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Dear Colleagues,

On behalf of the Hellenic Paediatric Neurology Association, as well as the Organising Committee and the Scientific Committee, it is my great pleasure and honor to welcome you to the 13th European Paediatric Neurology Society (EPNS) Congress 2019, in Athens, Greece.

The 2019 EPNS Congress’ title is “Paediatric Neurology and Rare Diseases: Genetics & Environment, Progression & Transition”. The Scientific Faculty presenting in EPNS is an exciting line-up of Local and Global experts, delivering the invited lectures, including topics covering full spectrum of Paediatric Neurology and many more Affiliated Specialties sessions. The multidisciplinary sessions are an important component of EPNS, followed by the presentations of original pieces of work in oral or poster format, selected by a large panel of experts among many submissions, ensuring cutting edge clinical and research information are presented during the 13th EPNS Congress.

Our venue, the Megaron Athens International Conference Centre (MAICC), offers the finest facilities, stunning aesthetics and cutting-edge technology. A landmark, in the center of Athens where major hotels are in close proximity, many within walking distance.

We hope delegates will profit from the 2019 EPNS Congress, and find the experience rewarding in terms of practice and research updates, as well as networking with friends and colleagues.

Sincerely yours,

Dimitrios I. Zafeiriou, MD, PhD
Professor of Child Neurology & Developmental Paediatrics
President of the Organising and Scientific Faculty of the 13th EPNS Congress 2019
EPNS Board Member
Past President of the Hellenic Paediatric Neurology Association

Dear Friends and Colleagues,

Welcome to Athens for the 13th European Paediatric Neurology Society (EPNS) meeting!

Prof. Dimitrios Zafeiriou, together with the Local Organising Committee from the Hellenic Paediatric Neurology Association, have been working with Professor Barbara Plecko, Chair of the EPNS Scientific and Research Committee, and her team, to put together a scientifically stimulating programme. The programme reflects the main theme of the Congress, which is “Paediatric Neurology and Rare Diseases: Genetics & Environment, Progression & Transition”.

This Congress will feature an exciting line-up of expert speakers and an excellent platform for the exchange of clinical and scientific knowledge on the latest developments and emerging challenges of Paediatric Neurology. In keeping with the tradition of the EPNS congresses