimating the probability of successful outcomes of neurological development of preterm. **Methods:** A study was made on the basis on data from 670 medical records of newborns, which were hospitalized after born in NICU and neonatology units. There were taken 64 sings, including anamnesis data of pregnancy, physical data at birth and during neonatal period. Also were taken into account data of clinical, biochemical, microbiological and instrumental assessments. Evaluation of the affected system conducted by the criteria proposed by Hankins G.D.V. et al., 2002 and Shah P. et al., 2004. At first stage were identified 33 variable signs. The next stage of statistical analysis was the method of binary logistic regression. As a final result, the following variables have been suggested as possible predictors: days on mechanical ventilation, FiO₂ more 40% (days), pH of blood, and blood urea

on the 1st day ($\chi^2=56$, 259, df=4, $p=0.000$). R2 Nagelkerke = 0.758. **Conclusion:** Percentage of correctly predicted outcome of treatment was 88.2%. The proposed model allows determining the outcome of a successful treatment in 90% cases, which influences the further neurological development.

P220 - 1639

Predicting features for normal development in preterm newborn

Nurmagambetova B, Bekkuzhinova G, Aralbaeva M, Dzhamanbekova D, Tortayeva G, Sagyndykova E, Jaxybayeva A. JSC "National Research Center for Maternal and Child Health", Astana, Kazakhstan – altynshash@gmail.com

Purpose: Identify predictors affecting the outcome forecasting neuropsychological development of preterm infants. **Methods:** We made an analysis of 338 preterm infants, who was treated in NICU, neonatology and neurology wards from January 2011 up to March 2013. The main information regarding baby's condition was taken from medical records, neurological assessment including anthropometric status, particularities of neonatal care. Neurophysiological assessment of the degree of maturity of the nervous system of preterm infants was carried by the following methods: long-term EEG monitoring (telemetry), general movements' analysis (Prechtl method), ophthalmological and audio logical screening. The study was conducted in three steps. **Conclusion:** During the study were identified prognostically important signs of further neurological development of premature infants. Also were developed the system for integrated assessment of preterm newborn with a goal for determination of time for corrective action.

P221 - 1594

Caffeic acid phenethyl ester blocks cell death and apoptosis in the developing brain of rat after pentylenetetrazole induced status epilepticus

Yiş U, Topçu Y, Özbal S, Tuğyan K, Bayram E, Karaoğlu P, Yılmaz O, Hız S. Dokuz Eylül University, School of Medicine, Department of Pediatrics, Division of Pediatric Neurology, Izmir, Turkey – ulyis@yahoo.com

Aim: Status epilepticus triggers a mixture of apoptotic and necrotic cell death within the developing brain which results in the development of epilepsy and cognitive deficits. Caffeic acid phenethyl ester is an active component of propolis obtained from honeybee and has neuroprotective properties. The aim of this study is to investigate the effects of caffeic acid phenethyl ester on hippocampus and prefrontal cortex of rat after pentylenetetrazole induced status epilepticus. **Material and methods:** Twenty-one dam reared Wistar male rats, 21-day-old were divided into three groups: control group, pentylenetetrazole induced status epilepticus and pentylenetetrazole induced status epilepticus and caffeic acid phenethyl ester treated group. Caffeic acid phenethyl ester treated group received caffeic acid phenethyl ester 30 mg/kg intraperitoneally 40 minutes after pentylenetetrazole injection for 5 days. Rats were sacrificed and brain tissues were collected at 5th day of experiment. **Results:** Neuronal cell death and apoptosis were evaluated. Histopathological examination showed that caffeic acid phenethyl ester significantly decreased neuronal cell death in CA1, CA3 and dentate gyrus regions of hippocampus and prefrontal cortex. It also diminished apoptosis in the hippocampus and prefrontal cortex. **Conclusion:** This experimental study suggests that caffeic acid phenethyl ester administration may be neuroprotective in status epilepticus in the developing brain.

P222 - 1588

Early visual stimulation for at risk babies – a step towards better visual development and visual perception

Depourcq M, Bonamie E, Keppens K. De Kade, Spermalie, Bruges, Belgium – katrien.keppens@mpi-spermalie.be

Early sensory input is essential in setting up the basic neural architecture that will eventually mediate sensitivity to both primary and higher visual functions. **Objectives:** Sensitization of medical and observation teams for early signals of delayed visual development in at risk babies. Timely reference to specialized early intervention teams within the sensitive period for development of selective (visual) attention, being 3–4 months. **Material and methods:** Presentation of an overview of "red flag" diagnoses with a list of distress signals for delayed visual development and the theory on sensitive periods in early visual development. **Results:** Normal development of (visual) attention is sensitive to experience early in life. Delayed development or absence of selective (visual) attention can lead to visual dysfunction ranging from mild to severe problems. The attention system can be stimulated or replaced by offering a specific visual stimulation program in severe cases or by simple adaptation of the environment and practical handling tips in mild cases. Specific early visual stimulation could eventually prevent mild visual dysfunctions in children with Delayed Visual Maturation (DVM) or decrease the level of visual dysfunction in children with Cerebral Visual Impairment (CVI). Subsequently sight-based motor, social and cognitive development also benefit from this approach. **Conclusions:** The delay between onset of symptoms and reference to a specialized team is often too long or nonexistent. We are convinced that increased awareness and early reference on visual dysfunction and/or delayed visual maturation can offer better support and service to the babies and their parents.

P223 - 1587

Motor development and (early) intervention in blind and severely visually impaired babies, toddlers and children

Dewerchin L, Keppens K. De Kade, Spermalie, Bruges, Belgium – katrien.keppens@mpi-spermalie.be

Visual impairment interferes with gross and fine motor development in children. This situation creates a paradox: on the one hand, the motor development is at risk, delayed and follows another sequence. On the other hand, a blind individual is highly in need of optimal motion possibilities in order to discover his/her world through moving, touching etc., and to achieve a maximum of self-reliance and independence allowing participation to daily social life. **Objectives:** Support and stimulation of blind children is typically provided by an early intervention team (Thuisbegeleiding Accent BC Spermalie). Providing targeted advice to these home care assistants is based on regular assessment of the child by a multidisciplinary team, coordinated by a paediatric neurologist. A physiotherapist is part of this team to evaluate the motor development. **Material and methods:** To map the motion possibilities, progress, and problems of the blind child, the physiotherapist relies on a few specific tests embedded in a neuro-developmental approach (Bobath) and on personal experience. We focus especially on self-initiated mobility, posture, locomotion and constructive play. **Results:** Based on literature and experience, we provide an overview of the most important findings concerning the achievement of the gross motor milestones for blind babies and toddlers, and concerning the general dynamic coordination of older blind children: gross motor milestones appear to be only slightly delayed during the first 6 months after birth. This delay becomes clearly more pronounced thereafter. We will list specific motor difficulties detected, for which special attention and stimulation is required by the caretaker. **Conclusion:** Stimulation and close monitoring of motor

development of blind and severely visually impaired children is essential. A specific yet varied motor education program for the individual child, initiated as early as possible, is necessary in order to maximize its motion possibilities.

P224 - 1560

Amino acids of spinal liquid at preterm with hypoxic-ischemic encephalopathy

Chuvakova T, Jaxybayeva A. National Research Center for Mother and Child Health, Astana, Kazakhstan – altynshash@gmail.com

Purpose: To study amino acids composition of spinal liquid at preterm newborns with hypoxic-ischemic encephalopathy and to define possibility of their use as indicators of brain damage. The amino acids structure of spinal liquid is studied at 90 prematurely born children with HIE. Investigation was conducted in the 1st day after the birth. It is shown that the greatest changes came to light at newborns with severe HIE and were characterized by substantial increase of level of glutamate, alanin, serine, glycine, proline whereas the content of asparaginate, histidine, glutamine, valine and phenilalanine didn't change in comparison with indicators at light degree of HIE. The majority of the specified amino acids is connected with a crebs cycle and plays an exclusive role in ensuring intensity of exchange processes in a brain and regulation of a brain blood circulation. The revealed imbalances create favorable conditions for accumulation of protein metabolites and destroy of brain metabolism. Therefore, changes of composition of amino acids in spinal liquor can be used as indicators of severity of HIE.

P225 - 1527

Significant cytokines in neonatal seizures induced by hypoxic ischemic encephalopathy; IL-1beta, IL-1Ra, IL-8 and IL-10

Youn YA, Kim SJ, Sung IK, Chung SY, Kim YH, Lee IG. Seoul, Korea – iglee@catholic.ac.kr

Objectives: We investigated changes in the levels of significant cytokines in relation to neonatal seizures induced by hypoxic ischemic encephalopathy (HIE), a pattern of cytokine concentrations serially and the severity of brain insult. **Material and method:** The HIE-induced seizure group consisted of 13 patients, and another 15 normal newborns were enrolled as a control group. All of the initial samples were obtained within the first 24 h of admission, and the second samples were obtained between 48 and 72 h in both groups. Only the third samples were taken in the seizure group on the 5th day. **Results:** During neonatal seizures, the levels of most cytokines increased within 24 h, and, in particular, the levels of interleukin (IL)-8 significantly increased ($P < 0.05$). After 48–72 h of seizure onset, the levels of most cytokines decreased, especially, IL-1Ra; however, IL-8 and IL-10 remained increased ($P < 0.05$). During the prognosis, one patient who was diagnosed with quadriplegic cerebral palsy at 6 months of age presented extreme elevation of IL-1beta, IL-1Ra, IL-6, IL-8, IL-10 and tumor necrosis factor-alpha in the initial sample, reflecting the severity of brain damage. **Conclusions:** A significant increase in IL-8 within 24 h and 48 to 72 h in seizure patients suggests that IL-8 may serve as a biomarker for earlier detection of brain damage in neonatal seizure.

P226 - 1526

New diagnostic technology in the prediction and evaluation of effective treatment of newborns with hypoxic brain lesions

Burov B. Tashkent, Uzbekistan – borei1970@rambler.ru

Background and aims: In connection with high rate of perinatal brain lesions in newborns and their consequences to the

present there are no absolute markers posthypoxic brain lesions. This has been our aim to develop new methods for predicting, diagnosing, correcting and evaluating the effectiveness of treatment of the effects of neurological disorders. **Methods:** A comprehensive examination 169 newborn infants with conducting neurological examination, Doppler ultrasound of the brain, determining the number of neuropeptide S-100 protein and factor neyrotroficheskogo brain BDNF levels. Established that the development and transformation of neurological disorders during postnatal neuroontogenesis occurs in correlation with a change BDNF production and protein S-100, disorders autonomic regulation and motor development Found that the rate of brain-derived neurotrophic factor in serum in children 3 months of age has prognostic significance for the further development of the engine, based on which a new method for predicting violations of motor development. **Results:** The study shows that the inclusion of neuropeptide preparation in complex rehabilitation therapy helps to reduce the production of protein S-100, has a positive effect on the autonomic regulation, cerebral hemodynamics, and optimizes the correction of neurological disorders in children. Such a way a result of the research has developed a system of activities for children in the first year of life with the consequences of perinatal hypoxic brain damage, which includes new technology forecasting, diagnosis, correction and evaluation of the treatment of neurological disorders.

P227 - 1524

Diagnostics and treatment of congenital dislocation of a hip at children of early age

Karabekova R. JSC Medical University Astana, Kazakhstan – rozakarabekova@gmail.com

Modern data on congenital dislocation of a hip shows the problem of early diagnostics and treatment of this disease continues to remain one of actual questions in orthoneurology practice. Under our supervision there were 901 children. We developed schemes of treatment, rehabilitation and medical examination: 1. Unripe coxofemoral joint – Frey's pillow, therapeutic exercise, massage during 2 months. Predislocation – Pavlik's stirrups within 2 months. Therapeutic exercise, massage, physiotreatment, ultrasonography control through 2, 6 and 12 months. 3. Incomplete dislocation – Pavlik's stirrups about 3 months, therapeutic exercise, massage, physiotreatment. 4. Dislocation - should be carried out step by step. At a treatment inefficiency Pavlik's stirrups or pathology identification at children 6 months are more senior conservative functional treatment by a clinic technique is carried out. Tactics is defined depending on the size of an index of stability. At an unstable coxofemoral joint, we expose indications to open reposition of dislocation. In cases when "a stability index" is more than 100 we impose adhesive extension within 2–3 weeks, after the bandage from an adhesive tape caste is applied under anesthetic. The immobilization in a bandage is carried out within 3–4 months, in dependence and on expressiveness of dysplastic process, with the subsequent transfer to the tire of the author. The tire was used by us for 20 patients for conservative treatment of congenital dislocation of a hip, for 5 children with an aseptic necrosis of a head of a hip, and for 10 patients after reconstructive operations on coxofemoral joints. **Conclusion:** Improvement of quality of treatment – to use the tire of the author which provides damped effect of a spring between two sliding cores, because the prevention of an aseptic necrosis of a head of a hip at the expense of improvement of quality of functionality of the device is carried out.

Neurogenetic disorders

P228 - 2031

Preliminary results of the study of Rett syndrome phenotype in 27 patients from a Romanian pediatric neurology clinic

Angheliescu C, Barca D, Burloiu C, Butoianu N, Darja M, Gherghiceanu R, Iliescu C, Gos M, Hoffman-Zacharska D, Iancu D, Minciu I, Motoescu C, Sandu C, Tarta-Arsene O, Todorova A, Craiu D. *Pediatric Neurology Department, Al. Obregia Hospital, Bucharest, Romania – dcraiu@yahoo.com*

Background: Rett Syndrome (RTT) is an X-linked neurodevelopmental disorder often caused by MECP2 mutations, characterized by acquired microcephaly, loss of purposeful hand skills and spoken language, gait abnormalities and stereotypic hand movements. Epilepsy affects 50%-90% patients. **Objectives:** Preliminary results of RTT study in Pediatric Neurology Clinic of "Al. Obregia Hospital", Bucharest, between 2010 and 2012 are presented. **Material and methods:** A Rett database was created in 2009. In 2010 the file template was improved according to the International Rett Registry. An evaluation protocol including clinical and neurologic examination, imaging, EEG, biochemical, genetic evaluation was designed, for homogenous approach of the Rett phenotype patients. Genetic testing was performed in Genica laboratory (Bulgaria) and Warsaw (Poland) within the Euroepinomics Consortium. **Results:** 27 female patients aged 8 month to 14 years at clinical RTT diagnosis were identified. 12 patients had a mutation in MECP2 gene; 11 are still being analysed. 15 patients (55%) had epilepsy. In 80% of patients, epilepsy started before age 5 years. Only 4 of them were seizure-free. 2 patients with seizures' onset before age 12 months and early psychomotor regression developed highly drug-resistant epilepsy. 73% of patients were receiving polytherapy. Two patients with p.R168X mutation were highly AEDs resistant. In other 2 patients with p.R255X (associated with epilepsy in the literature), only one had early onset resistant epilepsy and severe clinical regression; the other kept prehension and gait, mild mental retardation and no epilepsy. **Conclusions:** No significant clinical-genetic correlations may be realised, due to small number of identical mutations in our small group. Young age at epilepsy onset was a bad prognostic factor for response to AEDs. Phenotypic and genotypic variability are frequent in RTT. More factors may be involved in RTT clinical picture and outcome. This database created premises for future research in RTT in our clinic.

P229 - 2000

Different clinical progress and genetic mutations of Lafora disease

Poyrazoğlu HG, Per H, Karaca E, Canpolat M, Gumus H, Ozkınay F, Kumandas S. *Erciyes Univ. Child Neurology Department, Kayseri, Turkey – hgpooyrazoglu@yahoo.com*

Introduction: Lafora disease (LD) is a rare, autosomal recessive form of progressive myoclonic epilepsy characterized by a severe course. It is due to either the EPM2A or EPM2B gene mutations. The diagnosis of LD in our patient was based on the typical clinical picture and confirmed by not only showing polyglucosan inclusions in skin biopsy but also evaluating the molecular genetic findings. We describe two different genetic mutations and a fatal clinical course of LD with homozygote NHLRC1 mutation and a novel homozygote EPM2A mutation. **Cases 1 & 2:** Two siblings (16 year-old girl and 14 year old boy) followed up with juvenile myoclonic epilepsy were admitted to our department with intractable seizures and cognitive dysfunction. On neurological examinations; she was conscious and cooperated. Cognitive impairment, mild ataxia and dysarthria were determined. He was revealed no pathological findings except for mild mental retar-

dation. Their routine laboratory tests were normal. Her cranial magnetic resonance imaging (MRI) revealed mild cerebral and cerebellar atrophy and his MRI was normal. Their EEG showed multifocal localized, spike-polyspike wave discharges and burst of non-rhythmic slow activity. Lafora bodies were observed in their axillary skin biopsy. A novel mutation of EPM2A gene (homozygous p.Y112X(c.336C>A)) was identified. **Case 3:** 14 year-old girl was admitted to our clinic with therapy-refractory seizures with visual aura (sometimes) followed by generalized tonic-clonic seizures. Initial neurological examination was normal. After 6 months, cognitive impairment, ataxia in the trunk and limbs were added. Routine laboratory tests were normal. Her cranial MRI was also normal. EEG showed spike-multispike wave discharge. Lafora bodies were observed in the axillary skin biopsy. A mutation of NHLRC1 gene (homozygous c.199 G>T(p.E67X)) was identified. Clinical course developed rapidly progressive. She became bedridden and died after 18 months of her admission. **Discussion:** Generally, mutations in the NHLRC1 gene were associated with a more benign clinical course compared with EPM2A mutations. Here, we describe a rapidly progressive form of LD with NHLRC1 mutation.

P230 - 1840

Griscelli syndrome type 2, an exceptional onset

Olabarrieta N, Martinez MJ, Astigarraga I. *Hospital Universitario de Cruces (Barakaldo), Spain – naiara.olabarrietahoyos@osakidetza.net*

Introduction: Griscelli syndrome type 2 is a rare autosomal recessive disorder of partial albinism and immunodeficiency. This genetic disorder of lymphocyte cytotoxicity predisposes patients to haemophagocytic lymphohistiocytosis (HLH). Central nervous system involvement is frequent in HLH and neurologic symptoms may complicate and even dominate the clinical picture. We report a new case showing predominant neurological involvement. **Case report:** A 5-years-old girl, the only child of nonconsanguineous parents, with history of recurrent acute otitis media, perianal herpes and episode of gait disturbance, assumed as labyrinthitis. She was admitted because of vomiting, decreased level of consciousness and seizure, without fever. Neurological examination was normal. Cerebrospinal fluid test showed pleocytosis. EEG was normal. The brain MRI revealed diffuse changes of supra and infratentorial white matter in frontal, temporal and parietal bilateral lobes, cerebellum, thalamus and brainstem, with marked perilesional edema. Acute disseminating encephalomyelitis was suspected, and high doses of methylprednisolone were administered with good response. Three months later, she was readmitted because of vomiting and headache. Her examination persisted normal. MRI showed progression with a new giant pseudotumoral lesion in left frontal white matter that crossed through the corpus callosum. Oligoclonal IgG bands were not present. Laboratory evaluations were normal. Due to the neuroimaging findings with minimal involvement of the neurological examination, it is suspected a cerebral HLH, without systemic involvement. On examination, she was noted to have silvery grey hair. In her lactant period photographs she had white hair, supports partial albinism. Electron microscopy of hair shaft and genetic studies established the diagnosis of Griscelli disease type 2 with RAB27A mutations. **Conclusions:** We report a Griscelli syndrome type 2 case with an exceptional onset: severe neuroimaging findings without clinical involvement, and HLH compatible, without usual criteria of laboratory parameters. To sum up we presume the clinical spectrum of this pathology is enlarged.

P231 - 1834**P610T mutation in Nav 1.7 sodium channel in a family with primary erythermalgia**

Avez-Couturier J, Dalmas S, Deprez A, Vallée L. *Child Pain Consultation, CHRU de Lille, Paediatric Neurology, CHRU de Lille, Lille, France – jcouturieravez@gmail.com*

Objectives: Primary erythermalgia (PE) is a painful genetic disorder of autosomal dominant transmission, characterized by attacks of symmetrical pain, elevated skin temperature and redness in the extremities. PE is associated with mutations in SCN9A gene coding for voltage-gated sodium-channel Nav1.7, expressed in dorsal root ganglion (DRG) and sympathetic ganglion neurons (Drenth, 2007). Several SCN9A mutations have been described. P610T mutation was not considered as a pathogenic mutation or not at a highly penetrant way (Samuels, 2008). We report a family (father and daughter) sharing the same clinical characteristics with P610T mutation in SCN9A. **Material and methods:** The proband is a 3-year-old girl. She had, since her first year, typical attacks of erythermalgia. She had received several drugs (carbamazepine, gabapentine, nicardipine, propranolol) with no efficacy. Her father also had typical symptoms of PE but does not use any drugs. Patients were screened for SCN9A gene mutations (fluorescent sequencing analysis). **Results:** Heterozygous sequence variation at nucleotide C1828A in exon 12 (P610T) was detected in the proband and her father. Her mother was not carrying the mutation. We proposed to treat her with mexiletin. With 12 mg/kg/day mexiletin total improvement was obtained at 6 months and maintained at 1 year. Her father refused to take any drug. **Conclusions:** P610T mutation in SCN9A gene should be considered as a pathogenic mutation for primary erythermalgia. Based on our experience this mutation could be perfectly mexiletin sensitive.

P232 - 1823**Milder phenotype of pontocerebellar hypoplasia type 1 in an Indian girl**

Jain P, Sharma S, Kumar A, Aneja S. *Lady Hardinge Medical College and Associated Kalawati Saran Children's Hospital, New Delhi, India – puneet_mpa@yahoo.com*

Objectives: The rare association of Pontocerebellar hypoplasia with anterior horn cell involvement has been classified as Pontocerebellar hypoplasia type 1. Its classic phenotype is usually severe. We describe a young Indian girl who presented with a milder phenotype. **Methods:** The clinical details of a girl diagnosed with Pontocerebellar hypoplasia type 1 were reviewed and reported. **Results:** A 2-years old girl presented with delayed milestones and floppiness. She had no loss of previously acquired milestones. There was no history of convulsions, difficulty in feeding or breathing, or weak cry. On examination, there were no neurocutaneous markers, facial dysmorphism, spinal deformity or contractures. She had no bulbar dysfunction but had horizontal nystagmus and tongue fasciculations. There was global peripheral-type hypotonia. Her initial investigations revealed normal total creatine kinase, isoelectric focusing of transferrins and nerve conduction studies. The electromyography was neurogenic. The deletion of exon 7 of SMN1 (Survival Motor Neuron) gene was absent. The muscle biopsy was suggestive of spinal muscular atrophy. Her Magnetic Resonance Imaging of the brain showed cerebellar atrophy. A diagnosis of Pontocerebellar hypoplasia type 1 was made in view of mixed hypotonia, cerebellar atrophy on neuroimaging, and clinical, electrophysiological and pathological evidence of anterior horn cell involvement. **Conclusions:** The pontocerebellar hypoplasias type 1 may have wider variability in clinical and radiological features. There may be a genetic heterogeneity as well. We described here a young girl with relatively milder clinical phenotype with cerebellar atrophy

with absent pontine involvement, further adding to the clinical phenotype.

P233 - 1782**Mild phenotype and high-functioning autism in a boy with MECP2 duplication syndrome**

Zafeiriou DI, Ververi A, Vargiami E, Kalyva E, Kyriazi M, Gioula G, Gerou S, Al-Mutawa H, Kambouris M. *1st Department of Pediatrics, Aristotle University of Thessaloniki, Greece – athenaververis@yahoo.com*

Genetic syndromes, defined mutations and de novo copy number variations (CNVs) account for almost 20% of cases with autism spectrum disorders (ASD), whereas CNVs alone offer a diagnostic yield of 10% in non-syndromic isolated patients with autism. Duplication of Xq28, causing MECP2 duplication syndrome, is a recognized cause of autism and neurodevelopmental disorders, spanning 0.3 to 4 Mb in size and accounting for ~1.5% of X-linked mental retardation. Its clinical features include infantile hypotonia, severe mental retardation, ASD, poor speech development, seizures, progressive spasticity, recurrent respiratory infections, gastrointestinal complications and seizures. Autism is a defining feature of the syndrome, presenting in almost all male and the majority of female patients. Herein, a 5-year-old boy with high-functioning autism and two duplications in Xq28 and 10q11.22, spanning 1.3 and 1.5 Mb, respectively, is described. The index patient exhibited an unexpectedly mild phenotype with complete absence of seizures, recurrent infections or gastrointestinal disorders. His neurological exam, electroencephalogram and brain MRI were normal, whereas his verbal and practical skills, according to the Wechsler Preschool and Primary Scale of Intelligence, were average (raw scores provided, due to absence of a standardized Greek version). The clinical diagnosis of ASD was confirmed by the Autism Diagnostic Observation Schedule with an overall score of 8 and more severe difficulties in the area of social affect. This markedly mild phenotype may be associated with the absence of seizures and/or the presence of other compensatory genetic/epigenetic factors. Moreover, it must be underlined that the index patient exhibited high-functioning autism, which is rarely associated with an underlying genetic diagnosis.

P234 - 2113**A case of Ehlers-Danlos syndrome type VIA with novel PLOD1 gene mutation**

Tosun A, Kurtgoz S, Dursun S, Keskin E. *Adnan Menderes Medical School, Department of Pediatric Neurology, Aydin, Turkey – aysetosun2000@yahoo.com*

Objective: Ehlers-Danlos syndrome type VIA (EDSVIA), the kyphoscoliosis type is an autosomal recessive connective tissue disorder, clinically characterized by soft extensible skin, laxity of joints, severe muscle hypotonia at birth and kyphoscoliosis. **Material and method:** In this report was presented a 3 year-old Turkish girl diagnosed as EDSVIA whom parents were cross-cousin. She was born at term with breech delivery after a normal pregnancy and neonatal hypotonia and congenital kyphosis were observed. On postnatal second day, intracranial hemorrhage was detected on cranial MRI which was performed after she had convulsion. Strabismus, umbilical hernia, kyphos, laxity of joints, bilateral hip dislocation and muscular hypotonia were detected with insufficient head control when she was 18 months age. Control Cranial MRI revealed periventricular leukomalacia. When she was 3 years old, she had motor and mild mental retardation, she could sit without support but couldn't walk. Metabolic investigations were normal. Analysis of urinary cross-links showed an increase in the lysyl-pyridinoline to hydroxylysyl-pyridinoline ratio (LP/HP 7.42, control group LP/HP 0.193±0.03). Molecular

analysis of PLOD1 gene revealed that the patient had the novel homozygous p.622fsX624 (c.1888insCG) mutation on 17th exon which caused the EDSVIA. **Conclusion:** As a result, EDS type VIA should be considered in patients who have neonatal hypotonia, progressive kyphoscoliosis, eye abnormalities, unexplained joint laxities and neonatal vascular events. Besides, this paper reports a novel mutation on PLOD1 gene in patient with EDSVIA.

P235 - 2075

Prenatal onset of vanishing white matter caused by a novel EIF2B4 mutation

de Bruyn G, Régál L, Wouters L, Jansen K, van der Knaap MS, Lagae L, Buyse G. *UZ Leuven, Belgium – gwendolyn.debruyne@uzleuven.be*

We describe a prematurely born girl (GA 33 weeks) with unexplained IUGR, transient neonatal respiratory adaptation problems, transient icterus and bifrontal subependymal cysts on cranial ultrasound. She presented with epileptic attacks at the age of 3 weeks. Clinical examination showed an encephalopathic infant with a large fontanel, axial hypotonia and peripheral hypertonia with hyperreflexia and clonus. She developed refractory left temporal lobe complex partial seizures. Interictal EEG showed bitemporal spikes, no burst suppression. Bilateral hearing loss was detected. There was a progressive neutropenia. Magnetic resonance imaging revealed diffuse and symmetric involvement of the cerebral white matter (hypomyelination) with possible cystic degeneration and subependymal pseudocysts. The gyral pattern was immature for age. Based on the metabolic results and the MRI findings the differential diagnosis was narrowed down to congenital CMV infection or Vanishing White Matter disease (VWM). CSF findings (elevated glycine and protein level) and serial brain MRI further favored the VWM diagnosis. Genetic testing showed that the patient is homozygous for a mutation in EIF2B4 (c.978G>C, p.Lys326>Asn). Both parents are heterozygous for this mutation. The child deceased at the age of 4 months. In conclusion, VWM disease has a wide clinical spectrum and different ages of onset. Our patient showed a prenatal onset and a severe course with early onset refractory epileptic encephalopathy and rapidly fatal outcome.

P236 - 1972

Angelman syndrome – an update of our clinical experience

Barca D, Arghir A, Papuc SM, Tutulan-Cunita A, Iliescu C, Tarta-Arsene O, Minciu I, Craiu D, Duca D, Budisteanu M. *Pediatric Neurology Department, Alexandru Obregia Hospital, Bucharest, Romania – diana_barca@yahoo.com*

Purpose: Angelman syndrome (AS) is a complex neurodevelopmental disorder caused by various genetic mechanisms, involving the chromosome 15q11-q13, characterized by severe intellectual disability, epilepsy, speech impairment, movement disorder with ataxia and jerky movements, abnormal behavior, with happy disposition. In this paper we present our experience regarding the management of children with AS. **Material and methods:** The study included 16 children (6 boys and 10 girls) with AS, all with interstitial deletion of 15q11-13, aged between 6 months and 12 years, admitted in Pediatric Neurology Department of Alexandru Obregia Clinical Hospital, in the last 5 years (2008–2013). The clinical phenotype, epilepsy history (type of seizures, the EEG pattern, response to antiepileptic drugs) and the psychomotor development of all the patients were noted and analyzed. **Results:** All patients presented the typical clinical picture. 14 of 16 had epilepsy. The most frequent type of seizures were focal, but also atonic and atypical absences. The EEG proved to be very useful in the diagnosis of AS, showing characteristic pattern, similar in all cases with epilepsy, despite different

types of seizures. The epilepsy was controlled in most patients, only one presenting pharmacoresistance. As antiepileptic drugs, valproate was the first option, in monotherapy or in association with clonazepam, lamotrigine or levetiracetam. Corticotherapy was used in 4 cases. All children were included in individualized rehabilitation programs – physical and also psychotherapy, communication development through Picture Exchanging System (PECS). **Conclusions:** The early recognition of AS allowed the optimal antiepileptic therapy and also the initiation of physical therapy and cognitive stimulation, important for outcome improvement and for avoiding complications.

P237 - 1930

EAST syndrome (Epilepsia Ataxia Sensorineural Deafness Tubulopathy) caused by mutation in KCNJ10: an underdiagnosed illness?

Dorison N, Kleta R, Freudenthal B, Bockenhauer D, Burglen L, Billette de Villemeur T. *Paris, France – nathalie.dorison@trs.aphp.fr*

KCNJ10/Kir4.1 is an inwardly-rectifying K⁺ channel expressed in kidney distal convoluted tubule, cochlear stria vascularis and brain glial cells. KCNJ10 mutations cause an autosomal recessive disorder characterized by epilepsy, ataxia, sensorineural deafness and renal salt-losing tubulopathy similar to Gitelman syndrome (EAST syndrome). Very few patients were analysed; they invariably showed epilepsy from infancy, debilitating ataxia from an early age with difficulties in walking, sensorineural deafness and hypokalemic metabolic alkalosis with variable hypomagnesemia. Deafness and tubulopathy could occur after infancy. We report the first French patient with EAST syndrome. He is the second male child of consanguineous unaffected Algerian parents, born after an uneventful pregnancy and with perfect initial psychomotor development. The first seizure occurred at 4 months (tonicoclonic generalised); past 6 years old, he showed myoclonia, pharmacological resistant partial and generalised seizures. Ataxia became evident at 30 months, pyramidal signs appeared at 5 years old. At the age of 6, he lost his reflexes and myelinic neuropathy was objective. He had cognitive regression, lost language, developed mental retardation and severe autistic behavior. Progressive sensorineural deafness occurred after the age of 3. At 3 years old, he also had a hypomagnesemia and hypokaliemia, secondary to tubulopathy, needed substitution. A mitochondrial defect was suspected but not confirmed after muscular biopsy. A KCNJ10 homozygous missense mutation p. R65C (c.193C >T) was finally identified in our patient; both parents were heterozygous carriers (Pr Kleta, Londres). Prenatal diagnosis was performed for a further pregnancy. EAST syndrome should be considered in any patient with a renal Gitelman-like phenotype with additional progressive neurological signs and symptoms like ataxia, epilepsy or sensorineural deafness.

P238 - 1858

New mutations detected in primer microcephaly genes by whole-exome sequencing

Per H, Okay Caglayan A, Gumus H, Bilguvar K, Canpolat M, Kumandas S, Gunel M. *Department of Neurosurgery, Program on Neurogenetics, Yale University School of Medicine, New Haven, USA – huseyinper@yahoo.com*

Objectives: Microcephaly is the clinical finding of a decreased occipitofrontal head circumference (OFC) of less than -2 SD (ethnic, age and sex matched controls) and it could be genetic with called as true microcephaly, microcephaly vera or primary microcephaly. Thus far, studies have identified eight genes (chronologically listed and identified according to order of discovery, i.e., MCPH1-MCPH8) for primary microcephaly. **Material and methods:** We selected 4 consanguineous patients with mi-

crocephaly from our neurogenetics cohort and performed whole exome sequencing. **Results:** We identified novel mutations in four previously described microcephaly genes including WDR62, CDK5RAP2, ASPM, NDE1. **Conclusions:** Genetic heterogeneity is described in microcephaly, and the microcephaly proteins take varied pathways such as centrosome-related pathways or DNA repair. We revealed novel probably population specific mutations in known microcephaly genes as described above using whole exome sequencing.

P239 - 1816

Safety of everolimus by age category for subependymal giant cell astrocytomas (SEGAs) associated with tuberous sclerosis complex (TSC): results from the EXIST-1 trial

Jozwiak S, Brechenmacher T, Segal S, Franz DN. *The Children's Memorial Health Institute of Warsaw, Poland – sergiusz.jozwiak@gmail.com*

Objective: To present a 90-day safety update by age category for patients who participated in the EXIST-1 trial (NCT00789828). EXIST-1 demonstrated that everolimus is superior to placebo for reducing SEGA volume ($P < 0.0001$; cut-off 02 March 2011) with an adverse event (AE) profile consistent with previous reports in TSC. **Material and methods:** Patients (any age) with ≥ 1 SEGA lesion (≥ 1 cm in longest diameter) were randomized (2:1) to 4.5 mg/m²/day everolimus (target blood trough 5–15 ng/mL) or placebo. AEs were graded according to Common Terminology Criteria for Adverse Events v3.0. We report safety data for everolimus patients aged < 3 (n=13), ≥ 3 to 18 (n=55), and ≥ 18 years (n=10) and placebo patients aged < 3 (n=7), ≥ 3 to 18 (n=26), and ≥ 18 years (n=6). **Results:** As of 18 July 2011 (90-day update), median treatment duration was 52 weeks for everolimus and 47 weeks for placebo. For patients < 3 , ≥ 3 –18 and ≥ 18 years, the incidence of serious AEs was 54%, 18%, and 20% for everolimus and 29%, 12%, and 0% for placebo; incidence of drug-related grade 3–4 AEs was 46%, 13%, and 10% for everolimus and 14%, 8%, and 0% for placebo. Infections/infestations occurred in 100%, 71%, and 70% of everolimus patients and 100%, 69%, and 33% of placebo patients aged < 3 , ≥ 3 –18, and ≥ 18 years. Stomatitis (< 3 and ≥ 18 years) and mouth ulceration (≥ 3 –18 years) were the most common AEs for everolimus. For everolimus vs placebo, the incidence of stomatitis was 69% vs 43% (< 3 years) and 40% vs 17% (≥ 18 years) and mouth ulceration was 44% vs 8% (≥ 3 –18 years). **Conclusions:** The safety profile of everolimus is comparable among age categories with the possible exception of infections/infestations and stomatitis in younger patients, which may be an inherent underlying characteristic of the younger age group. Small sample sizes may have limited the results.

P240 - 1817

Safety of long-term everolimus treatment in toddlers with tuberous sclerosis complex (TSC)-associated subependymal giant cell astrocytomas (SEGAs)

Jozwiak S, Kotulska K, Chmielewski D, Borkowska J, Łojaszczyk B, Kuczyński D, Kmiec T, Berkowitz N, Dunin-Wasowicz D. *The Children's Memorial Health Institute of Warsaw, Poland – sergiusz.jozwiak@gmail.com*

Objectives: TSC is a multisystem autosomal dominant disorder that manifests with growth of benign tumors in several organs. In children with TSC, SEGAs, epilepsy, and neurodevelopmental delay present the most common causes of mortality and morbidity. TSC is characterized by increased mammalian target of rapamycin (mTOR) activation, and the mTOR inhibitor, everolimus, has recently been approved for the treatment of SEGAs associated with TSC in patients older than 3 years of age. The aim of this report was to show the safety of everolimus in younger

children with TSC-associated SEGAs. **Material and methods:** We present locally collected safety data from 8 children under the age of 3 who participated in the EXIST-1 (Everolimus in the Treatment of Subependymal Giant Cell Astrocytomas Associated With Tuberous Sclerosis Complex) study and were treated at our center with everolimus for at least 36 months. All children had growing SEGAs, and 5 patients presented with active, drug-resistant epilepsy at baseline. **Results:** There were no life-threatening or grade 4 adverse events throughout follow-up. All children are still on treatment. The incidence of adverse events and their severity were similar to that observed in older children and adults. The most common adverse events included aphthous stomatitis, upper respiratory tract infections, rash, and laboratory abnormalities. In 1 child with drug-resistant epilepsy, everolimus treatment resulted in cessation of seizures, and in 2 other children, at least a 50% reduction in the number of seizures was noted. Neuropsychological examination showed no significant differences between baseline and follow-up scores in the Psyche-Cattell test. **Conclusions:** Everolimus is a therapeutic option in patients with TSC and should be considered for treatment in children under 3 years of age.

P241 - 2093

Tuberous sclerosis complex: multiple tubers with no functional impact – a case report

Chemaly N, Grevent D, Hadj Rabia S, Ouss L, Boddaert N, Desguerre I, Nabbout R. *Neuropediatrics Department, Centre de référence des Épilepsies rares, Necker Enfants Malades Hospital, Paris, France – nicole.chemaly@nck.aphp.fr*

Tuberous sclerosis or tuberous sclerosis complex (TSC) is a rare multi-system genetic disease that causes non-malignant tumors to grow in the brain and on other vital organs such as the kidneys, heart, eyes, lungs, and skin. Brain involvement is frequent with seizures, cognitive impairment and behavioral disorders. Cognitive outcome is correlated to the occurrence of seizures, age of onset of seizures, infantile spasms occurrence and pharmacoresistance. Relationship between the localization of tubers and cognitive outcome is stressed out in many publications and autism seems to affect more frequently patients presenting with temporal tubers. A 16 year old girl who consulted for “malignant acne” was referred to our clinic for TSC. She presented facial angiofibromas and white spots. She had normal psychomotor development with normal scholar achievement. She had neither seizures nor other neurological symptoms. Her neurological examination was normal. Her neuropsychological test was normal for age and she presented no abnormal psychiatric behaviour. Renal ultrasound showed angiomyolipoma that were of small size and clinically asymptomatic. Cerebral MRI showed multiple cortical tubers (> 16) located almost in all brain regions with both temporal areas involved. She has also subependymal nodules with a small size SEGA with no ventricles asymmetry or dilatation. Tractography was performed and showed loss of anisotropy with modification of white matter fibers tracts. This report shows that the number of tuber and their localization does not seem to be the only predictive factors for cognitive outcome in TSC patients. In infants with prenatal diagnosis, functional aspects could prevail, and they must be closely followed on clinical and EEG basis in order to rule out and treat as soon as possible seizures, especially infantile spasms.

P242 - 1947**The natural history and traditional treatment outcomes of large renal angiomyolipomas in tuberous sclerosis complex**

Amin S, Robinson L, Merrifield J, Osborne JP, O'Callaghan FJK.
*Paediatric Neurology, University of Bristol, Bristol, UK –
 drsam05@yahoo.co.uk*

Aim: To study the radiological and clinical behaviour of angiomyolipomas (AML) ≥ 3 cm in diameter. It has been suggested that pre-emptive treatment with mTOR inhibitors should be recommended for AML > 3 cm; especially those that are still growing. **Methods:** This is a retrospective study of patients with tuberous sclerosis complex (TSC) with angiomyolipomas. More than 200 patients within the Bath TS clinic were reviewed. Ultrasound, MRI and CT scans were reviewed to identify those with AML ≥ 3 cm. Annual growth rates of individual lesions were measured. As the Bath TS clinic is a supra-regional referral clinic, we reviewed notes from referring centres looking for evidence of renal complications (e.g. haemorrhage) or interventions (e.g. embolization, nephrectomy). **Results:** We identified 54 patients with AML ≥ 3 cm and a definite diagnosis of TSC as defined by the modified Gomez criteria. 66 AML lesions ≥ 3 cm were identified. Follow-up ranged from 1 to 13 years (median = 4, interquartile range 2–5). 15 (22.7%) lesions did not show any radiological evidence of growth. Median growth rate was 0.4 cm per year, interquartile range 0.1–1 cm. 12/54 (22.2%) patients had bleeding. 8/12 patients had recurrent bleeding. 14/54 (25.9%) patients needed embolization, and 4/14 required more than one embolization. 4/54 (7.4%) patients had a nephrectomy due to renal bleeding. **Conclusions:** This study reaffirms that AMLs ≥ 3 cm in diameter have a high risk of haemorrhage. However, the majority of lesions did not show evidence of growth. Identifying those lesions ≥ 3 cm in diameter that are most likely to cause problems in the future will provide a rational basis for intervening pre-emptively with embolization or mTOR inhibitor therapy. Many lesions, however, will remain stable without intervention and a policy of intervention on a crude size criteria may not be justified.

P243 - 1944**Does tuberous sclerosis complex ever involve skeletal muscle? A case for discussion**

Amin S, Majumdar A, Cohen N, Phadke R, Sewry CA,
 O'Callaghan FJK. *Paediatric Neurology, University of Bristol, Bristol,
 UK – drsam05@yahoo.co.uk*

We report a 4 year old boy with Tuberous Sclerosis Complex (TSC). He suffers from seizures. He has no significant developmental delay. He has cardiac rhabdomyomas but no kidney angiomyolipoma. He developed right thigh and buttock swelling at 18 months of age [photos]. This was associated with overlying venous distension. He has been unable to weight bear. The swelling has been soft and non-tender, but feels warm. His creatinine kinase was normal. MRI scan showed uniform enlargement of the muscles of the thigh and buttock with contrast enhancement [MRI images]. Muscle biopsy showed myopathic fibre size variation, but there was no evidence of primary myositis or a dystrophy including normal protein analysis. The associated muscle mass was composed of adipose tissue and collections of blood vessels with abnormal vessel walls. There was no HMB45 immunopositivity [biopsy]. The biopsy was sent for a second opinion. A macrophage-rich infiltrate was noted in the perimysium, raising the possibility of myofasciitis. Steroids were suggested. He received high dose steroids for 4 weeks with no clinical response. Skeletal muscle involvement in TSC has not been reported before. However, activation of the mTOR pathway which is seen in TSC has been shown in vivo to cause muscle hypertrophy. If his muscle swelling is TS related, then

mTOR inhibitors such as Everolimus or Metformin may be an option.

P244 - 1755**Results of a families-researchers collaborative project in Lowe syndrome: ten patients with a wide neurological phenotype**

Serrano M, Perez-Dueñas B, Camino-León R, Maldonado E, Armayones M, Pousada M, Gomez-Zuñiga B, de la Fuente J, Nafria B. *Centre for the Biomedical Research on Rare Diseases, Hospital Sant Joan de Déu, Barcelona, Spain – mserrano@hsjdbcn.org*

Lowe syndrome, an ultra-rare X-linked disease due to OCRL1 mutations, causes multisystem disorder affecting the eye, the nervous system, and the kidney. There is scarce information about its natural history, genotype/phenotype correlations, complications' management... Parents of children with rare diseases develop considerable expertise and are advocating for formal collaboration in research. They can be important sources of information. **Objectives:** To increase biomedical knowledge on Lowe syndrome through Internet tools in a pilot Spanish study, collaborating families, doctors and researchers. **Methods:** 10 families participated in an online-community receiving periodical information about the disease and completing medical surveys thereafter. Vineland scales were performed through telephonic interviews. **Results:** Among eight genetically confirmed patients, three presented de novo mutations. Achievement of developmental milestones expressed in months were (mean age (range): head control 7.2 (3–17); sitting 11.7 (6–17); independent walk (8 patients) 35.5 (13–72); social smile 4.4 (3–6); ocular pursuit 5.2 (3–9); pincer grasping 14.4 (8–24). Among seven patients older than 3 years, four draw circles/crosses (5 years (4–7)); open a bottle top (4.8 years (4–6)); and say/understand more than 50 words (3.9 years (2–6)). Vineland scale gave wide heterogeneous results. Stereotypes were very varied. Three patients showed traits of autism disorder. One patient suffered febrile seizures. Two patients suffer refractory epilepsy causing neurodevelopmental regression in one. Neuroimaging was normal in two patients and showed white matter cysts in another. **Conclusions:** Enabling parents to reflect on and share with researchers their personal knowledge in ultra-rare diseases is an effective strategy to advance research, contributing to develop clinical guidelines and homogeneous medical assistance. This collaboration could reduce their suffering. Mutations in OCRL1 explain Lowe syndrome, with a huge heterogeneity of neurological symptoms, from no intellectual disability to profound mental retardation. New phenotypes are being described. Probably, Dent type 2 (caused by OCRL1 mutations) and Lowe Syndrome are comprised in a larger spectrum of OCRL1 related disorders.

P245 - 1999**A case report of TUBB2B mutation-associated polymicrogyria**

Diakogeorgiou A, Smits G, Jansen A. *Department of Pediatric Neurology, HUDERF, ULB Brussels, Belgium – nicolas.deconinck@huderf.be*

Introduction: Heterozygous dominant missense mutations in the TUBB2B gene were recently identified as causing a defined clinical and radiological phenotype. This includes congenital microcephaly, severe motor and intellectual disability and epilepsy associated with bilateral asymmetric and anteriorly predominant polymicrogyria on brain MRI. **Presentation:** A Turkish boy with no family history of neurological diseases, presented with global development delay and focal epilepsy first at the age of 2½ years. At age of 6 he had unsteady gait and poor bimanual coordination. He had limited language comprehension and used single words. He had difficulties in attention and in organizing meaningful play. He presented sporadic focal nocturnal seizures for which

he was treated with valproic acid and topiramate. EEGs showed focal epileptiform discharges over the left central regions. Brain MRI at age of 6 showed polymicrogyria in the anterior regions predominating in the right perisylvian region, enlarged ventricles, dysgenesis of the anterior limb of the internal capsule, thin corpus callosum, hypoplastic brain stem and cerebellar vermis. Sequencing analysis of TUBB2B revealed a de novo heterozygous missense mutation c.743C>T (p.Ala248Val) in exon 4. **Conclusion:** This report underlines the recently characterized association of TUBB2B mutations with bilateral, asymmetric polymicrogyria, corpus callosum dysgenesis, dysmorphic basal ganglia, brain-stem and vermis hypoplasia. These findings suggest implication of TUBB2B in neuronal migration processes.

P246 - 1918

EAST syndrome in a European child with KCNJ10 mutation

Foska A, Nagel M, Ioannou J, Dervenoulas G, Papavasiliou A.
Pendeli Children's Hospital, Greece – dkfoska@gmail.com

KCNJ10 gene mutations were described in five children with EAST syndrome (Epilepsy, Ataxia, Sensorineural deafness, Tubulopathy) and in 5 children with SeSAME syndrome (Seizures, Sensorineural deafness, Ataxia, Mental retardation, and Electrolyte imbalance). Most of them came from consanguineous families of non-European origin. The objective of this presentation is to present a European male with KCNJ10 gene mutation, born to non-consanguineous parents. He presented with Barter syndrome, developmental delay, epilepsy and sensorineural deafness. Earliest features were failure to thrive and epilepsy. Generalized seizures started at 3.5 months of age and responded well to anticonvulsants; he later exhibited secondarily generalized partial seizures. He walked at 19 months and had mild mental retardation. Spasticity was evident by age 14 years and produced gait instability while ataxia was much less prominent and developed in his late teens. There was mild sensory neuropathy. No abnormality was present on brain MRI. Sensorineural deafness was diagnosed at age 8 years. The molecular genetic analysis showed mutations that prove the clinical diagnosis of EAST syndrome. A missense mutation (p.R65C(CGC>TGC) is located at a codon position where a pathogenetic relevant missense mutation is already known. Next, a frame-shift mutation (p.F119GfsX25) creates a premature truncation of the protein and may cause protein dysfunction. The mutations are not yet in the database, but its pathogenetic relevance is obvious. In conclusion, this European patient with KCNJ10 mutation presented with features of EAST and SeSAME syndromes, but was also different from the reported patients in several ways; spasticity rather than ataxia was the most important motor manifestation, seizures were both generalized and partial. It remains to be demonstrated that both mutations belong to distinct alleles, which can be best accomplished by screening of both parents. The mutations are not yet in the database, but their pathogenetic relevance is obvious.

P247 - 1969

Feeding difficulties in Kabuki syndrome

Wacks M, Louw A, Rawat D, Fell J, Koggelmeier J, Kinali M.
Paediatric Neurology Department, Chelsea and Westminster Hospital NHS Foundation Trust, UK – michael.wacks@chelwest.nhs.uk

Background: Kabuki syndrome is a rare disorder characterized by distinctive facial features, postnatal growth retardation, hypotonia, developmental delay, congenital heart disease, renal, skeletal, gastrointestinal abnormalities, abnormal dentition and cleft palate. Feeding difficulties occur in 70% of patients with slow feeding, gastro-oesophageal reflux to requiring nasogastric tube (NGT) feeding or gastrostomy. MLL2 mutation positive

patients have more feeding problems than mutation negative patients. The natural progression of feeding difficulties has not been described in detail. We report our experience on the feeding difficulties of Kabuki Syndrome who attended our feeding clinic. **Design:** A case series of children (n = 3) with molecular and clinical diagnosis of Kabuki syndrome. **Results:** Feeding difficulties occurred in all three children. Children were referred to the clinic between 4 (n = 2) and 13 months (n = 1). All were female with congenital heart disease, hypotonia, gastroesophageal reflux disease, constipation, developmental delay, poor growth, oral food aversion, generalised sensory defensiveness, drooling and dysphagia. All three children presented with aspiration on thin liquids. Swallow function in all improved with repeat videofluoroscopy swallow studies indicating safe swallow function for thin liquids. All children required long-term enteral feeding support, initially via NGT/NJ tube and later via gastrostomy. Two children required Nissen's fundoplication. The age range for discharge was between 3.2–7.3 years. Progression onto exclusive oral feeding was slow due to oral food aversion as a result of gastroesophageal reflux disease, generalised sensory defensiveness and developmental delay. Two children were weaned off enteral feeding support. The other was lost to follow-up. **Conclusion:** Feeding difficulties are prevalent in children with Kabuki Syndrome. The cause of feeding difficulties is multi-factorial. Our experience indicates that feeding difficulties are long term in nature but children with this diagnosis do develop oral feeding skills, which can sustain growth without nutritional support via enteral feeding.

P248 - 1722

Hand stereotypies in Rett syndrome and autism – a preliminary comparative study using video motion analysis

Melo C, Calatróia R, Paula L, Cunha JP, Temudo T. Centro Hospitalar do Médio Ave, Portugal – crferrao.melo@gmail.com

Objective: Our aim was to characterize and compare hand stereotypies using not only direct observation but also quantitative analysis. **Background:** Autistic disorder and Rett Syndrome, both classified as neurodevelopmental disorders, share several clinical characteristics such as communication and repetitive behaviour problems. Hand stereotypies are common in both conditions. Studies based on direct observation claim that their stereotypies may be distinguishable. **Methods:** Children with autistic disorder (4 males) and Rett syndrome (4 females) were recorded during a 30 minutes session and their stereotypies were analysed by a two dimension video analysis system. Their velocity, amplitude, frequency, duration and total time of stereotypies were assessed. **Results:** We identified 81 stereotypies: 44 in Rett patients and 37 in the autistic patients. Stereotypies in autism were faster (median = 421.2 vs. 50.7 pixel/second), with a shorter duration (median = 1.7 vs. 7.6 seconds) higher frequency (median = 2.9 vs. 1.1 Hz) and greater amplitude of movement (median = 4990.6 vs. 877.5 pixel²) than in Rett. The median total time spent performing stereotypies per session was greater in the Rett group. **Conclusions:** Kinematic analysis allowed a distinction of the stereotypies in Rett syndrome and autistic patients. The slower and less extensive stereotypies of Rett syndrome patients may be in part explained by their greater motor deterioration when compared to autistic disorder. Differences in neuropathogenesis of both conditions may justify this fact. The explanation of the predominantly midline localization of hand stereotypies in Rett patients remains unknown. A better knowledge of the differences of stereotypies between these two conditions may help to clarify their pathogenic mechanisms.

P249 - 1533

A giant congenital melanocytic nevus associated with neurocutaneous melanosis

Kim SJ, Han JY, Son B-C, Eom TH. *Department of Pediatrics, St. Vincent's Hospital, College of Medicine, The Catholic University of Korea, Suwon, South Korea – Pedkim@catholic.ac.kr*

Neuromelanosis (cerebral melanosis), which relates to a congenital error in the morphogenesis of the embryonal ectoderm, describes melanocytic proliferation within the leptomeninges and brain parenchyma. Neurocutaneous melanosis (NCM) is neuromelanosis associated with congenital melanocytic nevi (CMN). It has been reported that many patients with symptomatic NCM die, with more than half of fatalities occurring within initial 3 years of diagnosis. However, asymptomatic NCM is known to have a favorable prognosis. It is uncertain that who will become symptomatic NCM among the patients with asymptomatic NCM. However, a report which studied the magnetic resonance imaging (MRI) finding of asymptomatic NCM patients showed that parenchymal NCM involving characteristic T1 shortening in medial temporal lobe, pons, medulla, and cerebellum had a stable and favorable prognosis. We report a case of a 10 year-old male patient with giant congenital melanocytic nevi (GCMN) and parenchymal NCM diagnosed in his infancy (3 months of age). His neurological condition deteriorated 10 years later with consequent development of leptomeningeal and spinal neuromelanosis. The MRI showed regression and stabilization of T1 hyperintensities (parenchymal NCM) in temporal lobe, cerebellum, and pons. On the contrary, it seemed that diffuse leptomeningeal involvement and enhancement ultimately caused hydrocephalus, seizures, and neurologic deterioration. As shown in our case, parenchymal NCM may not have a clinical significance even after 10 years after diagnosis and the leptomeningeal involvement seems to be a major determinant of the prognosis in patients with NCM.

P250 - 1974

Application of array-based comparative genomic hybridization to pediatric neurologic diseases

Byeon JH, Shin E, Kim G-H, Kim MK, Eun S-H, Eun B-L. *Department of Pediatrics, University College of Medicine, Neodine Medical Institute, Korea – bleun@chollian.net*

Purpose: Array comparative genomic hybridization (array-CGH) is a technique used to analyze the quantitative increase or decrease of chromosomes by competitive DNA hybridization of patients and controls. This study aimed to evaluate the benefits and yield of array-CGH in comparison with palliative karyotyping in pediatric neurology patients. **Material and method:** We included 87 patients from pediatric neurology clinic with least one of the following features: developmental delay, mental retardation, dysmorphic face, or epilepsy. Extracted DNA from patients and controls were hybridized on the Roche NimbleGen 135K oligonucleotide array and compared with G-band karyotyping. The results were analyzed with findings reported in recent publications and internet databases. **Results:** Chromosome imbalances, including 9 cases also detected by G-band karyotyping, were found in 28 patients (32.2%), and at least 20 of them seemed to be causally related to the abnormal phenotypes. Regarding each clinical symptom, 26.2% of 42 developmental delay patients, 44.4% of 18 mental retardation patients, 42.9% of 28 dysmorphic face patients, 34.6% of 26 epilepsy patients showed abnormal array results. **Conclusion:** Although there were a relatively small number of tests in patients with pediatric neurologic disease, this study demonstrated that array-CGH is a very useful tool for clinical diagnosis of unknown genome abnormalities performed in pediatric neurology clinics.

P251 - 1689

MASA syndrome – report of a two twin brother case

Kovac Sizgoric M, Sabol Z, Grmoja T, Bela Klancir S, Gjergja Z, Kipke Sabol Lj, Sabol F. *Sabol Clinic for Sick Children, Zagreb, Croatia – matilda.kovac.sizgoric@zg.t-com.hr*

Introduction: MASA syndrome, also called CRASH syndrome and Gareis-Mason syndrome, is a rare X-linked recessive neurological disorder. The acronym “MASA” describes four major symptoms - mental retardation, aphasia, shuffling gait, and adducted thumbs. A more suitable name for this syndrome is “L1 syndrome”. The disorder has been associated with mutations in the L1CAM gene. This syndrome has severe symptoms in males, while females are carriers because only one X-chromosome is affected. The aim of this report is to show similarities and differences between clinical manifestations in twins with the L1CAM gene mutation. Our patients: Born prematurely at 35 weeks gestation. Pregnancy was complicated with early bleeding and gestational diabetes. Immediately after birth hypertonus of the lower extremities in both twins was observed. Sixteen-year clinical follow-up showed spastic paraparetic form with shuffling gait, clumsiness, delayed speech development, with lower intellectual functioning at the level of light to moderate mental retardation, primary nocturnal enuresis, behavioral and sleep disorder (more pronounced in the second twin). Brain MRI in both twins showed complete agenesis of the corpus callosum, complete lack of the anterior commissure, and internal hydrocephalus. EEGs showed nonspecific slower dysrhythmic changes. Kidney ultrasounds showed mild dilatation in the channel system of both kidneys in both twins. Ophthalmologic examinations was normal. Molecular genetic testing (Karl-Franzens-Universität Graz) identified homozygous intron 26 L1CAM gene mutation IVS26-12G→A in both twins. The mother is a carrier of the same heterozygous mutations. **Conclusion:** Our patients, the twins show similar clinical changes typical of MASA syndrome. After identifying the specific genetic mutations this family has become informative for prenatal diagnosis.

P252 - 2076

Unusual neurological profile in Tunisian children with Williams syndrome

Ben Othmen H, Kammoun F, Belguith N, Elouz E, Hsairi I, Kamoun H, Triki C. *Research Unit “Neuropédiatrie” 01UR08-05, University of Medicine, Sfax, Tunisia – bothmenhouda@yahoo.fr*

Objectives: Williams syndrome (WS) is a neuro-developmental genetic disorder caused by the hemizygous deletion in chromosome 7q11.23. It is characterized by facial dysmorphism, physical abnormalities and a specific cognitive and behavioral profile. In this report, we look for neurological characteristics. **Material and methods:** We have reviewed retrospectively 4 girls with WS aged between 4 and 12 years. In all this cases, the diagnosis was based on facial dimorphism, behavior features and the deletion was confirmed by FISH study. We focus on neurological signs and brain investigations (EEG, brain imagery by Computed Tomography (CT) and MRI). **Results:** Initial consultations for our cases were psychomotor delay in three cases and other neurological abnormalities as hand mirror syncinesia in one case. All patients have abnormal intelligence quotient ranged from mild (n=3) to moderate (n=1). Hyperactive behavior was observed in all cases. CT show bilateral calcifications in the globus pallidus in one case and electroencephalographic abnormalities revealed a rapid diffuse rhythm in one case. **Conclusions:** Some neurological phenotype associated with mental deficiency can be suggestive of etiology like washing hand stereotypies in Rett and specific EEG patterns in Angelman syndrome. Unlike, previous studies have documented the absence of major neurologic signs in WS and some unusual neurologic profile can dominate the

clinical phenotype as hand mirror syncinesia in one of our case. The spectral analysis of the EEG may reveal an increased delta and slow wave activity and decreased alpha and sigma activity in patient without any clinical correlate. Interestingly, in another case, imaging studies revealed bilateral calcifications in the globus pallidus which may due to calcium metabolism disorders found in WS. In addition to dysmorphic and behavior features, a systematic neurological exam focused on soft signs and brain investigations seem to be indispensable to increase and spread knowledge about neuro-developmental abnormalities in WS.

P253 - 2074

Clinical characteristics of sleep disordered breathing in Moebius syndrome: case report

Sendon CS, Chocano JF, Sendon PM, Chocano E. *Eastern Virginia Medical School and Children's Hospital of The King's Daughters, USA – cssendon@hotmail.com*

Introduction: The Moebius Syndrome is an extremely rare congenital neurological disorder, its incidence is 2 cases per million births. It is characterized by facial paralysis and inability to move the eyes laterally due to underdevelopment of VI and VII cranial nerves. Limb abnormalities, chest-wall deformities (Poland syndrome), difficulty to breathe and swallow had been described. The combination of structural and cranial nerve dysfunction, makes sleep disordered breathing a complication. **Case presentation:** 5 years old African American male with Moebius Syndrome, presenting with central sleep apneas, tracheostomy and ventilator dependent. He has a frozen facial expression, aphonic-type voice due to inability to move his tongue and lips, vertical light follow but there was no lateral follow to the either side. By 3 years of age, he was referred for a reevaluation of the central sleep disorder breathing and to confirm the need of a tracheostomy tube. The overnight sleep study was performed with a capped thacheostomy, he did not tolerate being capped for more than 90 minutes. Study results showed obstructive events with oxygen desaturations. After 2 years, a repeated Polysomnogram showed severe obstructive sleep apnea without impairment of gas exchange. It was recommended not to decanulate and ENT evaluation of the upper airway to define the presence of malacia or granuloma formation around the tracheostomy site. **Discussion:** Moebius Syndrome had been associated with central apneas but it is important to evaluate also an obstructive component. A tracheostomy or its complications can produce obstruction in the airway and may responsible for sleep breathing problems. Patients with multiple comorbidities have central and obstructive components. The use of non-invasive methods such as nasal CPAP, BIPAP needs to be considered.

P254 - 2152

A new high water content leukoencephalopathy related to a basement membrane dysfunction

Tonduti D, Dorboz I, Renaldo F, Masliah-Planchon J, Elmaleh M, Dalens H, Rodriguez D, Boespflug-Tanguy O. *Centre de Référence des Leucodystrophies, Service de Neuropédiatrie et Maladies Métaboliques, Hôpital Robert Debré, AP-HP, Paris, France – davidetonduti@hotmail.com*

Basement membranes are specialized extracellular matrices. They have fundamental role in organization, stability and differentiation of many tissues. In human pathology many diseases related to anomalies of these structures are known, they variably affect skin, kidneys, eyes, muscles, central nervous system. We recently found two patients carrying a mutation in a gene involved in basement membrane constitution and presenting a new type of leukoencephalopathy. The younger sister presented a postnatal mild macrocephaly. From 8 months of age infantile spasms and then psychomotor delay associated to spastic

haemiplegia become evident. At 12 years she suffered of a recrudescence of epilepsy and started to progressively deteriorate; ophthalmological evaluation showed optic atrophy and bilateral subcapsular lens opacification. Neuroradiological exams, MRI showed a diffuse high water content leukodystrophy and also a large left porencephalic cavity. Her older brother presented an initial isolated macrocephaly and then a history of polymorphic pharmacoresistent epileptic seizures and slowly progressive deterioration started during late infancy. During adolescence two episodes of rapid degradation happened after an accidental traumatic fall. Ophthalmological evaluation showed the presence of retinal vascular tortuosities and bilateral subcapsular lens opacification. MRI showed a diffuse high water content leukodystrophy with temporal subcortical cysts. Whole-exome sequencing identifies compound heterozygous mutations in a gene crucial for basement membrane structure. Our patients suggest that a new phenotype presenting as a leukoencephalopathy should be added to the list of disease related to basement membranes malfunctioning.

P255 - 1787

Optic atrophy plus, a unique phenotype to a known mutation with early onset and rapid progression

Cohen Rappaport Y^{1,2}, Blumkin L¹, Leshinsky-Silver E^{1,3}, Lev D¹, Lerman-Sagie T¹. ¹Metabolic-Neurogenetic Clinic, Wolfson Medical Center; ²Hashalom Child Development Center, Maccabi HMO; ³Molecular Genetics Laboratory, Wolfson Medical Center, Holon, affiliated to Sackler School of Medicine, Tel-Aviv University, Tel-Aviv, Israel – yaelgadi@zahav.net.com

Autosomal dominant optic atrophy is characterized by selective degeneration of retinal ganglion cells. In 60–70% of ADOA cases, mutations in the optic atrophy 1 gene (encoding a dynamin like GTPase protein), are diagnosed. Defects in OPA1 cause optic atrophy type 1, and are the main cause of dominant optic atrophy plus syndrome; a neurologic disorder characterized by an insidious onset of visual loss and sensorineural hearing loss in childhood with variable presentation of other clinical manifestations including progressive external ophthalmoplegia, muscle cramps, hyperreflexia and ataxia in later decades. There is a marked intra and interfamilial clinical variability and an incomplete penetrance, estimated at 82% in the familial forms of the disease. We describe a 7 year old, who was evaluated for visual impairment at the age of 6 months, and was diagnosed with optic atrophy at the young age of 18 months was declared legally blind at 5 years. She has global developmental delay, she developed ataxia and tremor at the age of 2 years, and has a slight hearing impairment. She is the only affected patient in her family. Exome sequencing identified the heterozygous mutation, 1382M in the OPA1 gene. The mother and aunt carry the same mutation but are asymptomatic. Our case is unique because of the early onset, rapid progression, associated neurologic symptoms and low penetrance in the family. Exome sequencing is a powerful tool even in the identification of the cause of sporadic optic atrophy.

P256 - 1719

X-linked alpha thalassaemia-mental retardation syndrome with leukoencephalopathy: a new phenotype?

Aguilera-Albesa S, Díez-Bayona V, Yoldi-Petri ME, Esparza-Estáun J, Durá-Travé T, Elduayen-Aldaz B, Ramos-Arroyo MA, Gibbons RJ. *Paediatric Neurology, Navarra Hospital, Spain – saguilealea@navarra.es*

Objective: To describe the clinical and neuroimaging characteristics during long term follow up of two brothers affected by X-linked alpha thalassaemia-mental retardation syndrome (ATRX).

Cases studies: *Case 1.* A 17 year-old boy with profound mental retardation and repetitive stereotypic hands movements. Dysmorphic features were present: microcephaly, telecanthus, mid-face hypoplasia, flat nasal bridge, small triangular upturned nose, tented upper lip and everted full lower lip, hypospadias and talipes equinovarus. He presented with generalised hypotonia from infancy and non-progressive spasticity in lower limbs from early childhood. Extensive genetic and metabolic investigations were normal, excepting chronic microcytic anaemia. Cerebral MRI was performed at 2, 5 and 10 years old. They showed thin corpus callosum, periventricular and subcortical white matter T2 hyperintensities with sparing of arcuate fibers, with improvement over time. *Case 2.* An 11-yo boy with physical and behavioural phenotype similar to his brother (case 1). He also presented cryptorchidism, cold extremities and recurrent blepharitis. Chronic microcytic anaemia was also observed. Cerebral MRI performed at 18-mo and 8-yo revealed thin corpus callosum and an extensive symmetric posterior periventricular T2 white matter hyperintensities (hypo in T1) with significant improvement over time. Perinatal period was uneventful in both cases. Despite MRI findings, the phenotype suggested ATRX. Haemoglobin H inclusions were detected after incubation of red cells in brilliant cresyl blue. A missense mutation (C568G) of ATRX gene (Xq13) was confirmed in each case. **Discussion:** The diagnostic suspicion of ATRX is based on recognizable facial dysmorphism, genital abnormalities and chronic microcytic anaemia in a male with profound developmental delay. Brain imaging studies scarcely show abnormalities, like mild cerebral atrophy or hypo/agenesis of the corpus callosum. These two patients showed a predominantly periventricular leukoencephalopathy that improved over time. It has not been previously described in ATRX patients.

P257 - 1695

A novel MEF2C microdeletion in a case of Rett-like encephalopathy

Brighina E, Bonaglia MC, Arrigoni F, Borini S, Molteni M, D'Angelo MG. *Neuromuscular Unit, Department of Neurorehabilitation, E. Medea Scientific Institute, Bosisio Parini, Lecco, Italy – erika.brighina@bp.inf.it*

Objectives: MEF2C haploinsufficiency syndrome is an emerging neurodevelopmental disorder associated with severe psychomotor retardation, autistic features, epilepsy and abnormal movements, reported in only 43 patients by now (1). We describe the case of a 3.5 years child carrying a novel microdeletion in 5q14.3 region, encompassing part of MEF2C gene. **Methods:** Array-CGH analysis was performed using the Agilent array 180K and data analysis by Agilent Cytogenomics 2.5.8.1. **Results:** Our proband was born at term after an uneventful pregnancy to healthy unrelated parents with an unremarkable family history. At birth, head circumference was small (25° perc.), compared to weight and length (50° perc.). The neonatal period was normal. He underwent regular controls for convergent strabismus since 6 months (ms) of age. Motor milestones were slightly delayed (head control acquired at 5 ms, sitting position at 10, ambulation at 27 ms). Griffiths scale at 37 ms revealed severe intellectual impairment (GQ 26, MA 9.5 ms). He presented two episodes of febrile convulsions at 18 and 22 ms. EEG showed only irregular organization of activity during sleep. Brain MRI at 24 ms was normal. Last examination at 3.5 years showed diffuse hypotonia and hyporeflexia, lingual muscles weakness and unsteady gate. No evidence of dysmetria. Speech was absent and chewing impaired. Impermanent eye contact and stereotypic repetitive movements were present. The patient had a deletion of 88kb [arr 5q14.3 (8819525–88193351x1) dn] within MEF2C gene, resulting to be the second shortest deletion reported so far [1]. **Conclusions:** Our case supports the hypothesis that patients with smaller deletions in the 5q14.3 region involving MEF2C gene may show a milder motor

phenotype with possible ambulation (although wide-based and unstable, in the absence of any objective cerebellar signs), and a lower risk of presenting refractory and intractable seizures [2].

P258 - 1952

Kenny Caffey syndrome: expanding the clinical phenotype. A case with unusual severe lung involvement

Spyridou C, Wacks M, Mankad K, Deep A, Kinali M. *Paediatric Department, The Royal London Hospital, London, UK – maria.kinali@chelwest.nhs.uk*

Background: Kenny Caffey is a rare autosomal recessive syndrome reported almost exclusively in Middle Eastern populations, characterized by severe growth retardation – dwarfism, dysmorphic features, episodic hypocalcaemia, hypoparathyroidism, seizures, and medullary stenosis of long bones with thickened cortex. **Method:** We report the long term follow up of a 9.5 year old boy with Kenny Caffey syndrome and unusually severe respiratory system involvement. **Results:** Our patient was born by Caesarean section at term to second cousin Bedouin parents. Distinctive facial features were noted at birth, and his growth parameters were <5th centile, and remain so to date. He developed hypocalcaemic seizures when 2 months old. He has suffered multiple seizures types including status epilepticus, and requires antiepileptics. He had recurrent chest infections from the outset and has been CPAP dependent since aged 6. His respiratory function deteriorated in the last year with persistent hypercarbia, increasing oxygen requirement and progressive respiratory failure. This coincided with increased frequency and severity of recurrent lower respiratory tract infections and possibly chronic aspiration. He has severe psychomotor retardation and at 9.5 years he can sit with support, whereas up to a year ago he was able to walk unassisted. CT scan of his chest showed changes consistent with chronic aspiration, but no interstitial pulmonary fibrosis. He has required assisted invasive ventilation on several occasions. He requires long term ventilatory support via tracheostomy. He was found positive for a 12bp deletion of exon 2 of TBCE gene. 22q11 has been excluded. MRI brain showed bilateral hippocampal sclerosis, marked supratentorial volume loss and numerous calcifications, the latter in keeping with his diagnosis. Prolonged EEGs showed slow background activity, but no epileptiform activity. **Conclusion:** This case summarises the long term follow up of a patient with Kenny Caffey syndrome and expands the clinical phenotype describing unusually severe lung involvement.

Neurometabolic disorders

P259 - 2083

Whole exome sequencing study aids diagnosis of atypical pantothenate kinase associated neurodegeneration (PKAN)

Csanyi B, Kaminska M, Meyer E, Josifova D, Siddiqui A, Lumsden D, Kara E, Houlden H, Hardy J, Révész T, Kurian MA, Lin JP. *Great Ormond Street Hospital for Children, London, UK – doctorabarbara@gmail.com*

Background: Neurodegeneration with Brain Iron Accumulation (NBIA) comprises a heterogeneous group of rare disorders that present with a wide spectrum of classical and atypical clinical phenotypes. Clinical diagnosis and genetic confirmation can often be challenging. **Methods:** Clinical report of a patient with NBIA and results of molecular genetic investigations. **Results:** We present the case of a young girl born to distally related consanguineous parents. She presented with severe progressive dystonia and four limb spasticity from early childhood culminating in pharmacoresistant opisthotonic posturing and status

dystonicus by the age of 10 years. MRI brain scan showed generalised cerebellar and cerebral volume loss with excess iron deposition bilaterally within the globus pallidi, without convincing radiological eye-of-the-tiger sign. At age 11 years, after failing conventional oral medication, she had insertion of a deep brain stimulator (DBS). Insertion of DBS led to modest clinical improvements for a year but she died from pneumonia and acute respiratory complications at the age of 12 years. Post-mortem examination confirmed iron accumulation in both globus pallidi with extended neuroaxonal swelling (tau and alphasynuclein immunohistochemistry negative). Diagnostic testing of PANK2, PLA2G6 and DYT1 were negative. Research genetic studies were therefore undertaken. Autozygosity mapping studies did not reveal extended regions of homozygosity/linkage but subsequent whole exome sequencing revealed two mutations in PANK2: one novel mutation (p.Cys276Trpfs*15), and another previously reported mutation (p.Gly521Arg). **Conclusion:** We report a case of genetically confirmed PKAN where mutations in PANK2 were identified on research whole exome sequencing. Negative diagnostic screening of PANK2, parental consanguinity and lack of the classical eye-of the tiger radiological hallmark were confounding factors in making the correct diagnosis. Our report suggests that both research and future diagnostic whole exome sequencing is likely to play a role in the diagnosis of childhood neurological disorders.

P260 - 1615

Pantothenate kinase-associated neurodegeneration (PKAN): the “Eye-of-the-Tiger” sign may be absent in the early stages: a case report

Arslan M, Ünay B, Özcan E, Vurucu S, Gül D. *Department of Pediatric Neurology, Gülhane Military Medical School, Ankara, Turkey – mutluayarslan@yahoo.com*

Pantothenate kinase-associated neurodegeneration (PKAN) is a rare autosomal recessive neurodegenerative disorder associated with brain iron accumulation. ‘Eye-of-the-tiger’ sign, a central region of hyperintensity with surrounding hypointensity of the globus pallidus on T2-weighted images, is a highly specific magnetic resonance imaging (MRI) marker for PKAN. We report a patient affected by PKAN, in whom MRI examination demonstrated isolated T2 hyperintensity within globi pallidi in the early stages; the typical “eye-of-the-tiger” sign was detected only in the following examination. PKAN should be kept in mind in children who have progressive neurodegenerative symptoms, even in the absence of the “eye-of-the-tiger” sign, to benefit from early therapeutic options in paucisymptomatic patients.

P261 - 1589

A case of Hallervorden-Spatz disease initially presented with stammering and speech disorder

Sonmez FM, Donmez A, Ceylaner S, Aydin F. *Turgut Ozal University, Faculty of Medicine, Department of Child Neurology, Ankara, Turkey – mjpgsonmez@yahoo.com*

Hallervorden-Spatz disease (HSD) is a rare autosomal recessive neurodegenerative disorder characterized by progressive pyramidal and extrapyramidal manifestations associated with accumulation of iron complex. The most common psychiatric features are cognitive impairment as well as depressive symptoms. **Case:** 15 years-old-male patient was admitted with complaint of speech disorder and movement limitation on the left hand. He was born first degree parents as third child of family. Mental and motor development was normal until 7-years of age. At that time, progressive stammering has been started. Also he took the diagnosis of ADHD, so risperidone and speech therapy were started at another center. Family history revealed four other patients (one

daughter and one son of the mother's two uncle, one mother's uncle, one son of his uncle). Dystonia was observed on the left hand and peroral region during speaking on neurological examination. Cranial MRI showed eye of the tiger sign. Molecular genetic analyses revealed PANK2 mutation. **Conclusion:** Classical form of HSD is early onset, progressive type caused by a defect in the gene encoding PANK2. In atypical PKAN, both motor and verbal tics and obsessive compulsive behaviour have been described. In general, extrapyramidal signs in atypical PKAN cases are less severe than in typical cases and diagnosis can be long as similar in our case. We couldn't find any report about early onset with progressive stammering in HSD.

P262 - 2142

Episodic vomiting and ataxia and SLC2A1 mutation: further expanding the GLUT1 DS phenotype in a family with 3 affected members

Mewasingh LD, Houlden H, Leen WG. *Imperial College Healthcare NHS Trust, London, UK – leena.mewasingh@imperial.nhs.uk*

We describe a 7 yr old boy who presented at the age of 5 with paroxysmal episodes consisting of sweating, profuse vomiting, mildly impaired consciousness and ataxia. These could last from several minutes to hours, with no triggers identified. Father reported this had been occurring since early infancy. Clinical examination was unremarkable except for a head circumference on the 2nd centile. This child also has global developmental delay and attends a mainstream school with some support. An extensive neurometabolic work-up was negative. Fasting lumbar puncture under GA showed a CSF sugar of 3.5 mmol/l with a serum glucose of 5.3 (ratio 66%) and a CSF lactate of 1.1 mmol/l. This was not felt to be in keeping with GLUT1DS at the time and given that his episodes were highly suggestive of episodic ataxia type 2, he was screened for calcium channel mutations, CACNA1A. The latter was negative and the genetic team then went on to look at SLC2A1 gene. This showed a GLUT1 codon 60 heterozygous (T60M) mutation, which was confirmed as pathogenic and has not been found in 100 controls. **Family screening:** Father and a younger sibling also carry this pathogenic mutation. Father is currently asymptomatic, with no movement disorder. The younger 4 year old sibling has autistic spectrum disorder and is making good progress in a mainstream school with additional support. **Discussion:** This case further expands the mild phenotype of Glut1DS. Other reported cases in the literature of T60M mutation had a JME phenotype. This family highlights the variable penetrance of mutations in this condition. The relevance of this particular SLC2A1 mutation as regards the learning difficulties and autistic traits is difficult to ascertain; it could be relevant. More research is needed regarding this neurometabolic condition with such variation in the phenotypes.

P263 - 1945

Fahr fetched

Loughran C, Crozier D, Price J, Peake D, Mackin G. *Royal Belfast Hospital for Sick Children, Belfast Trust, Northern Ireland – clareloughran@doctors.net.uk*

Background: Fahr's disease (striopallidodentate calcinosis) rarely presents in children. It is a genetically dominant disorder of unknown aetiology. Fahr's syndrome is the combination of striopallidodentate calcinosis coupled with clinical manifestations. These include headache, seizures, movement, cognitive and psychotic disorders. Psychiatric symptoms usually precede neurological ones. **Aim:** We present two cases of Fahr's syndrome diagnosed in children from Northern Ireland. **Case report 1:** A 4yr old boy born of consanguineous parents presented with a prolonged febrile generalised seizure and subsequently developed

afebrile multifocal epilepsy. CT brain revealed calcification in the basal ganglia bilaterally, thalami and white matter of cerebral hemispheres. This was extensively investigated and no abnormalities were detected. Parents are very poor historians and were reluctant to disclose family history. His five siblings all have a diagnosis of ADHD. Recently his behaviour has deteriorated and he is being investigated for ADHD. Of note the patient's mother had a previous CT brain which demonstrated striking calcification in the basal ganglia, cerebellum and white matter felt to be consistent with the rare diagnosis of Fahr's disease. Case report 2: A 13 year old girl was referred to tertiary neurology with focal seizures. She had a background history of delayed motor milestones, stereotypical movements and marked Obsessive Compulsive Disorder manifestations. CT brain revealed bilateral basal ganglia calcification. **Discussion:** None of these children had significant neurological signs or symptoms but both have neuropsychiatric comorbidities; OCD and ADHD. In case two a heterozygous mutation of SLC20A2 gene has been identified, known to be associated with autosomal dominant intracranial calcification. This same mutation has also been identified in her father. Gene testing is currently awaited in case one. We conclude that CT brain scanning should be considered in all children with psychiatric co-morbidities, seizures and a family history of neuropsychiatric/neurological disorders to look for calcification.

P264 - 1791

Evolution of the disease under Miglustat treatment: timeline in two patients with early-infantile NPC in the Turkish cohort

Haliloglu G, Duzgun G, Oguz KK, Yuce A, Gurakan F, Topcu M. Hacettepe University Children's Hospital, Department of Pediatric Neurology, Ankara, Turkey – gtuncer@hacettepe.edu.tr

NPC is a rare neurovisceral disease characterized by progressive neurological manifestations. Miglustat can stabilize neurological manifestations in pediatric patients with late-infantile and juvenile-onset forms, however more experience is required in patients with early-infantile onset subgroup. In the NPC cohort of Hacettepe University Children's Hospital, among 24 patients diagnosed with NPC, we have 10 pediatric patients molecularly diagnosed as NPC1, who are currently treated with miglustat. We would like to present the course of the disease in two of the patients in the early-infantile onset subgroup who had a long-term follow-up. A 6-year-old girl, presented with difficulty in walking at the age of 3 years. Family noticed frequent falls at the age of 14 months. She had a mild oculomotor apraxia, splenomegaly, increased deep tendon reflexes, gait ataxia, and proximal weakness in lower extremities. Fibroblast culture showed "variant" NPC-phenotype. She had a compound heterozygous mutation in NPC1 gene. She had been on treatment for the last 28 months, and had a progressive course in terms of gait apraxia, and pyramidal involvement. A 7-year-old girl presented with motor and mental developmental delay, ataxic gait, splenomegaly at the age of 2 years. Family noticed frequent falls at the age of 14 months. She had hepatosplenomegaly, oculomotor apraxia, ataxia, distal atrophy, genu recurvatum deformity, wide-based gait. Fibroblast culture showed classical NPC- phenotype, molecular diagnosis was NPC1 disease. For the last 3.5 years, this patient had been on miglustat treatment. She had progressive worsening in her attention span and cooperation. During the last 12 months, the patient developed cataplexy resistant to tricyclic antidepressants and valproic acid. Neurological manifestations in pediatric patients with NPC can be modified especially in late-infantile, and juvenile-onset forms, however in line with other series reported, miglustat did not seem to modify the clinical course of the disease in early-infantile onset patients.

P265 - 1749

A novel suspicion index tool to aid diagnosis of Niemann-Pick disease type C (NP-C) in paediatric patients

Hendriksz CJ, Patterson MC, Kolb SA, Chadha-Boreham H. Salford Royal Hospital NHS Foundation Trust, Manchester, UK – Chris.Hendriksz@srf.nhs.uk

Objective: Niemann-Pick disease type C (NP-C) is a rare, autosomal, recessive lysosomal lipid storage disorder caused by mutations in NPC1 or NPC2 genes. The disease presents with various visceral, neurological and psychiatric symptoms and most patients with NP-C are diagnosed during childhood, but diagnosis can be delayed. Miglustat (Zavesca®) is the only approved treatment for the neurological manifestations of NP-C. Early diagnosis is vital as patients treated with miglustat at first onset of manifestations maintain a higher level of neurological function. We developed a paediatric NP-C Suspicion Index (SI) tool to provide a risk prediction score for clinicians in identifying patients aged 4 years or under with suspicion of NP-C for subsequent testing. This study aimed to collect additional data on these patients to provide an extended database with the aim of developing an improved NP-C SI tool in this paediatric age group. **Methods:** Data collection occurred as a retrospective chart review in 5–10 expert NP-C centres. Data included one measurement/patient and represents NP-C disease characteristics (signs/symptoms and family history of NP-C) in children aged 4 years or under. Children with suspected NP-C underwent filipin testing (ie, NP-C positive or NP-C negative); control patients were not tested. Signs/symptoms were categorised into three groups (≥ 40 patients/group): NP-C cases, NP-C non-cases and control. Data were summarised descriptively for the groups and kept anonymous to all parties involved in analysis/review. The relationship between a variable and likelihood of NP-C was modelled using one-sided logistic regression in two different models: NP-C cases (reference) versus NP-C non-cases, then versus controls. Psychiatric signs/symptoms were not used in modelling; they were summarised descriptively. **Results and conclusions:** The protocol was finalised in October 2012 and data collection began in November 2012, with data validation completed at the end of December 2012. The retrospective chart review study design will be presented.

P266 - 2077

AADC deficiency with oculogyric crises as the most specific presenting symptom

de Bruyn G, Régál L, Wouters L, Jansen K, Buyse G, Lagae L. UZ Leuven, Belgium – gwendolyn.debruyn@uzleuven.be

We describe a boy that presented at the age of 8 months old with failure to thrive, developmental delay, hypotonia, oculogyric crises and aberrant dystonic tongue movements. During hospitalization we noticed marked irritability worsening when tired, excessive sweating and ptosis. A neuroblastoma was excluded (normal MIBG scan). MRI of the brain was normal. Further analysis of the neurotransmitter profile in cerebrospinal fluid revealed the probable diagnosis of aromatic L-amino acid decarboxylase (AADC) deficiency leading to a severe combined deficiency of serotonin and catecholamines. AADC activity in plasma was absent. We also measured high levels of 3-methoxy-tyrosine, 5-hydroxytryptophan and a low level of serotonin in plasma which confirmed the diagnosis. Urinary vanillic acid which is elevated in some patients, was normal in this patient. First line treatment consists of vitamin B6, a cofactor of AADC and Elvornine to compensate for the high cerebral use of methyl-tetrahydrofolate. Our patient is currently 18 months old and is treated with Tranlycypromine (a MAO-inhibitor). His development is delayed and he still has sporadic oculogyric crises. AADC deficiency is a severe and rare neurometabolic disorder.

der and should be excluded in young children with oculogyric crises.

P267 - 2147

Maternal hyperphenylalaninemia

Yüksel D, Özel A, Okur I, Aksoy A, Ozkan M, Gunduz M. Dr. Sami Ulus Children's Health and Diseases Training and Research Hospital, Ankara, Turkey – drdeniz_yuksel@yahoo.com.tr

Untreated maternal phenylketonuria/hyperphenylalaninemia is an embryopathy which may result in nonphenylketonuric offspring with neonatal sequelae, especially intellectual disability, microcephaly, low birth weight and congenital heart disease. Dietary treatment to control phenylalanine concentrations can prevent these sequelae. This report present the case two brothers both diagnosed as maternal hyperphenylalaninemia who referred to our clinic because of microcephaly, neuromotor delay and epilepsy. Three and five years old boys were born to consanguinity parents who were second degree cousins. Perinatal history was insignificant. Physical examination both revealed head circumference below 3rd percentile, coarse face, cortical fisting, and increased deep tendon reflexes. Five years old patient was spastic quadriplegic. Analysis of urine and blood aminoacids, urine organic acids, tandem mass spectrometry, and lysosomal enzymes were normal. Magnetic resonance imaging of the brain showed enlargement of lateral and third ventricles, thinning of corpus callosum, and periventricular white matter volume loss on both brothers. Serum aminoacid analysis of mother disclosed elevated phenylalanine level ($359.1 \mu\text{mol/L}$ ($21\text{--}150 \text{ mmol/L}$)) cleared the diagnosis of maternal hyperphenylalaninemia. It's important to treat hyperphenylalaninemia to prevent pregnancy complications and embryopathy and undiagnosed women with hyperphenylalaninemia, unknowingly at risk for producing offspring with maternal phenylketonuria embryopathy.

P268 - 2073

Very long-chain fatty acids in patients with various central nervous system disorders

Stradomska TJ, Jamroz E, Paprocka J, Syczewska M. Department of Biochemistry, Radioimmunology and Experimental Medicine, The Children's Memorial Health Institute, Warsaw, Poland – justyna.paprocka@interia.pl

Background: Very long-chain fatty acids (VLCFA; $>\text{C}22:0$; $\text{C}24:0$, $\text{C}26:0$) incorporated in lipid compounds forming structure of the nervous system. Degradation of VLCFA are placed exclusively in peroxisomes. Detection of increased VLCFA levels in blood is a key biomarker for peroxisomal diseases, manifested by severe neurological signs (demyelination, epilepsy). **Purpose:** The aim of the study was to examine serum VLCFA in patients in developmental age with various central nervous system disorders. **Methods and patients:** Serum VLCFA was examined in 50 children (35 males and 15 females) aged from 2 months to 9 years. The children were diagnosed with refractory epilepsy $N=21$ (refractory symptomatic epilepsy: $N=18$, refractory epilepsy of unknown etiology: $N=3$), congenital brain abnormalities ($N=12$), developmental delay $N=11$, progressive encephalopathy $N=4$, cerebral palsy $N=2$. Serum VLCFA levels was detected by gas chromatography method. **Results:** The data show increased $\text{C}24:0/\text{C}22:0$ ratio and decreased $\text{C}22:0$ concentration in comparison to normal values at significant levels in investigated group.

P269 - 2062

Phenotypic variability in x linked adrenoleukodystrophy through clinic experience

Pomeran C, Tarta O, Motoescu C, Burloiu C, Barca D, Craiu D. "Prof. Dr. Al. Obregia" Hospital, Clinic of Pediatric Neurology, Bucharest, Romania – cristina.pomeran@yahoo.com

Motivation: X linked adrenoleukodystrophy (XALD) is a peroxisomal disorder caused by accumulation of very long chain fatty acids in plasma and various tissues. The most affected organs are cerebral white matter, adrenals and testis. The disease results from inactivating mutations on ABCD1 gene, located on Xp28 chromosome. The only effective treatment are bone marrow transplantation, during the pre-symptomatic phase of the disease, and just recently, hematopoietic stem cells gene therapy. Early diagnosis is essential for the possible therapeutic interventions. **Objectives:** To highlight the phenotypic variability among patients diagnosed with XALD. **Material:** Our case-study refers to a group of 8 patients diagnosed in our clinic for XALD during the last 5 years. Patients are 4 to 15 years old males at first presentation. Two patients are brothers, but the rest of them are unrelated. For all of them, the XALD diagnosis has been assessed in terms of clinical manifestations, biochemical features, magnetic resonance imaging (MRI) and spectroscopy (MRS) results. Personal and family history records have been also considered. Based on our observations and some correlations with the current literature we have succeeded to emphasize some connections between MRI/MRS findings and the clinical course of the disease. **Conclusions:** Only one patient was diagnosed in the pre-symptomatic phase. For all the others, bone marrow transplantation was not an option. All patients have had the onset of symptoms at the ages between 4 to 9 years. Five patients were diagnosed with adrenal insufficiency. One of them associated IGF1 deficiency, and also extensive cerebral calcifications. Another patient had familial phenotypic variability. For all our patients we found the same correlation between MRI findings and clinical course as currently accepted in the literature. The group exhibited a variety of clinical, biochemical and imaging features. Some unusual biochemical, imaging and familial peculiarities have been also revealed.

P270 - 2046

Therapeutic effects in tardive phase of cerebral folate deficiency

Tarta-Arsene O, Moisa G, Leanca M, Avram P, Tabacaru R, Craiu M. Pediatric Neurology Department, Clinical Hospital 'Al Obregia', Bucharest, Romania – otartaarsene@yahoo.com

Purpose: Cerebral folate deficiency is a progressive neurological disease associated with low cerebrospinal fluid 5-methyltetrahydrofolate in the presence of normal folate metabolism outside the nervous system. The authors will present the clinical response of therapy after 11 years of evolution of the disease. **Methods and results:** Anton is a 18 years old boy, with gradual onset of a diskinctic movements from the age of 7, initially as postural tremor of the left upper limb, then as generalized tremor. The movement disorder was progressive, so at the age of 17, he had a combined abnormal movements as truncal dystonia and asymmetric chorea of the limbs. The cerebral MRI was normal. It was excluded: Wilson disease, systemic lupus eritematosus, chronic exposure to toxics, infectious disease. Analysis of CSF showed deficiency of cerebral folate. After the anesthesia for cerebral MRI, he developed an acute respiratory deficiency and he needed oro-tracheal intubation and artificial ventilation. At that moment, he started treatment with folic acid, first intravenously, than orally, with semnificative clinical improvement from the first day (decreasing of amplitude and frequency of diskinctic movements). In the present time, after 12 months he is at home with motor autonomy with slight diskinctic

netic movements. **Conclusions:** The cerebral folate deficiency is a drug-responsive disease, even in a late diagnosis.

P271 - 1523

Acquired infantile bilateral striatal necrosis: a rare yet treatable disorder

Scott O, Hartfield D, Tang-Wai R, Goetz H. *Faculty of Medicine and Dentistry, University of Alberta, Edmonton, Canada – goez@ualberta.ca*

Introduction: Acquired Infantile Bilateral Striatal Necrosis (IBSN), is a rare entity manifesting as a movement disorder and basal ganglia imaging abnormalities, often following an infection. The pathophysiology of IBSN is not clearly understood; however, a defect in biotin metabolism has been implied in its aetiology. This is the case of a patient who was diagnosed with IBSN and treated with biotin successfully. **Case description:** A previously-healthy 4-year old boy presented with decreased level of consciousness and involuntary movements following febrile pharyngitis. Neurological examination showed a decline in mentation, posturing of left extremities, and involuntary tongue movements. Deep tendon reflexes were brisk and clonus was elicited in the lower limbs. Babinski and Hoffman reflexes were positive on the left, as well as Palmomental, Glabellar and Snout reflexes. Patient was started on Ceftriaxone, Vancomycin and Acyclovir, all of which were discontinued after cultures and serology returned negative. Laboratory workup was unremarkable, except for mild protein and WBC elevation in CSF. Brain MRI revealed cortical edema, which subsequently subsided, and abnormal signals in the lentiform and caudate nuclei bilaterally, which became more prominent over the next week. The patient's movement disorder persisted, with fluctuating level of consciousness (GCS 6–12). As IBSN was suspected, he was started on biotin, resulting in significant improvement. The patient was discharged after 9 days of treatment, being able to walk, feed and talk although articulation was still deficient and there was mild left arm dystonia. Brain imaging prior to discharge showed significant improvement in the T2 hyperintensity within the basal ganglia. **Discussion:** Due to its rarity, the diagnosis of Acquired IBSN is not commonly considered. We suggest physicians consider IBSN in patients presenting with acute movement disorder following febrile infections, as timely treatment with biotin is effective and may result in rapid improvement.

P272 - 1756

Molybdenum cofactor deficiency: four cases from Turkey

Gencpinar P, Duman O, Akcakus M, Karaali K, Ichida K, Haspolat S. *Akdeniz University Medical Faculty Department of Pediatric Neurology, Antalya, Turkey – pinargencpinar@yahoo.com.tr*

Introduction: Molybdenum cofactor deficiency is an inborn error of metabolism, which characterized severe mental-motor retardation, feeding difficulties and refractory seizures. The patients may be misdiagnosed such as hypoxic-ischemic encephalopathy because of their clinical features and MRI findings. We present clinical, radiological and genetic features of four Turkish patients diagnosed in early infancy. **Patients:** The first patient was five-day old male and presented with vomiting, poor feeding and fever. He had hypouricemia (0.1 mg/dl) and his urine sulfite level was positive. There was a diffusion limitation of cortical gray matter and basal ganglia in his magnetic resonance imaging. Homozygous gene mutation was found in gene MOSC1. The second case was a fifth month boy and presented with focal febrile tonic convulsion. Serum uric acid level was low (0.1 mg/dl). Urine sulfite level was positive. There were hyperintense lesions in bilateral cerebellum and globus pallidus. Bilateral lens subluxation was determined. He has homozygous in the MOSC2A and heterozygous mutations in the MOSC1. The third case was a five-month boy and pre-

sented tonic-clonic seizures. Serum uric acid level was low (0.2 mg/dl). There was a diffusion limitation of cortical gray matter. He has a homozygous mutation in the gene MOSC2A. The last case was male newborn and presented poor feeding, convulsions, bradycardia and hypotonicity. He had hypouricemia (0.2 mg/dl) and his urine sulfite level was positive. In his clinical follow-up, he was operated due to pyloric stenosis. There were subcortical and cortical cystic encephalomalacic changes in the bilateral cerebral white matter. He has homozygous MOSC2 mutation. **Conclusion:** Serum uric acid levels should be performed in all patients, who have clinical features such as hypotonia, hypoxic-ischemia-encephalopathy, intractable seizures after birth and motor-mental retardation and have the MRI findings supported hypoxia or diffusion limitation especially in our country because of high frequency of consanguinity.

P273 - 1998

TH-negative infantile-onset severe dopamine deficiency syndrome

Ng J, Tuschl K, Csanyi B, Kinali M, Devlin A, Carr LJ, Cleary M, Manzur AY, Gissen P, Garcia Cazorla A, Artuch R, Clayton PT, Heales SJR, Kurian MA. *Neurosciences, UCL- Institute Child Health, London, UK – j.ng@ucl.ac.uk*

Objectives: Defects in monoamine biosynthesis present with a range of childhood onset movement disorders associated with cerebral dopamine deficiency, and include Tyrosine Hydroxylase (TH) deficiency. This autosomal recessive disorder is caused by pathogenic mutations in the TH gene and has a biochemical hallmark of isolated low CSF Homovallinic acid (HVA) and low HVA:HIAA ratio (<1.0). Children with TH deficiency are categorised into 2 clinical phenotypes: infantile onset progressive hypokinetic rigid syndrome with dystonia (type A) and complex encephalopathy with neonatal onset (type B). We present a cohort of patients with TH-negative infantile-onset severe dopamine deficiency syndrome that mimic type B TH deficiency. **Methods:** Children presenting with an infantile-onset movement disorder were identified from UK and Spanish National Neurotransmitter Centres. Those with isolated low CSF HVA and negative for TH gene mutations were included for study, and clinical phenotype and neuroradiological features were delineated. **Results:** Eleven infants (6 males) were identified with an isolated low CSF HVA (range 13–73% lower limit of normal). Three infants were from 2 consanguineous families. 9/11 had a severe neonatal hypoxic ischaemic encephalopathy-like presentation but only 1 had significant abnormalities on MRI. Neonatal apnoeas were observed in 9/11 of whom 8 required ventilation. All had features of a generalised dystonic movement disorder with axial hypotonia and contractures in 4 infants. 8/11 infants had a trial of L-dopa with variable responses; sustained (1), partial response with improved motor function (5) and no response (2). 5 died due to respiratory insufficiency. **Conclusion:** These infants present with a life-threatening severe dopamine deficiency syndrome which appears distinct to TH deficiency with early death reported in just under half of the cohort. Possible pathogenic mechanisms in TH-negative infantile-onset dopamine deficiency syndrome include abnormal dopaminergic cell differentiation, impaired dopamine synthesis, dopamine receptor defects and dopaminergic tract degeneration. Future work is likely to identify the underlying genetic defect(s) in this cohort.

P274 - 2135**Acetyl Co A deficit: first prenatal diagnosis. Biochemical, molecular and ultrasound data in an affected fetus**

Pitelet G, Paquis V, Trastour C, Chami M, Rouzier C, Huppke P, Giuliano F. *Pediatric Hospital CHU-Lenval, Nice, France – pitelet.g@pediatrie-chulnval-nice.fr*

Acétyl CoA deficit: first prenatal diagnosis. Biochemical, molecular and ultrasound data in an affected fetus. Acetyl Co A deficit, AT-1, is a newly described anomaly in copper metabolism. Common biological hallmark, low plasma copper and ceruloplasmin is shared with the other inherited copper metabolism diseases previously known as Menkes, Wilson and aceruloplasminaemia. The inheritance is autosomal recessive and the implicated gene, SLC33A1, located in 3q25 has been identified by Huppke et al. [2011] and encodes for a ceruloplasmin transporter. AT-1 is responsible for severe developmental delay. Clinical signs probably begin during prenatal period, patients presenting with congenital cataract at birth. Cerebellar hypoplasia and deafness are also associated. The outcome remains fatal in early childhood. Only five patients, four from consanguineous families, have been described so far, but no prenatal diagnosis has been performed. We proposed a prenatal diagnosis for one of these families who already had 2 siblings dead from AT-1 deficit, and we present here our biochemical, molecular and ultrasound data from the fetus that happened to be affected.

P275 - 1996**Creatine transporter deficiency – a rare cause of developmental delay and seizures**

Funston LA, Peake D, O'Sullivan S, Flynn P. *Royal Belfast Hospital for Sick Children, Neurology Department, UK – lesley_annfunston@hotmail.com*

Introduction: Creatine deficiency is a rare but sometimes treatable cause of developmental delay and seizures, accounting for approximately 1–2% of males with intellectual disability. Disorders are autosomal recessive (creatine synthesis) or x-linked (creatine transport deficiency) and suspected following MR spectroscopy indicating markedly reduced creatine peak. We report the case of a male infant with creatine transporter deficiency. **Case:** History A 20 month old boy presented following a prolonged left focal motor seizure. He was an only child of non-consanguineous parents with a history of one simple febrile seizure aged 11 months. Gross motor and speech and language delay was noted 2 months prior to admission. He was crawling at 12 months, standing independently from 15 months but not walking independently, babbling but no words. There was no history of regression. He was macrocephalic (>90th percentile) with increased tone and pyramidal signs. Investigations MRI showed mild cerebellar vermian atrophy with diffusion restriction in the right internal capsule and corticospinal tract. Magnetic resonance spectroscopy (MRS) showed a markedly reduced creatine peak. Biochemical testing indicated increased urine creatine/creatinine ratio with normal guanidinoacetate, confirming creatine transporter deficiency. Genetic confirmation of SLC6A8 gene is awaited. EEG showed slow waves in the right temporal occipital region. **Treatment:** Treatment of creatine transporter deficiency is challenging with little objective, but some subjective evidence of neurodevelopmental improvement. In our case creatine, L-arginine and L-glycine were commenced. Objective neurodevelopmental outcome will be observed. Sodium valproate was started after a second nocturnal prolonged left focal seizure. **Conclusion:** This case presents the classical picture of developmental delay, macrocephaly and seizures associated with x-linked creatine transporter deficiency. We recommend MRS be considered in all children presenting with this pattern of developmental delay and seizures. Genetic confirmation can alter

management and guide with respect to prognosis. Case reports of this condition are limited.

P276 - 1590**Evaluation of the efficacy of Glycosade on epilepsy in 2 children with glucose transporter GLUT-1 deficiency**

Coppens S, Van Bogaert P. *Clinique de neurologie pédiatrique, Hôpital Erasme, Brussels, Belgium – sacoppen@ulb.ac.be*

Introduction: GLUT-1 deficiency syndrome (DS) is a cause of refractory epilepsy, often accompanied by developmental delay or mental retardation. Ketogenic diet is the gold standard treatment (KD), but is not always effective and tolerance can be difficult. One study demonstrated that seizures and EEG discharges are more frequent in the fasting state in GLUT1 DS. De Meirleir et al investigated the clinical efficacy of Glycosade, an high-amylopectin-containing cornstarch, in two patients, but without EEG seizure quantification, with encouraging results. **Objectives:** Evaluate the efficacy of Glycosade on clinical and EEG seizures in patients with refractory epilepsy secondary to GLUT1 DS. **Patients and methods:** Two patients were included, with genetically proven GLUT-1 DS, refractory epilepsy (absence seizures), mental retardation, and ineffectiveness or unacceptable side effects of KD. Seizure frequency was quantified by long term video-EEG monitoring, before and after the intake of Glycosade (2x30g) at short and long term. Blood glucose measurements were also obtained. **Results:** In patient 1, we did not observe a reduction in seizure quantification nor in the first days of administration of Glycosade, nor at one month of administration. In patient 2, we did not observe a decrease in seizure quantification in the first days, but we observed a 85% decrease of seizure number at month 3. We then stopped the administration of Glycosade and observed a return to baseline for seizure number. In both patients, we observed a stabilisation of glycaemia in the preprandial period at lunchtime. **Conclusions:** We have observed a significant decrease in seizure number after 3 months of administration of Glycosade in one patient. It would necessary to investigate several other patients. Glycosade could be an alternative treatment for refractory epilepsy in GLUT-1 deficient patients when ketogenic diet is ineffective or has intolerable side effects.

P277 - 1748**Usefulness of the ketogenic diet for metabolic diseases in children**

Uchikawa H, Takagi A, Mizuochi H, Suyama M, Fujii K. *Department of Pediatrics, Chiba University Graduate School of Medicine, Japan – woochikawa@yahoo.co.jp*

Objective: The ketogenic diet is known as the therapy for intractable epilepsy. But for metabolic diseases such as glucose transporter type 1 deficiency syndrome (Glut1 DS) and pyruvate dehydrogenase complex deficiency (PDHC deficiency), this diet which provides an alternative source of fuel is the important therapy. We report on the effectiveness of this diet for these diseases. **Material and methods:** Case1; A Japanese 1-year-old boy was diagnosed with Glut1 DS. He had the onset of recurrent generalized tonic seizures in the one month of age. While blood glucose was 107 mg/dl, CSF glucose was 25 mg/dl. In the genetic analysis, we identified c.517-2A>G mutation in the GLUT1 gene. The ketogenic diet with ketone index 2.9 started in the 2 months of age. Case 2; A Japanese 1-year-old girl was diagnosed with PDHC deficiency. She has severe developmental delay. Brain MRI revealed ventriculomegaly and agenesis of the corpus callosum. Blood lactate level was 85.7 mg/dl and pyruvate was 7.37 mg/dl, which were both elevated, but lactate/pyruvate ratio (11.6) was normal. We subsequently identified c.729 delC mutation in her PDHA 1 gene. We then started the ketogenic diet with ketone

index 2.3 at the 9 months of age. **Results:** Case 1; After starting the ketogenic diet, he achieved seizure freedom and CSF glucose was elevated in 37 mg/dl (blood glucose: 81 mg/dl). Developmental level is almost normal. Case 2; Blood lactate and pyruvate were quite decreased in 17.5 mg/dl and 0.95 mg/dl, respectively. Following reduction of the sleeping hours, she got active and showed smile at 18 months of age. Moreover, deterioration of brain atrophy has been stopped. **Conclusions:** The ketogenic diet is useful for the treatment of metabolic diseases. Early diagnosis and induction of the ketogenic diet are important for metabolic diseases especially in Glut1 DS and PDHC deficiency.

P278 - 1879

“Cetojaime.com”: A new shared website to simplify the calculation, the education, and to diversify the ketogenic diet

de Saint-Martin A, Burger MC, Vincent D. *Centre référent des épilepsies rares associé, Pédiatrie 1, Hôpitaux Universitaires de Strasbourg, France – anne.desaintmartin@chru-strasbourg.fr*

The efficacy of ketogenic diet is now recognized for some refractory childhood epilepsies and metabolic diseases, especially GLUT1 deficiency. However its application remains very constraining for the child, the parents, and time consuming for dietitians. With the help of website designers, of specialized dietitians of the French Society for Inborn Metabolic Diseases, and parents, a new website was created, online since November 2012. This protected website is open to specialized dietitians and parents in French neuropaediatric and metabolic pediatric centers. This website contains a large evolutive nutriment database (fresh and industrial food), and a large recipes database (different ratios), with video illustrations. In each center the dietitian becomes an administrator, can easily open new logins for each family, and has a rapid overview of all her patients. An electronic calculator helps to calculate or modify quickly the daily portion of the child. This tool is also helpful for the education. The parents can use the compatible recipes, easily transform recipes with different ratio, and create new ones. An electronic menu composer helps to calculate the right caloric portions of the ketogenic recipes. They can memorize all their meals and recipes on their session. As many parents have a large inventiveness, they can share their new recipes under the control of the dietitian. The use of this website, in several French centers really helps the dietitians, with a reduction of the duration of the education and calculation time. Most of the parents use this friendly tool daily and are usually glad to diversify their menus, according to their child palate. The access of the website is free, and we hope to continue its diffusion in France, and, why not, create English or German versions ...

P279 - 1864

Myopathic alterations in children and adults with glycogen storage disease type I and III

Sentner CP, van der Hoeven JH, Maurits NM, Verbeek RJ, Smit GPA, Sival DA. *Department of Pediatrics, Beatrix Children's Hospital, University Medical Center Groningen, University of Groningen, the Netherlands – d.a.sival@umcg.nl*

Background: Glycogen Storage Disease (GSD) concerns a group of autosomal recessive inheritable metabolic disorders resulting in abnormal glycogenolysis or glycogen synthesis. GSD I & III are characterized by liver-bound glycogen storage. Consequently, glycogen is stored in liver tissue and becomes unavailable for metabolic demand. GSD may result in neuromuscular alterations, but details are lacking, so far. In pediatric and adult GSD I & III, we aimed to elucidate neuromuscular involvement. **Patients and methods:** In 26 GSD I & III patients [12 children and 14 adults, aged: 7 (2–17) and 31 (18–42) years, respectively;

median (range)], we evaluated cross-sectional neuromuscular parameters [consisting of 1. sensory and motor nerve conduction assessment (EMG), 2. dynamometry (>4 years of age) and 3. muscle ultrasound assessment (muscle ultrasound density (MUD)]. Muscle force and MUD were expressed as Z-scores (corrected for gender and age). We associated neuromuscular GSD outcomes with metabolic parameters (by international metabolic GSD guidelines). **Results:** In GSD children and adults, sensory and motor nerve conduction was normal. In pediatric GSD, muscle force was decreased with a proximal to distal distribution (Z-scores <–2 SD; GSD III insufficient data >4 years) and MUD was increased (Z-scores >2.0 SD and >1.5 SD, for GSD I & III, respectively). Pediatric neuromuscular GSD outcomes were associated with parameters for metabolic derangement ($p < 0.05$). In GSD adults, muscle weakness persisted (more pronounced in GSD III than GSD I; $p < 0.05$), whereas metabolic conditions had stabilized. In GSD III patients, muscle weakness concurred with increased MUD ($p < 0.05$) and revealed an age-related deterioration ($r = .83$). **Conclusions:** In GSD I & III children, metabolic derangement can induce myopathic signs, implicating that muscle-tissue participates in glucose homeostasis during metabolic demands. Especially GSD III adults reveal additional signs of age-related myopathic disease progression, which occur independent of the metabolic condition.

P280 - 1775

Neurophysiological features in congenital disorders of glycosylation

Cusmai R, Pro S, Balestri M, Moavero R, Dionisi Vici C, Bevivino E, Vigeveno F, Martinelli D. *UOC Neurologia, Ospedale Pediatrico Bambino Gesù IRCCS, Rome, Italy – raffaella.cusmai@opbg.net*

Objectives: Congenital disorders of glycosylation (CDG) are a group of rare metabolic disorders with a widely variable phenotype. The clinical picture includes psychomotor delay, dysmorphic features, hypotonia, visual defects, disorders of coagulation. Epilepsy in CDG has been rarely studied, but it represents a frequent feature of this disease. The objective of this study is to analyze the electroclinical features of children affected by CDG type I. **Methods:** We retrospectively reviewed the complete clinical history of 9 children diagnosed with CDG type I. We analyzed their ictal and interictal EEG features, as well as the evolution of epilepsy, paying particular attention to age at onset and seizures' semiology. **Results:** All but one children presented epilepsy as the first symptom of their disease. Age at onset was widely variable, ranging from 3 weeks and 4 years of age. Two out of 9 children presented with infantile spasms, 1 partial migrating seizures, and 4 infants presented generalized seizures, initially with fever. One patient presented tonic clonic generalized seizures without fever at the onset. Interictal EEG showed multifocal epileptiform abnormalities. **Conclusions:** The epileptic phenotype appears to be highly variable, as well as the clinical course of the disease. In our patients the severity of the epileptic outcome appeared to be related to earlier age at onset.

P281 - 1761

Neurological presentations of nutritional vitamin B12 deficiency in infants

Pöder H, Part R. *Tallinn Children's Hospital, Estonia – haide.poder@lastehaigla.ee*

Vitamin B12 is the collective term for a group of chemical substances known as cobalamin. It has an important role as cofactor in homocysteine (Hcy), methylmalonic acid (MMA) and folate metabolism. Vitamin B12 is essential for cell division and tissue repair, the formation of red blood cells, synthesis mediators and myelin in central nervous system. The most frequent cause of

cobalamin deficiency in infants is poor nutrition. There are no specific symptoms for cobalamin deficiency. In the first year of life neurological manifestations are more frequent. Metabolic errors Hcy and MMA are strongly correlated to serum cobalamin, whereas the relation to serum folate is weak or absent. **Objectives:** To evaluate the main reason, neurological characteristics and laboratory abnormalities of infants with vitamin B12 deficiency. **Material and methods:** Cases of infants with B12 vitamin deficiency who had been hospitalized in the department of newborns and infants of Tallinn Children's Hospital during the 2012 were analysed. **Results:** All 56 infants who had been diagnosed vitamin B12 deficiency were breastfed. The average age at diagnosis was 5 months. The most frequent clinical symptoms were: irritability and disturbance of sleep occurred in 30 cases (53.6%); abnormal movements such as tremor, twitches etc in 17 cases (30%); developmental delay in 14 cases (25%). All patients had considerable decrease cobalamin level in serum accompanied by errors Hcy in 20 and MMA in 27 cases. The neurological manifestations and metabolic errors withdrew after vitamin B12 supplementation. **Conclusions:** Nutritional vitamin B12 deficiency among infants is an important health issue. Frequent manifestations are different neurological symptoms with metabolic errors. Timely diagnosis and treatment are presumptions to avoid irreversible damage of the nervous system. Nutritional vitamin B12 deficiency in infants can be avoided by mothers' adequate nutrition during pregnancy and breastfeeding.

P282 - 1760

The hyperhomocysteinemia in children treated by antiepileptic drugs

Winczewska-Wiktor A, Steinborn B. *Chair and Department of Developmental Neurology, University of Medical Sciences, Poznan, Poland*

Aim: The aim of study was to assess the relationship between the use of antiepileptic drugs and the variation found in the peripheral blood homocysteine (Hcy) level and estimate the percentage of patients with hyperhomocysteinemia (hHcy) in the pediatric population from the region of Wielkopolska, Poland. The final goal was to assess the validity of supplementation with folic acid and vitamins B6 and B12 at the start of therapy with antiepileptic drugs. **Material and methods:** In the study were 249 children aged from 1 to 18 years of age. 150 were treated with antiepileptic drugs. 140 suffered from epilepsy, of whom 122 received antiepileptic drugs. In 109 people has not been confirmed or excluded the diagnosis of epilepsy earlier diagnosis. In the group of patients without epilepsy, 28 were treated with antiepileptic drugs. The results were analyzed statistically (Chi2 test, Mann-Whitney test, two-sided Fisher's exact test, Spearman rank correlation). **Results:** The mean concentration of Hcy in the entire group was 11.00 ± 5.9 mmol/l. The percentage of patients with hHcy was 33% in the whole group. There was no statistically significant difference in mean serum Hcy and the percentage of patients with hHcy in both the treated and not treated with AEDs, as well as in patients with and without epilepsy. There were no clinically significant relationship between the drug and the occurrence of hHcy. **Conclusions:** There was no statistically significant relationship between the average concentration of Hcy and the proportion of patients with hHcy and the use of AEDs. None of the analyzed antiepileptic drugs did not affect significantly the concentration of Hcy in both observed groups. The obtained results do not allow the recommendation of routine supplementation with folic acid and vitamins B6 and B12 at the start of antiepileptic therapy.

P283 - 1746

Atypical presentation of a urea cycle disorder due to a homozygous mutation V622M in CPS1

Michaeli-Yosses Y, Lev D, Lerman-Sagie T. *Nes Ziona, Israel – yaelyos@gmail.com*

Objective: Carbamoyl phosphate synthetase I deficiency is an autosomal recessive inborn error of metabolism of the urea cycle which causes hyperammonemia. Two forms of carbamoyl phosphate synthetase deficiency are recognized: a lethal neonatal type and a less severe, delayed-onset type. We describe an atypical presentation in two sisters. **Material and methods:** Two sisters, of Samaritan origin, presented at the neonatal period with encephalopathy and hyperammonemia. The ammonia levels normalized following acute medical treatment. The elder sister developed normally, with no special medical treatment or follow-up, until her first labor, during which she developed an acute encephalopathy and elevated ammonia levels. She was admitted to the ICU and was intubated and ventilated. She was treated with dialysis and ammonia scavengers with good response. Ammonia levels normalized and she was discharged in good health and no further treatment. The younger sister was diagnosed with global developmental delay and later with an autistic spectrum disorder; her ammonia levels are consistently mildly elevated. She is currently treated with citrulline. The family noticed behavioral improvement while adhering to a protein restricted diet. **Results:** Metabolic work up showed: high glutamine, very low citrulline and normal orotic acid. Sequencing of the NAGS gene was normal, sequencing of the CPS1 (carbamyl phosphate synthetase) gene showed the mutation: V622M (missense substitution). **Conclusion:** This family demonstrates an atypical clinical presentation of acute neonatal hyperammonemic encephalopathy followed by recovery and a mild course, followed by postpartum deterioration.

P284 - 1564

Children with neurological disorders – when should we look for a neurometabolic disease?

Cvitanovic-Sojat L, Malenica M, Kukuruzovic M, Zigman T, Kuznik K, Tein I, Seneca S, Lissens W, Van Coster R, Lamhonwah AM, De Meirleir L. *Departments of Pediatrics, Department of Neuropediatrics, University Hospital Center Sestre milosrdnice, Zagreb, Croatia – ljerka-cvitanovic-sojat@zg.t-com.hr*

Objectives: To ascertain the presence of neurometabolic/genetic disorders in children presenting with intermittent encephalopathy aggravated by stressors, intractable epilepsy or neurodevelopmental regression. **Material and methods:** Retrospective analysis of clinical data was performed in patients hospitalized at Neuropaediatric Department, UHC Sestre Milosrdnice. **Results:** Primary systemic carnitine deficiency was confirmed in girl presenting with Reye-like syndrome due to homozygosity for single nucleotide deletion of g.17081C in exon 5 of OCTN2 gene. Homozygosity of 845-846delCT in exon 9 of SURF1 gene was found in girl with psychomotor delay, lactic acidosis and leukodystrophy. Diagnosis of Niemann Pick type C was confirmed by mutations c.2764 C>T (Gln922X) and c.3467 A>G (Asn1156Ser) in siblings who showed regression, ataxia and intractable epilepsy. Mutation in exon 4-5bp deletion (c.881-905del25) of the MECP2 gene was found in girl with autistic behaviour, mental deterioration and epilepsy. Homozygosity for c.502G>T substitution in exon 7 of ASAH1 gene was confirmed at boy with Farber lipogranulomatosis with joint swelling, neurological deterioration, myoclonus and cherry-red spot. A boy with elevated creatine kinase and intermittent muscle pain had m.5522G>A mutation in the MT-TW gene of the mitochondrial tRNA for tryptophan. Other diseases that were diagnosed for the first time in our region included: methyl malonic aciduria mut(o) form; Menkes

disease with a frameshift mutation c.1003_1004insGCAT in exon 4 of the ATP7A gene; Angelman syndrome with microdeletion or paternal uniparental disomy at 15 q11.2-q13; Mowat Wilson syndrome with frameshift (1352 delC exon 8) or truncating mutations of ZFXH1B gene. **Conclusion:** Intermittent encephalopathy precipitated by stressors, intractable epilepsy or neurodevelopmental regression should lead to a prioritized investigation for an underlying (neuro)metabolic/genetic disorder and require collaboration with specialized laboratories. All cases and their genetic mutations were novel diagnoses for Croatia. It is important to recognize these metabolic disorders early, as treatments are available for some with favourable outcomes.

P285 - 1521

Unknown leucodystrophy case at 11 months old girl: case report

Jaxybayeva A. National Research Center for Mother and Child Health, Astana, Kazakhstan – altynhash@gmail.com

Background: Leukodystrophy refers to a group of disorders characterized by dysfunction of the white matter of the brain. The leukodystrophies are caused by imperfect growth or development of the myelin sheath, the fatty covering that acts as an insulator around nerve fibers. Myelin, from which the white matter of the brain takes its colour, is a complex substance made up of at least ten different chemicals. Each of the leukodystrophies is the result of a defect in the gene that controls the production or metabolism of one (and only one) of the component molecules of myelin. **Purpose:** description of the case which we met one year ago. **Case report:** 11 month old girl was admitted to our hospital with total muscular weakness, consciousness disturbance (a very poor reaction to assessment). She was directed to MRI assessment from admission room. On MRI we found a very unusual picture with total destruction of white matter. Two days after admission she developed a coma for next three weeks. After that her consciousness was improved. She started react on pain stimulus and light. She had no problem with birthing but can't eat (swallow). EEG assessment showed a flat wave activity. Organic acids at urine did not detect any typical pathology. Genetically assessment on Canavan disease was not done. The girl was discharged to home and was died after 6 months. During last 6 months of her life were not reported any improvement in her condition. **Discussions:** we still have a big question about diagnosis of this girl? It was not a typical Canavan disease but definitely she had some kind of neurodegenerative disorder.

P286 - 2065

5-year follow-up in hematopoietic stem cell transplantation in 2 patients with late-infantile metachromatic leukodystrophy in comparison to an untreated cohort

Kehrer C, Groeschel S, Doering M, Krägeloh-Mann I. Department of Pediatric Neurology & Developmental Medicine, University Children's Hospital, Tübingen, Germany – Christiane.Kehrer@med.uni-tuebingen.de

Objective: While patients with juvenile Metachromatic leukodystrophy (MLD) are reported to benefit from hematopoietic stem cell transplantation (HSCT) when performed in an early stage, there is no consensus concerning treatment in late-infantile (LI) MLD. We report on 2 girls with LI MLD after infantile HSCT. **Patients and methods:** Diagnosis of LI MLD was done preclinically (4 months/prenatal) in both girls (now 75 and 51 months old) due to affected siblings. HSCT was performed at the age of 9 months. Relevant hematological complications did not occur. Outcome 5.5 and 3.5 years after HSCT was compared with natural course data of 21 untreated patients. Patient 1 additionally suffered from glutaric aciduria. **Results:** Aided walking was possible until the age of 70 (patient 1) and 48 (patient 2) months, while untreated LI

patients lost this significantly earlier (median age 29 months, 90%-percentile 32.2 months). Crawling and head-control was lost at the age of 72 months in patient 1 and is still preserved in patient 2, clearly beyond the untreated group (median age 31 and 33.5 months, 90%-percentiles 35 and 36.4 months). Patient 1 learned 2-word-sentences and is still able to speak single words, patient 2 speaks in whole sentences, while untreated children lost complete speech before the age of 4 years. MRI showed no MLD-typical lesions in patient 1, but in patient 2, mild demyelination was seen at 39 months, clearly later than in untreated controls. **Conclusions:** HSCT in the presymptomatic stage in LI MLD significantly delays onset and alleviates disease progression compared to untreated patients. However, risk and benefits have to be carefully balanced considering a severe and invasive therapy.

Neuromuscular disorders

P287 - 1966

Pompe disease (PD): clinical outcome in infants and children treated with recombinant human acid alpha-glucosidase (rhGAA)

Lianou D, Syrengelas D, Andreou N, Chantzopoulos I, Mavridou I, Michelakakis H. 1st Pediatric Department, "Aghia Sofia" Children's Hospital, Athens, Greece – lianou_d@yahoo.gr

Objectives: To review the efficacy and tolerability of rhGAA in treatment of PD and to highlight the phenotypic variability of the disease. **Material and methods:** 4 patients with classical infantile-onset (group 1) and 2 patients with non-classical form (group 2) were included in this clinical study. All patients received Enzyme Replacement Therapy (ERT) at the mean age of 3 mo and 17 mo, respectively. A standardized follow-up comprised Alberta Infant Motor Scale (AIMS) for gross motor assessment and left ventricular mass index (LVMI) for cardiac evaluation. **Results:** Group 1: 3/4 died. One patient (pt) died shortly after diagnosis after having received 2 doses of ERT. The second pt died after 18mo of treatment, though ERT was initiated early (2½ mo). The third pt, in an advanced stage of disease and delayed initiation of treatment (9 mo), survived beyond 2 y, after an initial improvement and stabilization. All pts showed a clinically meaningful improvement in cardiac function, with a steady decrease in LVMI. Normalization of cardiac parameters was seen in 1/4. All infants acquired motor skills, like sitting unsupported, although remained below 5th centile on the AIMS. The survivor is now a walker (2 year of age now). Group 2: ERT was initiated at 15 mo and 19 mo in 2 pts with non-classical form. Both showed AIMS scores on 95th centile, but one of them subsequently exhibited a steady decline of motor functions, with overt signs of myopathy after 5 years of treatment. Cardiac assessment showed normalization of LVMI after 12mo of treatment. No signs of decline were noted in the second pt. Only 1/6 pt experienced moderate infusion-associated reactions. **Conclusions:** Our results indicate beneficial effects of ERT on cardiac muscle, however the effect on skeletal muscles is extremely variable and less consistent. ERT clearly prolongs overall survival, as compared to untreated historical cohort.

P288 - 2100

A novel mutation in SCN4A gene in a patient with an unusual clinical presentation of myotonia permanens – expanding the clinical and molecular spectrum of SCN4A mutations

Ginzberg M, Vinkler C, Leshinsky-Silver E, Sagie Lerman T, Lehmann-Horn F. Pediatric Neuromuscular Unit, Wolfson Medical Center, Holon, Israel – mira_g@netvision.net.il

Congenital myotonias are a group of hereditary muscle disorders

that present in infancy and childhood, characterized by impaired muscle relaxation following a voluntary forceful contraction. The core symptoms either relate to myotonia or to periodic weakness. These disorders are caused by mutations in the genes encoding the skeletal muscle chlorides, sodium and calcium channels. We report a 7-year old boy with a severe early onset phenotype of myotonia permanens presented with neonatal respiratory failure, requiring mechanical ventilation and recurrent episodes of laryngospasm during infancy. Massive general muscle hypertrophy was present since early childhood, as well as eye lid myotonia and prolonged hand grip relaxation. Tongue hypertrophy was noted during infancy and reoccurred again after surgical resection. Clinical, biochemical, electrophysiology and genetic analysis of the proband and his parents were performed. A novel V717G mutation in SCN4A was identified in the proband, but not in his parents. This is the first case of myotonia permanens reporting recurrent tongue hypertrophy as a clinical feature in this disorder. Tongue hypertrophy results most probably from continued tongue contraction caused by his permanent myotonia. The novel mutation found in SCN4A in this case is suspected as the disease causing mutation, being located in a well conserved area of the gene and being absent in his parents. The mutation is located in the transmembrane helical part of the Sodium channel protein subunit. This mutation has not been described previously in SCN4A related disorders. This case further expands the genetic and clinical spectrum of myotonia permanens.

P289 - 2042

Merosin-deficient congenital muscular dystrophy type 1A (MDC1A): a case report

Graf von Kalckreuth C, Deconinck N, Goedseels J, Neuman A, Chevalier E, Kadhim H, Lê PQ. *Pediatric department, Etterbeek-Ixelles Hospital, Brussels, Belgium – clemenskalckreuth@gmail.com*

Congenital muscular dystrophies comprise a genetically and clinically heterogeneous group of disorders characterized by early onset of progressive muscular weakness. MDC1A is an autosomal-recessive condition and the commonest form of congenital muscular dystrophy in the European population with an estimated prevalence of 1/30,000. We report the case of a male newborn directly admitted after birth to our neonatology unit for general hypotonia. He is the third child of a Caucasian couple with two healthy siblings born at term. The mother's medical and obstetrical histories revealed hypothyroidism treated by levothyroxine and mild placental abruption in the third trimester respectively. The infant was born at term by vaginal delivery with an Apgar score of 5/6/9. His birth weight was 4.31 kg. Physical examination showed a floppy infant with generalized weakness and areflexia. Contact was excellent. Complementary investigations showed forty-fold increase of creatine-kinase level (19,241 UI/l), typical electromyographic signs of denervation, and muscle biopsy's merosine deficiency. Genetic analysis confirmed heterozygous mutations in the LAMA2 gene. Nevertheless, parental analysis is pending. Furthermore, neuroimaging was normal. Management was mainly symptomatic and multidisciplinary including enteral gavage feeding and physiotherapy. MDC1A is a neuromuscular disorder with a very poor prognosis. Respiratory insufficiency often complicates the clinical course and causes death among patients. Most of these patients die during infancy or early childhood. Creatine-kinase levels, electromyography and neuroimaging are important preliminary examinations, but the immunohistochemical analysis of a muscle biopsy is of utmost importance. Genetic and molecular analysis is of paramount importance to offer genetic and prenatal counseling to affected families. As there is no specific treatment management remains symptomatic.

P290 - 1926

Nine years experience in SMA – the basis for Romanian National Registry

Butoianu N, Barca D, Sandu C, Cimponeriu D, Stavarachi M, Toma M, Iliescu C, Burloiu C, Budisteanu M, Tarta-Arsene O, Minciu I, Craiu D. *Pediatric Neurology Department, Al. Obregia Hospital, Bucharest, Romania – nbutoianu@yahoo.com*

Aim: Spinal muscular atrophies are a group of neuromuscular disorders, which can now be reliably diagnosed by identifying homozygous deletions of SMN1 exon 7, chromosome 5. **Material and methods:** In Romania a National Register has been recently founded having as purpose, the analysis of patients with SMA hospitalized in our department between November 2002 and November 2011. All patients with clinical and laboratory criteria suggestive of SMA have been genetically tested for homozygous deletion of exon 7. Those with identified deletion were classified into SMA type I, II and III using as defining criteria the maximum functioning level achieved. **Results:** Of the 87 enrolled patients 42.5% were phenotype I, 29.9% phenotype II and 27.6% phenotype III. Sex ratio showed that male phenotype was predominant (59.5%) in group I, as for the group II and III females remains predominant (69.2% and 62.5%). Another important parameter is the average age of onset: 2.76 months (SD 2.0) for phenotype I, 10.8 months (SD 2.8) for phenotype II and 23 months (SD 30.5) for phenotype III. Of all patients tested for exon 8 deletion 94% of patients were confirmed in group I, comparing to 82.4% in group II and 70.0% in group III. Deletion of exons 7 and 8 was present in 70% of patients, data similar to those reported in other European countries. In patients tested for NAIP gene (exon 5), deletion was identified in 35.9%. Of these, deletion was present in 48.3% phenotype I, 25% phenotype II and 26.3% phenotype III patients. **Conclusions:** In Romania there is no current data regarding incidence and prevalence of SMA patients and there are no studies regarding clinical features and natural evolution of the disease. For this purpose National Register collects demographical, clinical, genetic and disease evolution data and allows patients to participate in clinical trials.

P291 - 2006

Preliminary data of National Romanian Registry of DMD patients

Butoianu N, Sandu C, Iancu D, Neagu E, Iliescu C, Barca D, Burloiu C, Budisteanu M, Tarta-Arsene O, Minciu I, Motoescu C, Gherghiceanu R, Barbarii L, Craiu D. *Pediatric Neurology Department, Al. Obregia Hospital, Bucharest, Romania – nbutoianu@yahoo.com*

Introduction: Duchenne muscular dystrophy is a progressive X-linked recessive disorder, with an incidence of approximately 1 in 3500 boys and a prevalence of approximately 1 in 18,000 boys. The purpose of national registry is to realize epidemiological and natural evolution studies, to enable general data collection and also to recruit patients for clinical trials. **Material and methods:** We now have in Romania two registries of DMD patients: DMD Patients Registry coordinated by Parents Association and DMD Patients Registry coordinated by the Ministry of Health. The Ministry of Health registry was built with proper funds as part of a national program of primary intervention in patients with Duchenne-type muscular dystrophy and prevention of hereditary transmission of the disease, all coordinated by the Pediatric Neurology Department from Alexandru Obregia Clinical Hospital, Bucharest. Clinical data comes from different pediatric neurology centers in the country and genetic data are obtained in one specialized laboratory. The information is processed and centralized by two curators, which add in clinical and genetic data, keeping up to date the registry. The collected items are: demographics, onset symptoms, diagnosis, motor function, cognitive level, CK level, muscle biopsy, scoliosis, cardiac and respiratory as-

assessment, molecular diagnosis, medications, ventilator support, enrolling in other registries. They were suggested and highly encouraged by Treat NMD and adapted to our country. The registry provides data for various clinical trials. There are currently 154 registered patients, of whom 118 patients from our Department of Pediatric Neurology, 60% had mutations detected by MLPA, and 10% by sequencing. **Conclusions:** National Register enables centralizing clinical and molecular data for DMD patients, recruitment for clinical trials and appropriate cooperation network (Treat-NMD).

P292 - 1807

Design of a Confirmatory Phase 3, multicenter, randomized, double-blind

Barth J, Reha A, Spiegel R, Elfring GL, Husain M, Peltz SW. PTC Therapeutics Inc., South Plainfield, New Jersey, USA – jbarth@ptcbio.com

Objectives: In ~13% of patients, Duchenne muscular dystrophy (DMD) is caused by a nonsense mutation (nm) in the dystrophin gene. Ataluren is an oral investigational drug designed to promote ribosomal readthrough of premature stop codons in mRNA, leading to production of full-length, functional protein. A confirmatory Phase 3 placebo-controlled study in nmDMD has been designed to assess the efficacy and safety of ataluren 10, 10, 20 mg/kg/day given tid. The study design reflects lessons learned from prior studies and targets a study population to best demonstrate the treatment effect over 48 weeks. **Material and methods:** Key study entry criteria require that patients are male with a nonsense mutation in the dystrophin gene, 7–16 years of age, receiving a stable dose of corticosteroids, screening 6-minute walk distance (6MWD) ≥ 150 meters and below the protocol-specified %-predicted threshold. These criteria were selected based on the results of a retrospective subgroup analysis of patients in the Phase 2b trial of ataluren in nmDMD meeting these criteria, in which the difference between the 10, 10, 20 mg/kg tid dose of ataluren (n=30) vs. placebo (n=31) in mean change in 6MWD over 48 weeks was ~50 meters. In the planned study, 220 patients will be randomized in a 1:1 ratio to placebo or ataluren. The primary endpoint is the 6-minute walk test. Secondary efficacy measures include: timed function tests, quality of life, North Star Ambulatory Assessment, and patient/parent-reported disease-related symptoms and activities of daily living. **Conclusions:** This study will be the largest clinical trial of an investigational drug in DMD and is designed to confirm the treatment effect of ataluren seen in the Phase 2b ataluren trial. This study will provide further knowledge of the natural history of DMD and of the performance and correlations of various outcome measures in a DMD therapeutic trial.

P293 - 2005

Epilepsy in Duchene muscular dystrophy patients

Sandu C, Tarta-Arsene O, Butoianu N, Craiu D, Iliescu C. Pediatric Neurology Clinic, Al Obregia hospital, Bucharest, Romania – carmensandu_u6@yahoo.com

Aim: Duchenne Muscular dystrophy (DMD) is a recessive X-linked form of muscular dystrophy caused by mutations in the dystrophin gene located on chromosome X, with progressive involvement of skeletal, cardiac and respiratory muscles. Recent researches showed that epilepsy might be more frequent in boys with Duchenne dystrophy compared with the general population. The aim of our study is to assess the prevalence of epilepsy in DMD patients with confirmed mutation from our clinic, to compare with recent published data and to emphasize onto history, clinical, laboratory features of those patients. **Material and methods:** We searched the Romanian DMD National

Registry and collected the data referring to patients diagnosed in our Pediatric Neurology Clinic. All included patients have been genetically tested and confirmed (118). Family history of epilepsy, age of seizures onset, type of seizures, EEG features, treatment, associated cognitive impairment and detected mutation have been analyzed. **Results:** Of all 118 DMD confirmed patients, 3 patients (2.54%) have been found to have recorded seizures in the files. Two patients are brothers and their mother also has epilepsy. Deletion of exons 48–50 was detected in both children and mother. Both had generalized tonic clonic seizures and generalized spike and waves EEG discharges were detected in one, during ILS. The third patient had no family history of epilepsy and point mutation has been detected using direct sequencing. There is history of prolonged staring episode and EEG recording revealed generalized spike and wave discharge during ILS. They had cognitive impairment and treatment for epileptic seizures. **Conclusions:** Based on data collected from National Registry the prevalence of epilepsy in our DMD patients (2.54%), was lower than in recent published data (6.3%) but higher than in general pediatric population (approximately 5%). Association of epilepsy and DMD in the same family is a further unusual feature.

P294 - 1740

A prospective natural history study of the progression of physical impairment, activity limitation and quality of life in Duchenne muscular dystrophy

Goemans N, Mercuri E, Morgan A, Eagle M, Lawrence F, Wilson R, Callandret L, Campion G. University Hospital Leuven, Leuven, Belgium – a.morgan@prosenza.nl

Duchenne muscular dystrophy (DMD) is the most common debilitating childhood disease, with 1/3500 boys affected at birth. It is characterized by a progressive and irreversible decrease in muscle function, with a predictable sequence of loss of ambulation followed by cardiorespiratory failure, leading to death by the late twenties. There is currently no cure; the standard of care recommends physical therapy, possible ventilatory support and the use of corticosteroids, which have been shown to delay disease progression. Mutations affecting the DMD gene, age at loss of ambulation, and muscle and respiratory function are all highly variable across the population. This study aims to describe the evolution of muscle strength and function over time, assessing quality of life (QoL) and measuring biomarkers in patients with DMD. A total of 250 patients, aged 3–18 years, ambulant or non-ambulant, will be enrolled at 16 sites in 10 countries and followed up every 6 months for 3 years. Standardized outcome measures including the 6-minute walk test, timed tests, pulmonary function testing, North Star Ambulatory Assessment, Performance of Upper Limb and QoL surveys will be assessed by experienced clinical evaluators. Exploratory biomarkers of disease progression will be measured from blood and urine samples, and magnetic resonance imaging/magnetic resonance spectroscopy will be performed at selected sites. Longitudinal data obtained (6-minute walk distance, pulmonary function and muscle scores, and QoL survey results) will be assessed by mutation type, age group and other factors. This large-scale study will generate a clear picture of the evolution of muscle function and disease progression in DMD that could possibly correlate with gene mutations. It may also indicate the best outcome measures for future trials. Furthermore, the results could be used as surrogate placebo data in clinical trials of investigational drugs, where rarity of eligible patients makes enrolment for pivotal studies challenging.

P295 - 1801**A single aminoacid deletion in the dystrophin protein associated with a mild clinical phenotype**

Pons R, Kekou K, Gkika A, Vogiatzakis N, Svigou M, Papadimas G, Youroukos S, Kanavakis M. *Agia Sofia hospital, First Department of Pediatrics, Genetics Department, First Department of Neurology, University of Athens, Athens, Greece – rosepons@otenet.gr*

Objectives: Clinical and molecular delineation of 6 patients of Greek origin with mild to moderate CPK elevations in whom MLPA analysis of the dystrophin gene disclosed a c. 5068-5070del leading to a single aminoacid deletion in the dystrophin protein (p.His1690del). **Material and methods:** Clinical assessment and metabolic studies were performed in all patients, EMG in 3 patients, muscle biopsy in 2 patients and muscle MRI in 2 patients. To confirm that the deletion was not a common polymorphism we screened 203 Greek male and 70 Greek female controls. **Results:** The majority of patients were asymptomatic or minimally symptomatic and two had episodes of myositis precipitated by febrile illness. Their CPK values ranged between 200 and 3800 IU/L. Two patients had mild exercise intolerance and weakness on exam, while fullness of the calves was detected in 4 patients. EMG showed mild myopathic changes in 2 and was normal in 1. Muscle MRI was normal in 2. Muscle biopsy showed normal dystrophin immunohistochemistry in 2 patients. Metabolic testing was normal in all patients except for low muscle carnitine values in 2. Analysis of 273 Greek controls was negative for the c. 5068-5070del mutation. **Conclusions:** The mutation c. 5068-5070del in the dystrophin gene is associated with a very mild phenotype. Further study is needed to evaluate the progression of this subgroup of dystrophinopathy patients.

P296 - 1679**Manifest female carrier with Duchenne muscular dystrophy with an unusual genetic background**

Trippe H, Wiczorek S, Kötting J, Kress W, Schara U. *Department of Neuropediatrics, Developmental Neurology and Social Pediatrics, University of Essen, Germany – heike.trippe@uk-essen.de*

Introduction: Female carriers with clinically manifest Duchenne muscular dystrophy (DMD) are rare in the pediatric population. Clinical severity varies from a Duchenne-like progression to a very mild Becker-like phenotype. Cardiac dysfunction and cognitive impairment can be present in nearly one-third of the patients, most often without skeletal muscle involvement. **Case report:** We report a girl that was first hospitalised at the age of four months because of failure to thrive. Further diagnostic work-up disclosed elevated liver transaminases and creatine kinase (23000u/l). At this time, neurological examination was normal. At the age of three the girl presented in our centre with proximal muscle weakness and exercise intolerance. Motor development was normal while speech development was delayed. Clinical examination, muscle biopsy and genetic analysis of the DMD gene was performed with following results: dystrophinopathy with dystrophic features and nearly absent expression of dystrophin using antibodies Dys1-3, negative results for MLPA-analysis and complete sequencing of the DMD-gene. Because of an additional mental handicap a chromosome analysis and molecular karyotyping were performed which showed a balanced translocation (X;4)(p21;q31).arr(1-22)x2 dn. Subsequent FISH analyses showed a breakpoint on the X-chromosome within an intron of the DMD gene between positions 31,838,166 and 31,854,846 (hg18). A skewed X- chromosome inactivation pattern in blood was shown on a cytogenetic level, resulting in a predominant inactivation of the non-derivative X-chromosome. Thus, cardiac involvement was assumed and a cardiac-MRI is pending. **Conclusion:** In girls with high elevated creatine kinase levels, developmental handicap and exercise intolerance a muscle biopsy

should be performed early and an appropriate genetic work-up is recommended which also includes rare genetic abnormalities possibly causing a manifesting carrier status of DMD. Chromosome analysis should also be recommended in boys with lack of dystrophin in muscle specimen but without a mutation detected in the DMD-gene on a molecular level.

P297 - 2002**Renal function in children and adolescents with Duchenne muscular dystrophy: a prospective study**

Braat E, Goemans N, De Waele L, Vermeersch P, Gheysens O, Levtschenko E. *University of Leuven, Leuven, Belgium – elke.braat@student.kuleuven.be*

Objectives: Improved life expectancy and the need for robust tools to monitor renal safety of emerging new therapies have fueled the interest in renal function in patients with Duchenne muscular dystrophy (DMD). We aimed to establish methodology for studying renal function in patients with DMD and using this methodology, to describe their renal function in detail. **Methods:** Twenty participants (6–21 years old) were selected for a prospective cross-sectional study. Medical history was obtained and all patients underwent a physical examination, 24-hour ambulatory blood pressure monitoring, ultrasound of the kidneys, 51Cr-EDTA for GFR measurement, blood evaluation and urinalysis. **Results:** From February 2013 until April 2013, 9 participants were tested. Another 11 participants are scheduled for the next months. Eight patients were treated with corticosteroids. Total protein/creatinine was increased in all patients, whereas 24-hour urine protein was normal in all subjects. Hyperfiltration, defined as GFR >1 SD, was found in 6/9 subjects. None of the patients had decreased GFR or proteinuria. Nephromegaly, defined as kidney length >2 SD for patient's length, was found in 5/9 subjects. Hypertension (blood pressure >p95) was found in 6/8 subjects and a non-dipping profile was found in 5/8 subjects. Plasma renin activity and aldosterone levels were elevated in 7/8 and 3/9 subjects. **Conclusions:** This small-scale prospective study demonstrates that urinary excretions expressed in mg creatinine are not reliable in DMD patients because of low urinary creatinine. Interpretation of kidney length and BP should be based on patient's length instead of age due to their short stature. We report a high prevalence of hyperfiltration, nephromegaly and hypertension. We emphasize that this study is still ongoing and therefore we expect that our current findings will be confirmed in a larger population, requiring further studies to investigate the pathogenesis, the confounding issue of chronic steroid treatment and long-term prognosis.

P298 - 1681**Diagnostic pitfalls in congenital myasthenic syndromes in children: clinical experience in an academic neuromuscular centre**

Ekker MS, Rietveld A, Kamsteeg EJ, Alfen N, Sie LTL, Erasmus CE. *Intern, UMC St. Radboud, the Netherlands – merel.ekker@gmail.com*

Background: Congenital myasthenic syndromes (CMSs) cover a group of heterozygous disorders in which the neuromuscular transmission is affected. We diagnosed congenital myasthenic syndromes in eight unrelated patients in the Netherlands. Five mutations were discovered in the CHRNE gene, two in the RAP-SYN gene and one mutation in DPAGT1. **Purpose:** We describe and show our struggles in the diagnostic work up in these children to others. Common diagnostic pitfalls, causing delay in diagnosis and treatment, are the lack of specificity of clinical features, technical drawbacks of invasive testing in young children, non-specific changes in muscle histology and false negative EMG results. Early initiation of treatment and alternative treatment

regimens can considerably improve the quality of life of patients with a CMS. **Methods:** Case series with emphasis on the pitfalls we encountered in reaching the DNA confirmed diagnosis of CMS in eight patients. **Conclusion:** We offer a description of eight patients, not described before, in which we learned a lot about diagnosing CMSs.

P299 - 1889

Congenital myasthenic syndromes: classification and therapy

Echenne B, Sternberg D, Richard P, Nicole S, Meyer P, Nougues MC, Walther-Louvrier U, Farmer M, Cieuta-Walti C, Hantai D, Eymard B, Rivier F. *Referral Center for Neuromuscular Disease, CHRU Montpellier, France – bernard.echenne0894@orange.fr*

Congenital myasthenic syndromes are an heterogeneous group of genetically transmitted disorders leading to neuromuscular transmission dysfunction and frequently to unusual and poorly known clinical pictures, as acute and relapsing cardiorespiratory distress, pseudoseizures, limb-girdle-like myopathy, chronic fatigue... Disease's course patterns could vary along time in a given patient, and therapy will be useful in some patients, but will worsen the neurological situation according to the genetic defect. The prognosis and therapeutic indications will be summarized from 15 patients with a long follow-up and extensive genetical investigations (CHRNE, CHRNA, DOK7, SCN4A, CHAT... Several presentations of these rare diseases will be done.

P300 - 1745

Charcot-Marie-Tooth in a pediatric population

Grenha J, Cardoso J, Vila Real M, Santos F. *Centro Hospitalar de Vila Nova de Gaia e Espinho, Maia, Portugal – joanagrenha@gmail.com*

Background and objectives: Charcot-Marie-Tooth (CMT) hereditary neuropathy is a group of disorders characterized by a chronic motor and sensory polyneuropathy. More than 100 genetic mutations are associated with CMT; these produce a wide spectrum of neurologic signs and symptoms. **Material and methods:** Eight cases of CMT in children are presented to emphasize the clinical diversity of this disorder and the difficulty of genetic confirmation. **Results:** In this study 5 girls and 3 boys were included. The age of onset of symptoms was 10.6 years (minimum 5 and maximum 17). The reason for neuropediatric consultation was high-arched feet in 6 cases, paresthesia in one case and motor discoordination in another. In the first visit, 7 patients presented hyporeflexia; 7 children had high-arched feet, 4 had muscular weakness, 2 had muscular atrophy and one had spasticity with hyperreflexia. 3 patients had sensory loss in inferior extremities and one had ataxia, dysmetria and trembling. 3 patients had previous history of motor delay. There was history of familial consanguinity in 3 cases. All children were submitted to electroneuromyography: 5 patients presented a predominantly axonal polyneuropathy and 3 patients presented a predominantly demyelinating polyneuropathy. It was performed genetic study in 6 cases (one abandoned the visits and one is waiting for the study in progenitors). Two cases were confirmed with genetic study: one case of CMT1A and another of CMT2A2. In another case it was found a mutation in gene MFN2 not yet described but probably pathological. The others are still waiting for results. The majority of cases presented progressive muscular weakness. **Conclusions:** the most prevalent clinical signs were high-arched feet, muscular weakness and hyporeflexia. Clinical and electrophysiology findings are important to conduct genetic tests due to the large number of genes implicated in this disease.

P301 - 1666

Alpha-dystroglycanopathies: Experience of a German patient group from Essen

Trippe H, Della Marina A, Lutz S, Hehr U, Kress W, Schara U. *Paediatric Neurology, Developmental Neurology and Social Paediatrics, University of Essen, Germany – heike.trippe@uk-essen.de*

Aim: Alpha-dystroglycanopathies show a broad clinical spectrum from mild limb-girdle to severe congenital muscular dystrophies with brain and eye abnormalities. Currently mutations in 9 genes are known which lead to defective glycosylation of alpha-dystroglycan: FKTN, LARGE, FKR, POMT1, POMT2, POMGnT1, DPM3, DPM2, WWP1, ISPD or encodes alpha-dystroglycan, DAG1. The diagnostic procedure using muscle biopsy and genetic hedging often requires a lot of time. Through the collection of our data, we would like to demonstrate clinical algorithms for a near-term diagnostic work-up in order to improve medical care of these patients. **Methods:** Since 2007, we attend 42 patients with a diagnosed alpha-dystroglycanopathy by clinical symptoms and muscle biopsy. We conducted a data collection on clinical symptoms, muscle biopsy findings and genetic analyses. **Results:** The largest group with 18 patients, 5–37 year-old, have mutations in FKR, six lost ambulation in teen age, two are mentally retarded, seven have cardiac problems, two needs non-invasive nocturnal ventilation. Further two patients, 9 and 12 year-old, have mutations in FKTN, two, 17 and 19 year-old, in POMT1 and one 8 year-old in POMT2. In another 19 patients an alpha-dystroglycanopathy could be confirmed clinically and by muscle biopsy findings, a final genetic diagnosis is pending. **Conclusion:** Withal the increase of known genetic defects in alpha-dystroglycanopathies, the detection rate is at least not 100%. Although this will be improved by upcoming next generation sequencing, clinical clues and best phenotype characterization are necessary for an optimized therapeutic approach addressing specific complications in every single patient.

P302 - 1593

Evaluation of the cases with congenital muscular dystrophy associated with defective dystroglycan glycosylation and collagen VI deficiency

Yiş U, Uyanık G, Rosendahl DM, Çırak S, Çarman KB, Karaoğlu P, Çakmakçı H, Özer E, Hız S. *Dokuz Eylül University, School of Medicine, Department of Pediatrics, Division of Child Neurology, Izmir, Turkey – ulyis@yahoo.com*

Aim: To evaluate clinical, genetic and radiologic features of our cases with congenital muscular dystrophy associated with defective dystroglycan glycosylation and collagen VI deficiency. **Material and method:** The data of cases who were diagnosed with congenital muscular dystrophy associated with defective dystroglycan glycosylation and collagen VI deficiency in the Division of Pediatric Neurology of Dokuz Eylül University School of Medicine and Gaziantep Children Hospital between 2005 and 2013 were analyzed retrospectively. **Results:** A total of 30 cases were evaluated. Among 30 cases, sixteen (53%) were girls and fourteen (47%) were boys. Twenty one patients (70%) were in the defective dystroglycan glycosylation group and nine patients (30%) were in the collagen VI deficiency group. The mean age of cases was 7.3 ± 6.2 years (1 month–19 years). Among the defective dystroglycan glycosylation group, three patients (14%) were in the Walker Warburg group, three patients (14%) were in the Fukuyama congenital muscular dystrophy group, twelve cases (52%) were in the muscle eye brain disease group and diagnosis in three patients (14%) could not be categorized. Mean serum creatine kinase value in the defective dystroglycan glycosylation group was 2331.26 ± 1179.04 (700–4267) IU/L. The most common ophthalmologic and radiologic abnormalities in defective dystroglycan glycosylation groups were cataracts, retinal detachment,

periventricular white matter abnormalities, ventriculomegaly, pontocerebellar hypoplasia and multiple cerebellar cysts. Regarding genetic study, one patient (5%) had homozygous POMT1 mutation, three patients (15%) had homozygous Fukutin mutation and twelve patients (63%) had homozygous POMGNT1 mutation. In the collagen VI deficiency group, the most common findings were developmental motor retardation, contractures, distal hyperlaxity and respiratory deficiency. Conclusion: Congenital muscular dystrophy with defective dystroglycan glycosylation and collagen VI deficiency should be kept in mind in cases with combined eye and brain malformations, developmental motor retardation, contractures and distal hyperlaxity.

P303 - 1565

The pseudo-poliomyelitis of the 21st century

Teoh H, Sampaio H. Sydney Children's Hospital, Randwick, NSW, Australia – sakesushi@yahoo.com

It has been 12 years since enterovirus 71 haunted the hallways of our hospital, with 18 of 200 children affected experiencing neurologic complications. Between Jan 2013 to March 2013, 30 children presented with neurologic symptoms and enterovirus positivity on faeces, throat swab, serum or CSF. 14 out of the 30 were genotyped and found to have enterovirus 71. Of the 18 patients who had an MRI scan, two thirds showed an abnormality with increased T2 signal intensity in the brainstem +/- spinal cord involvement seen. Symptoms of these patients were varied and included: neurogenic pulmonary oedema with quadriparesis, seizures, myoclonic jerks (almost invariable), monoplegia, unilateral cranial nerve 6 palsy, generalised weakness, irritability and neurogenic bladder. Treatment was also variable with 3 needing full cardio-respiratory support with intravenous immunoglobulin (IVIG) and high dose methylprednisolone, 4 receiving IVIG and high dose methylprednisolone, 4 receiving only high dose methylprednisolone and 4 receiving only IVIG and 15 receiving no special treatment. 29 children improved in their clinical course. All patients presenting with limb weakness, although improved, continue to have residual weakness at follow up in the presence of a normal MRI, regardless of treatment. Follow up is on-going.

P304 - 1516

Lambert-Eaton myasthenic syndrome in a 13-year-old girl with Xp11.22-p11.23 duplication

Verbeek S, Vanakker O, Mercelis R, Haerynck F, Dullaers M, Van Coster R, Verhelst H. University Hospital Ghent, Belgium – helene.verhelst@ugent.be

Lambert-Eaton myasthenic syndrome (LEMS) is a presynaptic autoimmune disease of the neuromuscular junction typically seen in adults as a paraneoplastic syndrome. Only rare cases have been reported in childhood. In most childhood cases, malignancies have not been detected and an underlying propensity to autoimmune disease is suspected. Nevertheless, little is known about genetic factors that may contribute to the susceptibility of an individual to develop LEMS. We report on a 13-year-old girl, known with the Xp11.22-p11.23 duplication syndrome, who presented with severe non-neoplastic LEMS. The potential role of this microduplication syndrome in development of LEMS is explored. Literature review of twelve patients with Xp11.2 duplication syndrome showed that three of them suffered from various autoimmune diseases. The common duplicated region in those three patients and the presented case comprises 12 disease associated genes including the FOXP3 (Forkhead Box P3) gene and the WAS (Wiskott-Aldrich syndrome) gene, both implicated in immune function. However, it is unclear whether increased gene dosage of one or both genes can cause susceptibility to autoimmune diseases. In conclusion, the presented case

emphasizes that autoimmune disease is a recurrent feature of the Xp11.2 duplication syndrome, which should be considered in the follow-up of these patients. The exact mechanism underlying this autoimmune propensity remains to be elucidated.

P305 - 2007

A male with mild intellectual disability and hyperckemia

López Písón J, Monge Galindo L, Torres JA, Rodríguez Valle A, García Jiménez M^oC, Peña Segura JL. Hospital Universitario Miguel Servet, Zaragoza, Spain – jlopezpi@salud.aragon.es

Danon disease is a rare X-linked dominant disorder caused by primary deficiency of lysosome-associated membrane protein-2 (LAMP-2) characterized by cardiomyopathy, myopathy, and variable mental retardation. We present a case of a boy and his mother with Danon disease. An 11-year-old boy with mild intellectual disability and increase of CK, ranging between 400 and 960. X-fragile and Steinert genetic studies normal. His mother underwent a heart transplant after a postpartum cardiomyopathy. Our study protocol of hiperCKemia, without etiologic diagnosis, required a muscle biopsy, that showed autophagic vacuolar myopathy and no detectable LAMP-2 in immunohistochemistry analyses. The genetic study identified a mutation A314GfsX2 in exon 8 of the LAMP2 gene, in the boy and his mother (with normal CK levels and intelligence). The only sister has no mutation. Danon disease is a rare disorder with substantial morbidity and early mortality due to arrhythmia and cardiomyopathy. Male patients usually suffer severe cardiomyopathy, mild myopathy and mental retardation. Men have a high morbidity rate and are unlikely to reach the age of 25 years without a cardiac transplantation. Women are less severely affected but have higher than expected levels of cognitive and skeletal muscle complaints and manifest an equal prevalence of dilated cardiomyopathy and hypertrophic cardiomyopathy. We highlight the importance of studying hyperCKemia, the need for cardiac surveillance in different muscle diseases and the importance of concern for muscle disease in families with cardiomyopathy, due to the implications of diagnosis, management, prognosis and genetic advice.

P306 - 9999

A positive Gowers sign mimicking a primary neuromuscular disorder for 17 years.

de Rijk-van An del JF, de Coö IFM, van der Laar I. Erasmus Medical Center, Rotterdam, the Netherlands

Niels was born in september 1989 after a normal pregnancy and delivery from Dutch non-consanguineous parents. His two older sisters are healthy. In his family there are no neuromuscular diseases. His development was normal until the age of 3 years, when he developed walking problems and a positive Gowers sign. An intensive neuromuscular work-up in three academic centres with muscle biopsy and DNA analysis followed, but did not show any specific disorder. Symptoms suggested a SMA type III, but no deletion was ever found in the DNA analysis. At the age of 20 years he complained of pain in his legs. On examination the circumference of the upper legs were the same as the circumference of the lower legs. Then an X-ray of the bone showed bone dysplasia. Finally, the diagnosis Camurati-Engelmann (CED) was confirmed by the clinical genetics. There is a c.652C>T mutation in the TGFβ1-gene. This is the coding gene for the transforming growth factor TGFβ1. In the symptoms of CED muscle weakness is described in about 1/3 of the patients due to a high TGFβ1 activity which inhibits muscle and fat development. The biggest challenge of the moment is the pain treatment.

Oncology

P307 - 2153

Severe methotrexate encephalopathy – response to aminophylline and dextromethorphan

Mari J, Morgan M, Joy H, Forrest K. *Pian Brown Paediatric Haematology and Oncology Unit, Southampton, UK – katharine.forrest@uhs.nhs.uk*

Background: Methotrexate encephalopathy (MTX-E) is a potentially fatal complication of treatment incorporating intrathecal methotrexate (IT-MTX) for acute lymphoblastic leukaemia. Most often presenting with headache and seizures, a stroke-like syndrome is recognised, typically occurring 2 to 14 days after IT-MTX. The pathogenesis is poorly understood and probably multifactorial, with increased extracellular adenosine release, hyperhomocysteinaemia, NMDA-receptor excitation, and altered bipterin metabolism. Histological findings have revealed demyelination, myelin vacuolation, axonal spheroids or macrophage infiltration and necrosis. Treatment is supportive as most cases are mild or moderately severe with spontaneous resolution. **Objectives:** We present the clinical and radiological features of a 15 year old girl with CNS negative ALL who presented 10 days after her sixth dose of IT-MTX with acute onset of slurred speech and right upper limb weakness preceded by headache. Additional cases of MTX-E are reviewed retrospectively. **Results:** Clinical examination of index case revealed right upper motor neurone facial weakness, moderate dysarthria, right upper limb weakness with preserved deep tendon reflexes. Initial MRI Brain demonstrated no parenchymal lesion nor restricted diffusion with normal intracranial artery flow voids. Over the next 3 days she deteriorated, and became mute with decerebrate posturing. Neurointensive and neuroprotective measures were instituted. Repeat MRI brain demonstrated progressive diffusion weighted imaging changes with features typical of MTX-E. Aminophylline (inhibits phosphodiesterase and antagonises adenosine receptors) was administered with minimal improvement of left upper and lower limb neurology. Dextromethorphan (NMDA-antagonist) 1.5mg BD was commenced as Robitussin Dry Cough Mixture. She was extubated that day, had recovery of right sided limb function the following day, and recovery of speech 2 days later. Dextromethorphan was discontinued after 7 days, and she was discharged home 12 days after admission to PICU with minimal neurological deficit. **Conclusion:** Aminophylline and dextromethorphan is well tolerated in MTX-E and dextromethorphan may expedite clinical recovery and improve outcome.

P308 - 2060

Primary central nervous system lymphoma: radiology based diagnosis and treatment when tissue diagnosis is not possible

Maras H, Yalcin EU, Anik Y, Kara B. *Kocaeli University Medical Faculty, Department of Pediatrics, Division of Child Neurology, Kocaeli, Turkey – hulyamaras@gmail.com*

Primary central nervous system lymphoma (CNSL) is a B-cell type lymphoma with an aggressive course which requires rapid diagnosis and treatment. We present a 17-year-old healthy boy who presented with headache and vomiting. The physical examination was normal except papilledema. The cranial MRI revealed a mass lesion in the right temporooccipital lobe, with vasogenic oedema, midline shift, contrast enhancement, and diffusion restriction. The radiological diagnosis was either encephalitis or CNSL. There were no systemic signs of inflammation in the patient, and tumour and infection work-up were negative. Lumbar puncture was not feasible and anti-oedema treatment was started including steroid and mannitol. The stereotactic biopsy performed after steroid treatment revealed reactive changes with

no neoplastic infiltration. Consequent cranial MRI's showed dynamic lesions with some of them regressing, and newer lesions appearing in the basal ganglia and cerebellum. Diagnosis of CNSL was made according to MRI perfusion, diffusion and spectroscopy findings. Chemotherapy combined with radiotherapy was started. Soon after therapy, brain lesions regressed markedly. The cerebrospinal fluid analyses during the course of treatment were normal. Now it had been a year since the therapy started, and there are no residual lesions in the final MRI. Although CNSL has specific radiological features, histopathological diagnosis of primary CNSL remains obligatory for treatment. Even single dose of steroid may mask the histopathological diagnosis, so it is crucial to perform tissue diagnosis before steroid therapy. If steroid therapy is given for intracranial hypertension before tissue sampling; then normal pathological findings should not rule out CNSL if there is strong clinical suspicion for CNSL.

P309 - 1913

Imaging anaplastic oligodendroglioma by diffusion tensor imaging analysis: case study of an 11-year-old boy with Li-Fraumeni syndrome

Bregant T, Benedik Dolnicar M. *Department of Pediatric Neurology, University Children's Hospital, University Medical Centre Ljubljana, Slovenia – tina.bregantdrmed@gmail.com*

Objectives: Diffusion tensor imaging (DTI) can be used to determine the preoperative viability or resectability of the tumour-adjacent white matter (WM) tracts. Prior to biopsy the DTI can give some information on tumour histology. **Material and methods:** We present an 11-years old boy with anaplastic oligodendroglioma localized in the left parietal lobe. The boy had been previously treated for 3 different cancer types. We confirmed Li-Fraumeni syndrome, a rare autosomal dominant syndrome, with a new genetic mutation 825T>A in exon 8 of coding region of the gene TP53 on chromosome 17p13. The decision on surgery was based upon DTI analysis as we were able to determine preoperatively whether the motor tracts for the boy's right hand were salvageable. **Results:** Brain MRI showed a 52×57 mm round, large, cystic, partially necrotic tumour left parietally with edematous border of 11 mm. It seated superficially, was well vascularized, infiltrating into parenchyma with a large cyst in the centre. Pathohistology showed anaplastic oligodendroglioma with numerous mitoses, nuclear polymorphism, vascular and pericital proliferation (WHO malignancy grade III). Postoperative MRI showed contrast accumulation posteriorly and medially, so decision for further resection was based upon DTI, where the corticospinal tract for the right hand was displaced and the surgeon was able to avoid it. The boy had no focal neurological signs after the operation. Despite successful reoperation, few months later the sarcoma of the right calf emerged, oligodendroglioma reappeared and the boy succumbed. **Conclusion:** In older children with brain tumours who cooperate well during the paradigm performance, DTI can give additional information on WM integrity and can also alter surgical approach and decision for the surgery.

P310 - 1753

Gliomatosis cerebri can be caused by primitive neuroectodermal tumor in childhood

Takagi A, Arahata Y, Kitazawa K, Fujii K. *Department of Pediatrics, Chiba University Graduate School of Medicine, Japan – asahipedia@yahoo.co.jp*

Background: Gliomatosis cerebri is a rare brain tumor defined as a diffuse neoplastic glial tumor cell infiltration of the brain, involving more than two cerebral lobes. This is usually composed of astrocytoma or oligodendroglioma, but there has been no report of primitive neuroectodermal tumor (PNET). We herein

describe a first case of gliomatosis cerebri histologically proven as PNET. **Case report:** A Japanese 10-year-old girl was admitted to our hospital because of recurrent complex partial seizures. She was previously a healthy girl and family history was unremarkable. Brain MRI showed diffuse T2 high intensity areas in left frontal and temporal lobes with partially enhancement. Biopsy was performed two months later, and pathological diagnosis was anaplastic astrocytoma at that time. We then started oral temozolomide and radiation therapies. However, nine months later the tumor size became enlarged and brain edema was deteriorated to the coma state of the patient. To reduce the mass volume, surgical operation was performed and tumor sample was taken to decide the precise tumor classification. The final pathological diagnosis at the operation was PNET. After the operation she received three courses of carboplatin and etoposide therapies but another mass appeared. She received ifosfamide, carboplatin, and etoposide therapies, but the tumor became enlarged. At fifteen months since first symptoms appeared, she died because of the tumor enlargement causing to brain stem compression. **Discussion:** To our knowledge, this is the first report of gliomatosis cerebri caused by histologically proven as PNET. The reason why this tumor demonstrated the diffuse extension like gliomatosis cerebri remains to be elucidated, but in childhood such malignancy progression should be kept in mind especially in PNET. Although the therapy in gliomatosis cerebri has not been well established, early biopsy or repeated biopsy is critical to decide appropriate chemotherapy and may improve the prognosis in children.

P311 - 1500

Germ cell tumor presenting like Bell palsy

Erol I, Ozkale Y, Yazıcı N, Saygi S, Demir S. *Baskent University Faculty of Medicine, Department of Pediatrics, Neurology Division, Adana Teaching and Medical Research Center, Turkey – ilknur_erol@yahoo.com*

Introduction: Causes of peripheral facial nerve palsy (PFNP) in children include trauma, infection, congenital anomalies, systemic disease, malignancy, middle ear surgery, and idiopathic reasons. Malignancy is one of the rare causes of facial palsy in childhood. In this case study, we present an infant with a germ cell tumor who initially presented with unilateral PFNP and normal brain and internal acoustic MRI at admission. **Case:** A 2-month-old-girl with unremarkable medical history presented with right sided PFNP. Upon examination, both her vital signs and physical examination were normal except for right sided PFNP grade 4 House-Brackmann scale. On neurological examination, the other cranial nerve functions were normal, and no signs of meningitis were detected. Laboratory analyses revealed normal blood leukocyte count serum C-reactive protein and erythrocyte sedimentation rate. Viral and Lyme serology were normal. Neither computed tomography nor magnetic resonance imaging (MRI) of brain and internal acoustic canal revealed any mass lesion. She was diagnosed with idiopathic PFNP and was administered steroid treatment. Two months following the first admission, she presented with new neurologic findings, with head tilting to the right and bilateral sixth nerve palsy. However, fundoscopic evaluation revealed no papil edema. MRI scans showed a heterogenous mass adjacent to the inner ear structures, reaching to the internal acoustic canal at the right temporal fossa. Histological examination of the tumor revealed malignant atypical teratoid tumor with no rhabdoid differentiation. The patient was treated for malignant teratoma with adjuvant chemotherapy. The patient presently remains under treatment. **Conclusion:** malignancy is rare but should be considered in the differential diagnosis of unilateral peripheral facial nerve palsy, particularly in the infant population. In the present study, the attention of pediatricians and pediatric neurologists to

the importance of a high level of suspicion for this diagnosis is warranted, even when initial imaging results are normal.

P312 - 2027

Seronegative myasthenia gravis in an adolescent after curative treatment of B-cell lymphoma

Maras H, Uysal NC, Imal M, Mulayim S, Kara B. *Kocaeli University Medical Faculty, Department of Pediatrics, Division of Child Neurology, Kocaeli, Turkey – hulyamaras@gmail.com*

Myasthenia gravis is an autoimmune disease mediated by antibodies to acetylcholine receptors (AChRs) or muscle specific kinase (MuSK). The relationship between myasthenia gravis and thymoma is well recognized, but the association of myasthenia and other malignancies has not been well known. In the literature, there are some case reports about the relation of lymphoma and other lymphoproliferative disorders with myasthenia gravis. Myasthenia gravis may be a part of the paraneoplastic syndrome in a synchronous fashion with lymphoma, but it may occur after the therapy of lymphoma as a non-synchronous fashion. Genetic factors may play a role for the pathogenesis of non-synchronous myasthenia gravis in lymphoid malignancies, but also perturbations in the immune mechanisms that normally prevent the emergence of autoimmunity. In this presentation, we want to discuss the relationship between myasthenia gravis and lymphoid malignancies, according to a 15-year old boy. He was diagnosed as B-cell lymphoma and treated with complete cure 5 years ago. He presented with severe systemic and bulbar muscle involvement. Serologic tests for anti-AChR and anti-MuSK antibodies were negative. Electromyography revealed decremental responses at the orbicularis oculi and ala nasi muscles. Residual tumour investigation was negative. Myasthenic symptoms could be controlled with oral prednisolone and intravenous immunoglobulin therapies.

Sleep

P313 - 2070

Sleep evaluation in a patient with chromosomal disorder duplication (17) p11.2

Sendon CS, Chocano JF, Sendon PM, Chocano E. *Eastern Virginia Medical School and Children's Hospital of The King's Daughters, Norfolk, USA – cssendon@hotmail.com*

Introduction: The duplication 17p11.2 Syndrome is a contiguous gene syndrome. Potocki-Lupski Syndrome (PTLS) was the first reciprocal of a homologous recombination. Its reciprocal disease is Smith-Magenis Syndrome (SMS), in which the chromosome portion duplicated in PTLS is deleted altogether. Both syndromes are extremely rare, characterized by multiple congenital abnormalities and mental retardation. A key feature is autism spectrum disorder. Other features include infantile hypotonia, sleep apnea, structural cardiovascular anomalies, learning disabilities, attention-deficit disorder, obsessive-compulsive behaviors, malocclusions, short stature and failure to thrive. Disrupted sleep patterns are characteristics of SMS due to an inverted melatonin circadian rhythm. **Case presentation:** 3 years old African American male with a history of PTLS/SMS Syndrome, with developmental, speech, and motor delays. He has hearing loss and myopia. Mom referred that her son gets up and walk around during the night. A sleep study showed mild snoring, obstructive respiratory events, and few periodic leg movements. Patient fall asleep very quick but have awaken several times. He woke up at the last part of the night and he did not go back to sleep. Time in bed was 7.1 hours; total sleep time 6.2 hours; Sleep efficiency was 87.5%; Arousal index was 25.8; Stage 2 was

60%; stage 3 was 11%; REM was 29%; SpO2 mean was 97% and SpO2 minimum was 84%; Apnea/Hypopnea index was 12.8; Apnea/Hypopnea index in REM was 34.0; ECO2 mean was 31.7 and ECO2 max was 53.0. No sleep walking, no sleep talking, no seizure activity. **Conclusion:** The polysomnography evaluation of a patient with Smith-Magenis/Potocki Lupski Syndrome allows us to understand the sleep pattern of an affected individual. The Obstructive Sleep Apnea syndrome is related to structural mid-face defects. Awakenings and arousals may disrupt sleep pattern modifying sleep architecture. Polysomnography study should be included in the evaluation of patient's with SMS/PTLS Syndrome.

P314 - 1862

Clinical and behavioral characteristics of childhood narcolepsy

Dhondt K, Verloo P, Verhelst H, Van Coster R. Ghent University Hospital, Pediatrics, Div. Child Neurology & Metabolism, Pediatric Sleep Center, Belgium – karlien.dhondt@ugent.be

Narcolepsy is a sleep disorder characterized by severe daytime sleepiness, cataplexy, hypnagogic hallucinations, sleep paralysis and fragmented night sleep. Approximately one third of patients experience symptoms prior to the age of 15 years but only 4% is diagnosed before that age. Difficulties in recognition of this sleep disorder are responsible for the underdiagnosis in young patients. In our pediatric sleep center, 12 children between the age of 5 and 16 years were diagnosed as having narcolepsy/cataplexy in the period 2005–2013 (10 primary, 2 secondary narcolepsy/cataplexy). In this study, a detailed clinical description is given from disease onset to treatment. The major clinical features and difficulties in recognizing this disorder are discussed. Special attention is drawn to the typical behavioral aspects and cataplectic features that occur in childhood narcolepsy and that differ significantly from those in adults. The cause of the diagnostic delay will be clarified. Diagnostic tools such as polysomnography and hypocretin-1 detection and the different treatment options adapted to the individual patient are described. In addition, interesting research topics within this field are cited.

P315 - 1796

Melatonin in Angelman syndrome

Paprocka J, Jamroz E, Kijonka M, Sokó M, Pêcka M. Child Neurology Department, Medical University of Silesia, Katowice, Poland – justyna.paprocka@interia.pl

Background: Melatonin (MLT), based on its properties as chronobiotic, antioxidant, or analgesic all of which have been confirmed in numerous experimental studies, may have an influence on epileptogenesis (modulation of GABA and glutamate transmission), maturation oligodendrocytes, developing of alpha rhythm. The interaction between sleep and epilepsy remains unclear. In several disorders like Angelman syndrome, autism spectrum disorders, Rett syndrome, and tuberous sclerosis sleep problems have a relative high prevalence. **Purpose:** The aim of the study was to access melatonin secretion in children with Angelman syndrome and to compare it to the children with and without epilepsy. **Material and methods:** Study group consist of Angelman syndrome group (AG; n=8), epilepsy group (EG; n=72), comparison group (CG; n=33). The melatonin level was by radioimmunoassay method. The blood samples were drawn every 3 hours through an intravenous catheter. To describe the melatonin secretion during the day estimation of nonlinear least squares method was used. The Levenberg-Marquardt algorithm was chosen to adjust parameters of model curve. Obtained parameters were statistically analyzed using the Mann-Whitney-Wilcoxon test and Spearman's rank correlation coefficient. **Results:** Comparison of the data from the CG and AG showed longer duration of sleep and the higher value of the phase shift of melatonin

release in Angelman syndrome. In the next step AG was divided into two subgroups: with and without epilepsy. Statistical analysis showed that the comparison group and Angelman syndrome without epilepsy group are similar ($p > 0.05$ for all parameters of melatonin models). However, the differences between Angelman syndrome group and the comparison group correspond to the symptoms of epilepsy in Angelman group. **Conclusions:** This clinical observation adds to the growing data showing melatonin secretion in Angelman syndrome, epilepsy and in comparison group.

P316 - 1649

Evaluation of the effect of the standard treatment of sleeping disorders in children

Vinding R, Debes NM. Paediatric Department, Naestved Hospital, Denmark – nanettemol@hotmail.com

Objectives: In this study, we will evaluate the effect of the standard treatment of sleeping disorders in children without comorbidity. The study is still ongoing and the examinations will be finished in July 2013. **Background:** Sleeping disabilities are common in children. Sleep is extremely important for the psychomotor and cognitive development of children. In our clinic, ball blankets are the first choice of treatment and with insufficient effect, melatonin is tried. However, in the present literature, there are only a few studies examining treatment of sleeping disorders in children without co-morbidity. Melatonin is shown to be effective in children with insomnia. **Material and methods:** We include 10 children with sleeping disorders without any comorbidity. The children are between 10 and 16 years old. They are examined with ARMBAND analysis during three nights and with a structured questionnaire about quality of sleep. Afterwards, the children will be treated according to the standard treatment procedure in our clinic, namely initially with a ball blanket and if the effect is insufficient, treatment with tablet melatonin will be started. The children are reexamined with ARMBAND analysis during 3 nights and questionnaire after 6 weeks treatment with ball blanket and after 3 weeks treatment with melatonin. **Results and conclusions:** By the end of this study, we hope to increase the knowledge about treatment of sleeping disorders in children and we hope to be able to optimize the treatment and give more sufficient information to parents and children.

P317 - 1633

Geniospasm associated with tongue biting during sleep

Nechay A. Neurology department, Paediatric Hospital No. 1 of c.Kiev, Ukraine – allanechay@ukr.net

Geniospasm is a movement disorder presenting with episodes of involuntary tremor of the chin and lower lip, which usually start in infancy, may be precipitated by stress or emotions and is considered benign. Genetic heterogeneity has been suggested. To our knowledge, association of geniospasm and other paroxysmal disorders had not been performed before. Video of episodes of chin trembling that started in healthy boy aged 19 months who also had a scar on his tongue from its biting during sleep will be presented and shortly discussed.

P318 - 1604

Sleep disorders in children with attention-deficit/hyperactivity disorder (ADHD) – a retrospective polysomnographic study

Prihodova I. Department of Neurology, 1st Medical Faculty and General University Hospital in Prague, Czech Republic – iprih@lf1.cuni.cz

Objective of study: Retrospective assessment of sleep disorders

in patients with attention - deficit/hyperactivity disorder (ADHD) referred to nocturnal polysomnography. **Patients and methods:** 80 children, 60 males, age range 4–18 years, mean age 10 ± 4.2 . We evaluated presenting complaints, subjective sleep problems, polysomnographic findings and final diagnosis. **Results:** Presenting complaints were parasomnia – sleep terrors, somnambulism (28% patients), insomnia with difficulty in falling asleep (25%), obstructive sleep apnea – OSA (13%) and excessive daytime sleepiness (11%). The most frequent polysomnographic findings were periodic limb movements in sleep – PLMS (25%), parasomnia – disorders of arousal from NREM sleep (24%), OSA (18%) and delayed sleep phase disorder (11%). 10% of patients had normal polysomnography. Comparison of sleep parameters of the whole ADHD group and subgroups with various sleep disorders did not reveal any statistically significant changes in polysomnographic results. 70% patients presenting with insomnia had a diagnosis of various sleep disorders (delayed sleep phase disorder – 8 patients, periodic limb movements disorder – 4 patients, restless legs syndrome – 2 patients). **Conclusion:** Sleep disturbances (PLMS, parasomnia, OSA) represent other comorbid disorders of ADHD and nocturnal polysomnography plays an important role in their diagnostics. Insomnia in ADHD can be a manifestation of sleep phase delay, periodic limb movement disorder or restless legs syndrome.

P319 - 1503

Types and prevalence of sleep disorders in school children in the city center of Trabzon

Ozgun N, Sonmez FM, Can G, Topbas M. *KTU Medical Faculty, Department of Child Neurology, Trabzon, Turkey – mjgsonmez@yahoo.com*

Objectives: Insomnia and parasomnia are the most commonly seen sleep disorders in childhood. The prevalence of sleep disorders in childhood is 25–40%. A limited number of studies have been made on this issue in Turkey. This study aimed to define the prevalence and factors involved in the etiology of insomnia and parasomnia. **Material and method:** An 84-item questionnaire was administered to 5200 school children from different socio-economic levels in 10 primary schools and 10 secondary schools. The questionnaire included items that elicited about the symptoms, findings of sleep disorders and the factors that predispose to them according to ICSD-2 diagnostic criteria, sleeping habits, demographic, social and economic conditions of children. Of the 5200 questionnaires, 4144 were evaluated after the inappropriate questionnaires were eliminated. **Results:** The mean of age was 11.30 ± 3.28 years. 780 (18.8%) of the subjects were diagnosed with insomnia and 1980 (47.8%) were diagnosed with parasomnia according to ICSD-2 diagnostic criteria. There was no gender difference between the patients diagnosed with insomnia and parasomnia. Snoring was seen more often in males and sleep talking and nightmares were seen more often in females ($p < 0.05$). Sleep talking was the most commonly seen parasomnia type with a ratio of 28.4%, followed by bruxism in 14.1%, nightmares in 12.9%, primary snoring in 7.2%, night terror in 5.7%, enuresis in 4.7%, and sleepwalking in 4.2% of the patients. Total sleep duration and prevalence of parasomnia decreased and prevalence of insomnia increased significantly with increasing age ($p < 0.05$). **Conclusion:** In our study, the effect of the parameters that affect the prevalence of sleep disorders is similar to the literature. We believe that prevalence studies made from different areas of Turkey will be very important in having an insight into the importance of sleep disorders in childhood and their treatment methods.

Stroke and vascular disorders

P320 - 2156

Recurrent anterior arterial stroke

Kirkham F. *International Paediatric Stroke Study and European collaboration, London, UK – Fenella.Kirkham@ucl.ac.uk*

Risk factors for arterial ischaemic stroke (AIS) in children include congenital heart malformations, arterial cerebrovascular disease (CVD), infectious diseases, collagen tissue diseases, metabolic disorders, and prothrombotic risk factors. The relevance of these factors to a second AIS event is not known. Data on recurrent AIS from the databases held in Toronto, Utrecht, Rotterdam, St Etienne, Paris (Bicetre), Ljubljana, Sydney, Switzerland, Germany and the United Kingdom were pooled. Children with sickle cell disease were excluded. Data were available from 1168 patients with a median age at first AIS of 6 years and a median follow-up of 36 months (1 day to 256 months). Seventy-two (10.6%) had recurrence after a median follow-up of 3.3 months (1 day to 76 months). Recurrence was significantly higher in those with CVD (Cox regression: hazard ratio (HR) 3.06, 95% confidence intervals (ci) 1.90, 4.93, $p = 0.001$) but not in those with congenital cardiac disease. The presence of any prothrombotic risk factor doubled the risk of recurrence (HR 2.04, 95%ci 1.24, 3.35, $p = 0.005$). Individual laboratory tests associated with increased risk of recurrent AIS included high fibrinogen, homocysteine and lipoprotein(a) but not protein C, protein S or antithrombin deficiency or any of the tested polymorphisms e.g. Factor V Leiden, prothrombin 20210, thermolabile methylene tetrahydrofolate reductase. CVD (HR 1.8, 95%ci 1.0, 3.8; $p = 0.04$) and multiple prothrombotic disorders (HR 2.5, 95%ci 1.2, 5.1, $p = 0.01$) were independent risk factors for recurrent AIS. Children with AIS should have an MRA at the time of MRI to stratify stroke risk. Although testing for individual prothrombotic disorders may have low yield for the relatively high cost, comprehensive testing informs physicians and families about the risk of recurrence in time to consider appropriate prophylaxis. Vascular imaging and prothrombotic testing may guide strategies to reduce the risk of recurrence after paediatric AIS.

P321 - 2129

Stroke in children from a public hospital network: a series of cases

Souza DB, Siqueira ES. *Pediatric Neurology, Secretary of Health Hospital Regional da Asa Sul, Brasília, Brazil – denizebomfim2006@gmail.com*

Introduction: Stroke in childhood is an event of low prevalence with an incidence of 2–14 cases in 100,000 children^{1,2}. However, it is among the 10 leading causes of death in this population^{1,2}. Early diagnosis requires high clinical suspicion, since the signs and symptoms may be nonspecific, unlike in adults¹. The prognosis depends on the extent of brain damage and underlying disease, which can result in complications, risk of sequel and death^{1,2}. **Objective:** To describe a series of children with stroke in a public hospital in Brasília, Brazil. **Methodology:** Retrospective Study of 13 children in a universe of 17,500 patients admitted to the emergency department, from November 2006 to November 2011. Children with a previous diagnosis of sickle cell disease were excluded. All patients were diagnosed with stroke by clinical and neuroimaging abnormalities. They were also subjected to additional tests in search for the etiology of stroke: EEG, thrombophilia tests, electro and echocardiogram, abdominal and renal ultrasound, search for organic acidemias. **Results:** The sample consisted of six females and seven males, ages ranged from 2 to 10 years with a mean of 4.2. All the children had neurological signs and symptoms: 4 had seizures, 9 had motor deficit

syndrome. They all underwent Computed Tomography, Magnetic Resonance and a neurological examination by a pediatric neurologist. All children had abnormal neuroimaging. The heart tests, nephrology and thrombophilia tests of all children were normal. A boy presented hiperlactemia, a girl had multiple cavernomas and a boy Moya-Moya disease. Three children have evolved without neurologic sequel. **Conclusion:** This case series showed the need for adequate knowledge of disease pathophysiology, natural history, diagnostic methods as essential tools for early diagnosis and appropriate management to minimize the risk of sequelae.

P322 - 2069

Long-term MRI follow-up of arterial ischemic neonatal stroke

Hertz-Pannier L, Dinomais M, Chabrier S, Kossorotoff M, Husson B, Nguyen S. INSERM, U663 NeuroSpin, CEA, Saclay, France – synguyen@chu-angers.fr

Objective: The objective was to describe the cerebral MRI evolution of children having suffered from arterial ischemic unilateral neonatal stroke. **Material and methods:** The AVCnn cohort was composed in 2003 of 100 children with symptomatic arterial ischemic stroke confirmed by an early MRI. These children are currently being followed up to age 8, with a clinical evaluation and a 3T MRI (3DT1, 3DFLAI, DTI). We have reviewed the 22 first cases available to date. **Results:** There were 16 boys (72%). The stroke was most often left (13 cases, 60%), in the territory of the middle cerebral artery (MCA) in 19 cases (86%). Seven children had hemiplegic CP (30%), 8 were left handers (36%), among which 7 children had left lesions, including 2 with right hemiparesis. The topography was concordant between neonatal and childhood MRIs, but the lesions were strikingly smaller and more subtle at age 8. There were few large porencephalies. The strokes were mainly located in the post central region, with opercular and parietal involvement (posterior branch of the MCA) (72%), and without motor deficit when isolated (35%). The precentral location was less frequent (18%), rarely isolated (involvement of temporal and posterior branches) and then always accompanied by hemiparesis. Obvious peduncular atrophy was associated with hemiplegia. Minor peduncular asymmetries were possible in non-hemiplegic children. A decreased volume of the posterior part of the lesioned hemisphere was noted suggesting a restricted growth remotely from the stroke. **Conclusion:** A focal and isolated post central localization of neonatal strokes is associated with the “good” motor prognosis (only 1/3 of hemiplegia). The involvement of the precentral gyrus, and/or of several branches of the MCA, is associated with a poorer prognosis, especially when associated with a peduncular atrophy. The link between the growth restriction of the lesioned hemisphere and cognitive deficits should be further explored.

P323 - 2023

Growing skull fracture: an unusual cause of a large intraparenchymal bleed in a child

Flanagan M, Kaliaperumal C, Nabialek T, Leonard J, Crimmons D. Temple Street Children's University Hospital, Dublin, Ireland – marflanagan@gmail.com

Background: Growing Skull Fractures (GSFs) or Post Traumatic Leptomeningeal Cysts (PTLMC) are very rare complications of skull fractures, constituting ~0.05–0.6% of all skull fractures. The majority of GSFs present as progressively worsening scalp masses or scalp defects. GSFs tend to occur mostly in the parietal skull and are usually associated with an underlying dural tear and a widely separated fracture. If left untreated GSFs can present later as neurological symptoms of deficit/seizures/headache, etc. We describe a case of a large intra-parenchymal bleed secondary to GSF. **Case description:** A 21-month-old girl presented with right

sided hemiplegia and dysphasia following a fall down a staircase. She had a history of a significant fall at the age of 16 months of age resulting in left parietal and bilateral occipital fractures with subgaleal haematoma, which was managed conservatively. She failed to attend for a follow up skull x-ray. CT brain at the current presentation showed a large left sided intra-parenchymal haematoma extending to the site of a left parietal GSF with surrounding oedema, mass effect and mild midline shift. There was a widening of the previous parietal fracture and scalloping of the bone edges. She underwent a craniotomy and evacuation of her haematoma with dural repair. Her right sided hemiplegia slowly improved with rehabilitation. **Conclusion:** We believe that the GSF contributed to the severity of this girl's intraparenchymal bleed. We also believe that the bleed may have originated from a small connecting cortical vessel to the leptomeningeal cyst. Our case demonstrates the importance of reviewing skull fractures in the paediatric age group particularly children below three years of age. Skull fractures re-imaging within 6 months is therefore recommended.

P324 - 2012

The French National Reference Centre for Childhood Stroke: a new tool to improve management of stroke in children?

Kossorotoff M, Chevignard M, Vuillerot C, Zerah M, Husson B, Saliou G, Debillon T, Renaud C, Chabrier S. National Reference Centre for Childhood Stroke and Paediatric Neurology Department, University Hospital Necker-Enfants Malades, APHP, Paris, France – manoeille.kossorotoff@nck.aphp.fr

Background: Up to 1000 paediatric strokes occur each year in France, including perinatal stroke. Acute phase management and diagnosis delay, but also long-term individual care plan and referral to rehabilitation facilities, may be very different within managing teams. **Methods:** Under a national 5-year stroke plan (Stroke 2010–2014), the French Ministry of Health approved a multi-site National Reference Centre for Paediatric Stroke, coordinated by the University Hospital (UH) of Saint-Etienne. The centre involves experts from the Paediatric Neurology and Paediatric Neurosurgery departments at Necker-Enfants Malades Hospital (Paris UH - APHP), from the Imaging department at Bicêtre Hospital (APHP), from the Paediatric and Neonatal ICU at the UH of Grenoble, and from the Paediatric Physical Medicine and Rehabilitation departments at Lyon UH and Saint-Maurice Hospitals. Operating according to a model developed for rare diseases, the centre was attributed several missions: to develop collaborative activities to bring together, coordinate and formalize the organization of local and national care pathways; to provide expertise for complex cases; to educate all professionals involved in paediatric stroke to reduce the clinical and radiological diagnostic delay and favour optimal management; to collaborate with adult neurovascular professionals; to train and inform school professionals, families and the general public about the consequences of paediatric stroke; to collect epidemiological data and to coordinate research in this field. The centre is now the first interlocutor of the Ministry of Health, the regional health agencies, the healthcare professionals involved in paediatric stroke care, as well as patients' representatives. **Discussion:** The centre was appointed in January 2013 for five-year. Multidisciplinary video-conference meetings started early 2013 to discuss issues requiring expertise. A website is under construction. Regional groups are encouraged to plan their local organization. Different endpoints and quality criteria will evaluate the centre activity and the impact concerning paediatric stroke management in the country.

P325 - 1859**Clinical and laboratory features of the transient ischemic attacks in children**

Lvova OA, Kovtun OP, Voroshilina ES, Orlova EA, Abilova MY, Semenova AP. Ural State Medical Academy, Ekaterinburg, Russia – mashaabilova@yandex.ru

Background: The etiology of transient ischemic attacks (TIA) in children is not investigated thoroughly. The aim: to estimate the clinical features and frequency of thrombophilic single nucleotide polymorphisms (SNPs) in patients with TIA. **Methods:** Case-control study. 32 patients were compared with 83 controls. 12 SNPs of hemocoagulation and folic acid cycle's enzymes by polymerase chain reaction and homocysteine's level were identified. **Inclusion criteria:** TIA at the age under 18 y.o.; slavic origin; no changes on brain CT (MRI) and spinal tap. **Results:** The average age of disease's onset was 11 y.o. Smoking (n=2), overweighting (n=4) and dyslipidemia (n=0) are very rare as risk factors for TIA. The following symptoms were identified: cerebral (n=20; 62.5%), face and extremities' dysesthesia (n=18; 56.3%), cranial nerves' (n=18; 56.3%) and extremities' paresis (n=5; 15.6%), speech difficulties (n=7; 22%). Only 4 patients had embologenic syndrome on ultrasound TCD and 4 children had congenital cerebral vessels' malformation. Patients had 2.8 ± 0.7 thrombophilic and 2.2 ± 0.5 folic acid enzymes' SNPs in the homozygous or heterozygous state: F2:G20210A 0 vs 2, F5:G1691A 0 vs 1, F7:G10976A 6 vs 8 (OR=2.16, p=0.11), F13:G103T 12 vs 39 (OR=0.68, p=0.74), PAI-1:-675 5G/4G 25 vs 68 (OR=0.79, p=0.38), FGB:G-455A 14 vs 28 (OR=1.53, p=0.11), ITGA2:C807T 23 vs 50 (OR=1.7, p=0.05), ITGB3:T1565C 10 vs 34 (OR=0.65, p=0.77), MTHFR:C677T 11 vs 31 (OR=0.88, p=0.53), MTHFR:A1298C 22 vs 38 (OR=2.6, p=0.006), MTRR:A66G 24 vs 58 (OR=1.3, p=0.13), MTR:A2756G 13 vs 31 (OR=1.15, p=0.29). All patients had combinations of prothrombotic SNPs: FGB:G-455A and PAI-1:-675 5G/4G 11 vs 24 (OR=1.3, p=0.24), FGB:G-455A+ITGA2:C807T+ ITGB3:T1565C+PAI-1:-675 5G/4G 3 vs 5 (OR=1.6, p=0.33), FGB:G-455A+ITGA2:C807T+ITGB3:T1565C+PAI-1:-675 5G/4G+ MTHFR:C677T 2 vs 4 (OR=1.3, p=0.48), FGB:G-455A+ITGA2:C807T+ITGB3:T1565C+PAI-1:-675 5G/4G+MTHFR:C677T+MTHFR:A1298C 2 vs 3 (OR=1.8, p=0.38). Homocysteine's average level was 11.6 in patients under 10 y.o. and 15.7 $\mu\text{mol/l}$ under 10 y.o. **Conclusion:** TIA is still very difficult diagnosis and remains multifactorial disease in children. Although some prothrombotic SNPs may increase the chance of TIA, they don't play the main role in their onset as well as their severe combinations.

P326 - 1856**A case of spontaneous spinal epidural haematoma mimicking Guillain-Barre syndrome**

Uzun M, Düzenli Kar Y, Renklişık B, Aygün MS. Konya Education and Training Hospital, Turkey – meltempirti@yahoo.com

Spontaneous spinal epidural haematoma (SSEH) is a rare cause of spinal cord compression in children. Presenting symptoms are usually pain followed by progressive bilateral motor weakness, with sensory loss. Guillain Barre Syndrome (GBS) is an acute inflammatory polyradiculopathy and rapidly progressive. Early diagnosis, and treatment may result in decreased morbidity and mortality. We describe the clinical course and treatment of spontaneous epidural haematoma mimicking GBS in a 10 year-old boy. CASE A 10-year-old previously healthy male presented with back pain, progressive limb weakness and inability to walk of 4 days duration. There was no history of trauma or of bleeding diathesis, any infection. Neurological examination revealed decreased muscle weakness bilaterally, both upper (2/5) and lower (3/5) extremities. Deep tendon reflexes were abolic. **RESULTS** Laboratory studies and analysis of the cerebrospinal fluid was normal. F wave could not be obtained in on electromyography. The clinical

course simulated GBS so intravenous immunoglobulin therapy was started. The magnetic resonance imaging (MRI) was done and showed an subacute extradural haematoma extending from C6 to T1 with compression of the spinal cord. Intravenous immunoglobulin therapy was stopped. The patient underwent an emergency laminectomy and showed gradual improvement within 1 weeks. **CONCLUSIONS** Spinal epidural haematoma is presented as a GBS. During the course of the first few days, completely normal nerve conduction studies can be found in GBS. The earliest evidence suggesting that EMG F responses could not be obtained. MRI is very important in the differential diagnosis of such diseases with very similar signs and symptoms such as GBS and SSEH. MRI should be the first diagnostic test to be applied in the case of a paraplegia or tetraplegia. this can reduce the morbidity and mortality in cases of acute cord compression such as SSEH, which can be corrected with urgent surgical intervention.

P327 - 1843**Magnetic resonance spectroscopy in predicting outcomes for children after cardiac transplantation**

Pichon P, Emily Brandt E, Chinnock R, Holshouser BA, Ashwal S. Department of Pediatrics, LLU School of Medicine, Linda, California, USA – sashwal@llu.edu

Objective: We performed a retrospective chart review of children undergoing cardiac transplantation (1999- 2011) who had pre-transplantation proton Magnetic Resonance Spectroscopy (MRS). **Methods:** MRS was done at a mean age of 7.9 months. Pediatric Cerebral Performance Category Scale (PCPCS) scores were determined on average at 5.3 years post-transplant. N-acetylaspartate (NAA), creatine (Cre), choline (Cho), myo-inositol (Ins), presence of lactate (Lac), and metabolite ratios (NAA/Cre, NAA/Cho, Cho/Cre) were evaluated in the mid- occipital gray matter, basal ganglia and thalami. MRS data were correlated to pertinent clinical data and neurologic outcome (PCPCS, dichotomized as poor: moderate/severe disability, vegetative state, or death; n=7; vs. good: normal, mild disabilities; n=18). **Results:** We studied 25 patients (mean age 11.3 months at transplant) and compared their MRS findings to age-matched controls. The presence of lactate and reduced NAA in occipital gray matter or basal ganglia correlated with poor outcomes (χ^2 ; p=0.016). The presence of lactate correlated with a higher PCPCS score (Pearson; p=0.004) and with poor outcome in the dichotomized PCPCS (Pearson; p=0.014). Seizures pre or post transplantation correlated with a higher PCPCS score (p=0.04) and a poor PCPCS categorized outcome (p=0.02). **Conclusions:** Pre-transplant elevated lactate levels signifying altered energy metabolism and reduced N-acetylaspartate levels signifying neuronal loss or dysfunction correlated with poor outcomes for children who had heart transplantation. The presence of pre or post-transplant seizures was a predictor of poor outcome. MRS performed prior to heart transplant may be used with clinical data (e.g., seizures) to determine long term-prognosis.

P328 - 1842**Automated quantification of ischemic core and penumbra in neonates with arterial ischemic stroke**

Ghosh N, Obenaus A, Ashwal S. Loma Linda, California, USA – sashwal@llu.edu

Objective: Neonatal arterial ischemic stroke occurs in about 1/2300 live births and is associated with significant morbidity. MRI has improved our ability to detect neonatal AIS and future treatments will be predicated on determining the degree of irreversibly injured (core) from salvageable (penumbra) tissues using different MRI modalities. In recent translational/human studies we have shown that Hierarchical Region Splitting (HRS),

a computational analysis method, can differentiate core from penumbra based on diffusion and T2 weighted imaging (Ghosh et al, *J Cereb Blood Flow Metab.* 2012; 32:2161). **Methods:** HRS recursively partitions the apparent diffusion coefficient (ADC) maps into uniform-diffusivity regions that allows detection of total ischemic lesion volume and allows quantification of ischemic core and penumbra based on subtle ADC variations within the lesion. **Results:** Our pilot data from 6 AIS neonates (studied ~3–5 days after birth) showed considerable variations in total lesion and core/penumbral volumes and no emerging correlation between lesion volume and the percentage of tissue that was core/penumbra (i.e., some neonates with large lesions had large penumbral volumes). Ongoing HRS analysis is being concluded on an additional 20 neonates. **Conclusions:** We have demonstrated that HRS can quantify ischemic core and penumbra volumes in neonates with AIS. Ongoing work is aimed at determining the relation between time post-injury and the relative core/penumbra volumes as well as the relationships between total lesion volume and the degree of salvageable tissue. Such data are clearly needed for using any therapy to treat neonatal AIS.

P329 - 1804

Initially suspected intoxication in a patient with thalamo-mesencephalic stroke

Perković-Benedik M, Kopač L, Gradinik P, Podnar T. *University Medical Centre Ljubljana, Slovenia – mirjanap.benedik@gmail.com*

Objectives: We report a 14 years old boy who presented with coma without focal neurological signs. The correct diagnosis was delayed because intoxication was initially suspected. Authors discuss the clinical presentation of this rare stroke syndrome and how a delay in diagnosis could be omitted. **Case report:** A 14 years old boy experienced sudden speech and gait difficulties followed by loss of consciousness while attending school. On admission to a local hospital he was unresponsive and had a GCS score of 7 without focal neurological signs. CT scan was performed 2 hours after the onset of symptoms and was normal. Extensive evaluation of suspected intoxication was done but all tests came out negative. The patient was transferred to a university medical centre where stupor and upward gaze palsy were found. Seven days after the onset, the MRI brain scan was carried out and showed infarction in the region of the ventral rostral mesencephalon, crus cerebri bilaterally and in the left thalamus. Extensive diagnostic evaluation was done to find possible stroke risk factors. Only large patent foramen ovale was found with important right-to-left shunt. Patient improved substantially, mild upward gaze palsy have persisted. **Conclusions:** A thalamo-mesencephalic stroke is rare in pediatric population and according to data from adult patients our patient had the most common clinical presentation: loss of consciousness, decreased alertness and coma, visual disturbances, particular vertical gaze palsy. The case indicates two important facts: that normal initial CT scanning, performed very early on, can not eliminate the diagnosis of acute stroke, therefore brain MRI should be considered as a first-line imaging procedure in pediatric patients with acute neurological deficits. Secondly, horizontal eye movements are regularly checked in a drowsy or comatose patient, but also an examination of vertical eye movements is important and can lead to the correct diagnosis.

P330 - 1744

Chorea and primary antiphospholipid syndrome: case report

Pilarska E, Lemka M, Zawadzka M. *Department of Developmental Neurology Medical University of Gdańsk, Poland – mlempka@wp.pl*

Objectives: Primary antiphospholipid syndrome is characterised

by arterial or venous thrombosis and/or pregnancy losses, in the presence of elevated levels of antiphospholipid antibodies when there is no evidence of associated diseases. Different other clinical symptoms have been related to this syndrome. Chorea is not so frequent phenomenon, but antiphospholipid syndrome should be excluded in all unexplained cases of chorea, even when the associated clinical signs are absent. **Material and methods:** A girl aged 13 years with involuntary movements was admitted to the Clinic of Developmental Neurology in Gdańsk, in Poland. Choreiform movements of four extremities, face, neck, tongue and mouth were present at rest, more marked during emotions. No other neurological deficits were established. Routine blood tests with haematological parameters were normal. Serological studies and clinical signs did not show SLE. Anticardiolipin antibodies, beta 2 glycoprotein antibodies and lupus anticoagulant were positive with normal brain MRI. **Results:** Primary antiphospholipid syndrome is a probably one of the unrecognised causes of choreatic syndroms in childhood and adolescence. Assessment of anticardiolipin antibodies and/or circulating lupus anticoagulant in blood tests should be an obligatory part of our diagnostic process of such patients. **Conclusions:** Early diagnosis of primary antiphospholipid syndrome, even when the clinical signs are absent, may improve clinical management and treatment to avoid or minimise complications in adult life.

P331 - 1726

Central retinal artery occlusion in childhood diagnosed by laser tomography and fundus examination

Mizuochi H, Fujii K, Takagi A, Suyama M, Inoue Y, Uchikawa H. *Department of Pediatrics, Graduate School of Medicine, Chiba University, Japan – hiromi_miz@yahoo.co.jp*

Objectives: Central retinal artery occlusion (CRAO) is a rare disease in children. Early diagnosis has been supposed to be critical not to leave the permanent visual loss. However, appropriate technique to diagnose CRAO has not been well established. **Material and methods:** We examined a 12-year-old Japanese girl who exhibited sudden loss of right vision repeatedly after her mild exercise without eye pain. She lost right vision completely, and revealed mydriasis with elimination of light reflex. To elucidate the etiology of this sudden vision loss, we performed several examinations, including MRI, MR angiography, blood analysis, cardiac echogram, electroencephalogram, retinal laser tomography, and fundus examinations. We finally investigated the most useful method to diagnose CRAO correctly among these examinations. **Results:** Physical examination of anterior eyes was unremarkable. Fundus examination showed retinal whitening with cherry-red-spot in her right eye, which was typical for retinal ischemic damage. Retinal laser tomography showed retinal edema in her right eye. The fundus fluorescence angiography showed prolonged retinal circulation time and retinal vessels filled with fluorescent dye at late phase, suggesting the existence of prolonged retinal ischemic changes. In blood examination, they showed no immunological disorder, nor coagulation disorder. Her cardiac echogram was normal. MRI and MR angiography revealed no abnormality in the eye and the brain. Extensive medical work up showed no evidence of diabetes, cardiovascular, hematologic, or collagen disease. Based on these examinations, we finally diagnosed her as having central retinal artery occlusion in childhood. **Conclusion:** Diagnosis of CRAO is clinically important to treat patients efficiently. Our study clearly showed diagnostic value of fundus examinations and laser tomography, which was able to perform in the outpatient clinic. We conclude that even in children, combinations of these examinations lead to prompt diagnosis and enables them to apply the appropriate therapy in patients with CRAO.

P332 - 1717

Intracranial aneurysm in children with sickle-cell anaemia

Kossorotoff M, Brousse V, Grevent D, Zerah M, Naggara O, Brunelle F, Ozanne A, Blauwblomme T, De Montalembert M. French Reference Centre for Paediatric Stroke, Paediatric Neurology Department, University Hospital Necker-Enfants Malades, APHP, Paris, France – manoelle.kossorotoff@nck.aphp.fr

Background: Intracranial aneurysms in sickle-cell anaemia (SCA) have been reported in about 50 adult patients, and only in one teenager, mostly presenting with subarachnoid haemorrhage (SAH). Aneurysms in those patients have a tendency to be multiple, to involve the posterior circulation more frequently than in the general population and to be diagnosed at a younger age. In SCA children a chronic stenotic vasculopathy leading to ischaemic events is much more frequent than cerebral haemorrhage. Actually, SAH has scarcely been reported and no evident link with the classical stenotic cerebral vasculopathy demonstrated. **Material and methods:** we conducted a retrospective study in a single sickle-cell clinic to record cases of SCA children with intracranial aneurysm (ICA) diagnosis during 2005–2012. Clinical and radiological data concerning SCA characteristics and markers of cerebral vasculopathy (transcranial Doppler, brain MRI/MRA) were collected. **Results:** Nine ICA were found in 5 children (1 had 4 ICA, 4 had 1), aged 5–13. 6/9 were located on the posterior circulation (posterior cerebral artery, basilar artery) and 3/9 on the anterior circulation (intracranial carotid artery, ophthalmic artery), mostly with saccular or nipple shape (8/9). Brain imaging was prompted by non-traumatic SAH in 2/5 children, transcranial Doppler abnormalities in 3/5. Transcranial Doppler (TCD) or brain MRI were suggestive for concurrent SCA-associated chronic stenotic cerebral vasculopathy in 4/5, in a mild (conditional TCD, white matter T2 hypersignals <3 mm) or severe form (abnormal TCD, arterial ischemic stroke, unilateral moyamoya syndrome). Various ICA management and subsequent haematological treatment modifications were decided, in the absence of recommendations in this setting. **Conclusion:** Intracranial aneurysm may not be exceptional in SCA children. In our short series, they bore similar characteristics with ICA described in adult patients. They were mostly associated with stenotic vasculopathy, suggesting common pathophysiological mechanisms. Further studies are needed to determine clinico-radiological features, pathophysiology and adequate management.

P333 - 1685

Genes' condition in infants with the operated congenital heart diseases and ischemic stroke

Lvova O, Gusev V, Nesterova A, Partyulova E, Voroshilina E. Ural State Medical Academy, Yekaterinburg, Russia – olvova@bk.ru

Introduction: Congenital heart malformations and thrombophilia are described to be the most frequent reasons for stroke's debut in infants. But interaction between them is not investigated thoroughly. **Methods:** Case-control study. 13 patients' blood samples (5 boys and 8 girls) with acute ischemic stroke (AIS) were compared with 83 controls. 12 single nucleotide polymorphisms (SNPs) by polymerase chain reaction and homocysteine's level were investigated. **Inclusion criteria:** age 0–12 month; AIS developed immediately after cardiac surgery and confirmed by brain CT scan; no changes in embologenic mode on ultrasound TCD. **Results:** Patients had 4.4 ± 0.7 thrombophilic and 2.9 ± 0.5 folic acid enzymes' SNPs in the homozygous or heterozygous state: F2:G20210A 1 vs 2 (OR=3.4, 95% CI 0.3–42.2; $p=0.35$), F5:G1691A 1 vs 1 (OR=6.8, 95% CI 0.4–123.2; $p=0.25$), F7:G10976A 8 vs 8 (OR=15, 95% CI 3.8–58.5; $p=0.00008$), F13:G103T 4 vs 39 (OR=0.5, 95% CI 0.1–1.8; $p=0.92$), PAI-1:-675 5G/4G 13 vs 68 (OR=2.9, 95% CI 0.3–24.7; $p=0.27$), FGB:G-455A 11 vs 28 (OR=10.8, 95% CI 2.2–53.8; $p=0.0007$), ITGA2:C807T 11 vs 50 (OR=3.63, 95% CI 0.7–18; $p=0.06$), IT-

GB3:T1565C 4 vs 34 (OR=0.6, 95% CI 0.2–3.3; $p=0.84$), MTHFR:C677T 10 vs 31 (OR=5.6, 95% CI 1.4–22.5; $p=0.009$), MTHFR:A1298C 5 vs 38 (OR=0.7, 95% CI 0.2–2.5; $p=0.75$), MTRR:A66G 11 vs 58 (OR=1.6, 95% CI 0.4–6.3; $p=0.37$), MTR:A2756G 7 vs 31 (OR=1.95, 95% CI 0.6–6.5; $p=0.2$). All patients had severe combinations of prothrombotic SNPs: FGB:G-455A+PAI-1:-675 5G/4G 11 vs 24 (OR=13.5, $p=0.0002$), FGB:G-455A+ITGA2:C807T +ITGB3:T1565C+PAI-1:-675 5G/4G 5 vs 5 (OR=9.8, $p=0.003$), FGB:G-455A+ITGA2:C807T+PAI-1:-675+MTHFR:C677T 7 vs 4 (OR=23.0, $p=0.00003$) and so on. Homocysteine's average level was $13.3 \pm 2.1 \mu\text{mol/l}$ and the age limit was doubled. **Conclusion:** We assume prothrombotic and procoagulant genes' polymorphisms to be the main reason of early life stroke's debut: seven significant candidate genes were identified, their OR were 1.6 and more. Combination of "sticky platelets" syndrome with defective fibrinolytic system and with folic acid enzymes' cycle have the most diagnostic value in these patients. The operation technique can be considered to be an essential risk factor for stroke in those children but thrombophilia most likely will become "the last straw".

P334 - 1677

Parry-Romberg presenting as giant intra-cerebral aneurysm

Van Oploo T, Halbertsma F, Wagenaar L, Roos F, Bok LA. Veldhoven, the Netherlands – l.bok@mmc.nl

Introduction: Parry-Romberg is a rare slowly progressive syndrome characterized by hemi atrophy of the face including subcutaneous tissue, skeletal muscle, bones, various ocular abnormalities (ptosis, uveitis, iridocyclitis, exophthalmos and retrobulbar pain) and central nervous system symptoms in up to 15% of patients. The reported central nervous system symptoms include epilepsy, hemiparesis, language deficits, cognitive difficulties, hemianopia, and Rasmussen's encephalitis. On MRI this can be seen as cerebral hemiatrophy, white matter lesions, cortical calcifications and meningeal enhancement (Gambichler BMC dermatitis 2001;1:9–13). Intracranial aneurysmata in Parry-Romberg are rarely reported (Pichiechio, Aoki, Bosman, Schievink), and is reported to be progressive and multiple in one Parry-Romberg patient (Schievink). **Case:** We report a 10 year old girl, with a small temporal intradermal capillary haemangioma without skin hypotrophy, that presented with mild headache and right sided slowly progressive abducens paresis. MRI of the brain showed a giant aneurysma of the right arteria carotis interna; including white matter abnormalities right occipital resembling gliosis with right occipital located calcifications on CT. She had successful neurosurgery. Postoperative period was characterized with serious headache, and right sided miosis and ptosis. The headache resolved over months after administration of carbamazepin. Six years later she reported right sided slowly progressive hypotrophy of the subcutis of the forehead. Only a that time a diagnosis of Parry-Romberg was established. Currently she is 16 years at age, doing well at school but suffering from an anxiety disturbance for which she is using esitalopram. So far no other aneurysmata are seen on 2-yearly follow-up cerebral imaging. **Conclusion:** We confirm the association of Parry-Romberg and cerebral aneurysm and conclude that in case of a giant intracerebral aneurysm a diagnosis of Parry-Romberg should be considered. As giant aneurysmata in Parry-Romberg can be multiple and progressive this implicates follow-up in these patients.

P335 - 1675

The role of thrombophilic and procoagulant genes' polymorphisms in children's stroke with Moyamoya disease

Lvova O, Gusev V, Tsoriev A, Golovaneva A. Ural State Medical Academy, Yekaterinburg, Russia – olvova@bk.ru

Background: It considered that Moyamoya disease (MMD) itself

has enough reasons for stroke and TIA in children. The aim was to assess the incidence of prothrombotic genes' polymorphisms in patients with MMD. **Methods:** Type of study: clinical cases. 5 children 5–13 y.o. with MMD I-IV type (Matsushima, MR angiography confirmed) were investigated for 12 single nucleotide polymorphisms (SNPs) by polymerase chain reaction and for the level of homocysteine. Patients had 2–6 TIA and 1–2 stroke in the past. **Results:** Patients had more than three thrombophilic genes and more than two genes of folic acid cycle's enzymes. The frequency of genes' polymorphisms were: F2: G20210A (n=0), F5: G1691A (n=0), F7: G10976A (n=4), F13: G103T (n=3), PAI-1: -675 5G/4G (n=5), FGB: G-455A (n=2), ITGA2: C807T (n=5), ITGB3: T1565C (n=3), MTHFR: C677T (n=4), MTHFR: A1298C (n=0), MTRR: A66G (n=4), MTR: A2756G (n=3) both in the homozygous and heterozygous state. Nobody was suspected as having thrombophilia before the stroke occurred. All patients had SNPs' combinations including coagulation factors (FGB, F7, F13), platelets receptors (ITGA or ITGB) and fibrinolytic system (PAI). As well as their hemostasis states showed hypercoagulation: fibrinogen >4.3 g/l, aPTT <27 seconds. The level of homocysteine were 12–37 $\mu\text{mol/l}$ and the age limit was doubled. After genotyping patients were prescribed anticoagulants and antiplatelet drugs (aspirin, clopidogrel, warfarin or sulodexide) and 200–400 μg folic acid daily which have not been administered before. Two years monitoring showed no stroke, no TIA, normal level of homocysteine ($4.78 \pm 0.21 \mu\text{mol/l}$) and normal- or hypocoagulation in hemostasis. **Conclusion:** Five and more SNPs of inherited thrombophilia genes that have been realized as stroke, TIA and homocysteinemia were revealed in children with MMD. We assume procoagulant genes' SNPs to be the main reason of early life debut and thrombosis' recurrence in these patients. Detection of these SNPs, homocysteine's rate and blood clotting system must be administered to all patients with identified MMD.

P336 - 1667

Acute brain stem infarction with atypical Wallenberg syndrome in a boy revealing Lyme neuroborreliosis

Baumann M, Hetzer B, Brunner J, Cartes-Zumelzu F, Rostasy K. Department of Paediatrics I, Medical University Innsbruck, Innsbruck, Austria – matthias.baumann@uki.at

Case report: We report a 14 year old boy who presented with balance perturbation and gait unsteadiness after getting up in the morning. Neurological examination revealed an anisocoria with a small pupil and a mild ptosis on the right (Horner's syndrome, descending sympathetic fibers), a right sided ataxia and falling tendency to the right (anterior spinocerebellar tract), a deviation of the soft palate to the left and change of his voice (nucleus ambiguus) and a hypoaesthesia (especially temperature sensation) of the left side of the body (lateral spinothalamic tract) and the left side of the face (ventral trigeminothalamic tract). The neurological symptoms were indicative of an atypical (ipsilateral sensory deficit of the face) lateral medullary syndrome (Wallenberg syndrome). **Results:** The MRI showed a right sided dorsal lateral medullary infarction. CSF analysis revealed a high protein content, lymphocytic pleocytosis (116 cells/ μl) and oligoclonal IgG bands not present in the serum. The specific *Borrelia burgdorferi* IgG antibody index was elevated (38.7) confirming the diagnosis of a neuroborreliosis. Treatment with intravenous ceftriaxone for 14 days was initiated in combination with 200 mg acetylsalicylic acid for 3 months. Neurological symptoms improved within a few weeks. Two months later he still had a mild sensory deficit on the left side of the body with dysaesthesia, especially for temperature sensation. **Conclusions:** Ischemic stroke in children due to neuroborreliosis with inflammation of intracerebral arterial vessels is rare and localisation in the brain stem like in our patient has been reported only in isolated cases. Therefore Lyme neuroborreliosis should

be included in the differential diagnosis of paediatric cerebral infarction.

P337 - 1642

Valuable diagnostical tools for strokes at children of first year of life

Kenzhagulova R, Jaxybayeva A. National Research Center for Maternity and Child health, Astana, Kazakhstan – altynshash@gmail.com

Stroke is going to be a huge problem of children leading to motor disability and epilepsy. We observed 32 cases. 2 children has ischemic stroke while the rest children – hemorrhagic type. The majority of the children has stroke at the age of 2 months. 4 children developed disturbance at the age of 5–7 months. The aim of the research is to evaluate the valuable diagnostical tools for strokes at children of first year of life. We assessed data of anamnesis. According them - 7 mothers (22%) had a respiratory infection without fever while 12 mothers (37%) had cases of fever and did not receive any treatment. 7 mothers tested for TORCH infection, in five of them was found CMV infection, in three patients - herpes infection. The majority of the children were born health and full term. But one month after birth they developed a stroke. Clinically all children have had movement disorders and different level of developmental delay. Most of them (72%) had seizures and microcephaly (65%). On EEG children with stroke had a different sings. All the children revealed focal changes in the form of suppression of bioelectric activity, reduce of the waves amplitude, and the predominance of slow waves in 20 (62%) children were lateralized (diffuse by one hemisphere), in the other cases they had localized according to stroke location. In 70% of children there were recorded the extended focal epileptiform activity as a sharp waves on the "affected" zone of the hemisphere, 45% had also epileptiform changes on the "intact" side of the hemisphere. EEG data were identical with those MRI findings, which suggest the diagnostic value of the EEG.

P338 - 1586

A retrospective review of a series of patient with Moya-Moya syndrome in Durban, South Africa

Govender R, Mitha A, Mubaiwa L. Department of Paediatric Neurology, Nelson R Mandela School of Medicine, University of Kwa-Zulu Natal, Durban, South Africa – govenderr2@ukzn.ac.za

Moya-Moya syndrome (MMS) is a rare, progressive disease with a high risk of disability. **Objectives:** To document the clinical profile, laboratory and imaging findings of children with MMS. **Methods:** This was a retrospective review of children with MMS identified from our database of 2000 children. **Results:** Ten (5 males and 5 females) children were identified. The average age at the time of diagnosis was 4.2 years (range: 14 months– 7 years). The presenting features were focal seizures (n=4), hemiparesis (n=5) and headaches (n=1). Other neurological deficits included: bulbar palsy (n=2), facial nerve palsy (n=2), sixth nerve palsy (n=1), cortical visual impairment (n=2), aphasia (n=1). Eighty percent of patients had an associated risk factor identified: protein C/S deficiency n=2, Down's syndrome n=3, Neurofibromatosis Type 1 n=1, HIV infection n=2. One patient with Down's syndrome had anti-phospholipid antibody syndrome. All other auto-immune/pro-thrombotic screens were negative. Seven children had iron deficiency anaemia. All patients had evidence of developmental delay (predominant cognitive n=4, predominant motor n=2, predominant speech n=2, global delay n=2). Eight had bilateral chronic cerebral infarcts, 3 had acute right watershed infarcts and 1 patient had no infarcts. Predominant right hemispheric involvement was noted in 8 patients. All patients had

vascular occlusive changes of the anterior circulation to varying degrees (additionally 6 of these patients had posterior circulation involvement). Seven patients had involvement of the cavernous portion of the internal carotid artery. Seven patients had the classical “puff of smoke” appearance on MRA. Pial collaterals on the post-contrast scan were evident in 2 children. Treatment was supportive in all patients- 2 children were on aspirin prophylaxis, 4 children were on anti-convulsant therapy. No surgical intervention was offered to any of the patients. **Conclusion:** MMS is a rare phenomenon in our setting. Ischaemic hemispheric strokes and seizures are the commonest presenting features.

P339 - 1563

Cerebral sinovenous thrombosis in children and neonates: clinical experience, laboratory findings, treatment, and outcome

Bektaş Ö, Teber S, Akar N, Uysal LZ, Arsan S, Atasay B, Deda G. *Department of Pediatric Neurology, Ankara University Medical School, Ankara, Turkey – gulhisdeda@gmail.com*

Aim: To present the etiology, risk factors, radiological findings, anticoagulant therapy, and treatment outcome in patients with cerebral sinovenous thrombosis (CSVT). **Material and methods:** The study included 12 patients that were treated for CSVT at Ankara University, School of Medicine, Department of Pediatric Neurology. All patients underwent echocardiography and hematological investigation, including prothrombin time, partial thromboplastin time, fibrinogen, protein C, protein S, antithrombin III, lipoprotein(a), factor VIIIc, factor IX, homocysteine, and prothrombotic gene mutations. **Results:** The study included 5 girls (41.7%) and 7 boys (58.3%) with a mean symptom age of 5.2 ± 6.29 years (range: 0–18 years) that were followed-up at our institution for a mean period of 1.8 ± 1.73 years (range: 1 month–6.5 years). According to etiologies, neonates was classified as intracranial hemorrhage to 3, hypernatremic dehydration to 2, protein S deficiency to 1. Three (25%) patients had hemiparesis or hemiplegia, 7 (58.3%) had seizure, 2 (16.6%) had cranial nerve involvement, and 2 (16.6%) had headache. Among the patients, 3 had no risk factor, 2 had 1 risk factor, and 7 had multiple risk factors. Anticoagulant therapy was administered to 4 patients, of which 1 had neurological sequelae; neurological sequelae occurred in 3, exitus in 1 of the 8 patients that did not receive anticoagulant therapy. **Conclusion:** The present findings show that appropriate prophylaxis in appropriately selected patients reduced the rate of recurrence. We think that anticoagulant therapy should be given to CSVT patients during the acute phase of disease, unless major hemorrhage is observed.

P340 - 1556

Sporadic hemiplegic migraine: hypoperfusion demonstrated by susceptibility weighted magnetic resonance imaging and CT perfusion study

Kim YM, Lee YJ, Nam SO. *Busan, Korea – pink2129@naver.com*

Sporadic hemiplegic migraine (SHM) is defined by migraine attacks with aura including a gradual progression of any degree of hemiparesis or other neurological deficit without family history of similar attacks. The mechanism of hemiplegic migraine has not been elucidated. Cerebral perfusion change in hemiplegic migraine has been postulated as a possible cause of encephalopathy and hemiplegia. We describe a 19-year-old male with a SHM. When he was a 17-year-old, he was admitted for right hemiplegia and aphasia. Brain MRI (T1/T2) with diffusion-weighted imaging (DWI) was normal, while susceptibility weighted magnetic resonance imaging (SWI) demonstrated prominent vessels in the left hemisphere during the attack. On the next day, [99mTc] HMPAO-SPECT showed increased tracer uptake over left cerebral hemisphere and this finding was not compatible with

findings in SWI. Follow-up EEG on day 11 was normal. Brain MRI (T1/T2, DWI) with SWI and [99mTc] HMPAO-SPECT on day 14 day were normal and there was no significant difference of perfusion between two cerebral hemispheres. Two years later, he showed right hemiplegia, aphasia, and dizziness again. At that time, we checked brain MRI with DWI and SWI and computed tomography (CT) with perfusion sequences within 2 hours after onset. SWI demonstrated increased venous vasculature in left hemisphere and CT perfusion study showed decreased perfusion in left middle cerebral arterial territory. These studies during the acute phase of hemiplegic migraine revealed hypoperfusion at the left cerebral hemisphere. Hypoperfusion may explain the clinical features in the acute phase of hemiplegic migraine.

P341 - 1555

Total occlusion of the middle cerebral artery associated with Mycoplasma pneumoniae pneumonia

Kwon YS, Kang B, Son BK. *Department of Pediatrics, School of Medicine, Inha University, Incheon, Korea – ysped@inha.ac.kr*

Introduction: Arterial ischemic stroke (AIS) is a rare extrapulmonary complication of Mycoplasma pneumoniae infection, especially in the pediatric population. **Case:** A 5-year-old girl was admitted due to left hemiparesis and facial palsy that had developed on that day. She had developed symptoms of cough and fever 6 days before. Physical examination revealed coarse breath sounds with crackles on both lung fields. Motor grade were both 3 in the left upper and lower extremities. There was central type facial palsy on the left side. Chest radiography showed pneumonic infiltration with pleural effusion in the left lung. Brain magnetic resonance imaging revealed acute infarction in the right middle cerebral artery (MCA) territory. Brain magnetic resonance angiography and transfemoral cerebral angiography showed total occlusion of the right MCA at the M1 portion. Initial serum antibody titers to M. pneumoniae were 5021 U/ml for immunoglobulin M (IgM) and 5.5 AU/mL for IgG. The patient received antibiotic treatment with intravenous ceftriaxone and clarithromycin and antithrombotic treatment with oral aspirin. Rehabilitation therapy was initiated on the fifth hospital day and the patient showed gradual improvement of motor weakness. Laboratory exams to identify other inherited or acquired predisposing factors of stroke were all negative. Serum antibody titers to M. pneumoniae conducted three weeks after admission were 7300 U/ml for IgM and 26.65 AU/mL for IgG, showing a 4-fold increase in serum IgG antibodies compared to the initial exam. At discharge, although there were remaining mild neurologic deficits regarding fine motor skills, both left hemiparesis and left facial palsy had improved to a level of motor grade 5 on all extremities and independent gait. **Conclusion:** We report a case of AIS in a pediatric patient in which total occlusion of the right MCA had occurred 6 days after the onset of serologically proven M. pneumoniae infection.

P342 - 1498

Central retinal artery occlusion in a 13-year-old child as a presenting sign of hyperhomocysteinemia together with high lipoprotein(a) level

Erol I, Karatas MC, Ozkale Y, Yazıcı N. *Baskent University Faculty of Medicine, Department of Pediatrics, Neurology Division, Adana Teaching and Medical Research Center, Adana, Turkey – ilknur_erol@yahoo.com*

Introduction: Central retinal artery occlusion which is a devastating ophthalmological event leading to severe impairment of vision present with acute, painless loss of monocular vision. It is mostly seen in the elderly with clinical findings suggestive of atheromatous emboli. It is an extremely rare diagnosis in the

pediatric population. **Case report:** A previously healthy 13-year-old girl referred to the pediatric emergency department with sudden onset of vision loss of the left eye after her basketball exercise 3 days ago. She had no history of infectious diseases, trauma, systemic malignancy or other systemic complaints. On her ophthalmologic examination, her best-corrected visual acuity was 1.0 in the right eye and counting fingers 0.5 meters in left eye. Intraocular pressure was 14 mmHG in both eyes measured with Goldmann applanation tonometry. Slit lamp examination revealed no obvious inflammation in the anterior chamber or vitreous. Fundus examination revealed normal findings in the right eye and pallid retinal edema and cherry red spot in the macula of the left eye. Relative afferent papillary defect was detected on the left eye. Fundus fluorescein angiography showed delayed arterio-venous transit time was on the left eye. Optical coherence tomography disclosed diffuse macular edema on the left eye. Magnetic resonance imaging of brain and orbita were also in normal range. Evaluation for potential stroke factors revealed elevated serum homocysteine and lipoprotein(a). The patient was found to be homozygous mutant for MTHFR 677T. She received enoxaparin, folbiol and vitamin B12. **Conclusion:** To our knowledge, this case study is the first report of central retinal artery occlusion associated with hyperhomocysteinemia caused by MTHFR C677T mutation and high lipoprotein(a) level in a child. This case mentions the need for a systemic evaluation for hyperhomocysteinemia and lipoprotein(a) level in children with retinal vascular occlusion of uncertain etiologies.

Trauma

P343 - 2047

The paediatric head injury referrals audit: our 12 months experience

Aziz M, Kaliaperumal C, Allcutt D. *Children's University Hospital, Temple Street, Dublin, Ireland – mohdazli@me.com*

Objective: This audit is a follow-up to the 6 months experience. Our aim is to observe any change in referrals pattern of head injury to neurosurgery in the last 6 months compared to the same period in 2011 and to observe any neurosurgical interventions carried out and highlight learning points of same to improve the efficiency of head injury referrals and management in terms of costs, admission to second hospital and inconvenience to families. **Methods:** All head injury referrals are recorded in the neurosurgical registrar On-call logbook from 01st July to 14th November 2012. Each referral is entered into an EXCEL spreadsheet to include demographic data, date and time of referral, referring hospital, baseline Glasgow coma scale (GCS), clinical signs, imaging and plan of transfer to neurosurgical units in CUH and BH, neurosurgical intervention and discharge. The same data from the same period last year is used as comparison. **Results:** In 2012 there were 78 head injury telephone referrals. 51 patients

were transferred to neurosurgery units. Only 5 patients required neurosurgical intervention. Data from 2011 showed 103 referrals. 79 patients were transferred and 24 patients remained in referring hospital. Out of 79 patients transferred only 7 required intervention. **Discussion:** There has been a 24% reduction in number of telephone referrals between the two periods. The presentation of our 6 months experience have given more awareness to clinicians to be more selective prior to making the referral and general reflection of the general public's awareness of head injury prevention. The transfer rates have also reduced by 11%. **Conclusion:** This positively reflects the willingness and confidence of referring physicians to observe the patients based on baseline clinical examination and GCS.

P344 - 2149

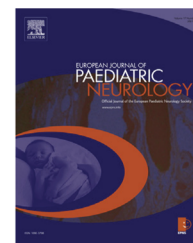
Virtual rehabilitation after brain injury?

Mackie S, Geary M, Kirkham F. *Southampton, UK – Fenella.Kirkham@uhs.nhs.uk*

Rehabilitation after brain injury is an increasingly important priority but commissioners of services are reluctant to pay for prolonged inpatient stays after the acute phase. The use of tablet computers and the internet might allow children to continue therapy at home or in local facilities but with specialist input from experienced therapists. We report our experience after a 6 month service delivery pilot of this type of service involving Physiotherapy, Occupational Therapy, Speech and Language Therapy (SALT), Neuropsychology and Psychiatry as well as Neurology services based in University hospital Southampton and children, parents and therapists in local hospitals. Important aims are to evaluate the effects of the technology on length of stay, and patient/parent satisfaction and outcome. The NHS firewall precluded the use of commercially available video software and most conferencing programmes were of inadequate definition for assessing movement but Facetime was successfully used on iPads using 3G hubs. SALT was feasible in assessing progress in (1) a child with word-finding difficulties after limbic encephalitis (2) 2 children with bulbar difficulties post surgery. Occupational therapy was impossible online in a shy 6 year old with a stroke but was useful in allowing repetitive practice of skills, in combination with SALT and Neuropsychology, in another child with stroke. Physiotherapy experience was limited because of safety concerns as well as lack of definition and size of available screens but one child with a complex movement disorder a year after streptococcal infection was successfully reintegrated into school with thrice weekly physiotherapy sessions for 3 weeks after 6 weeks of inpatient rehabilitation. Feedback from families was generally positive. There are currently technical limitations to rehabilitation over the internet. Future developments include exploration of a large screen VideoConferencing system for Physiotherapy and assessment of cognitive function in children at least 6 months post-head injury.



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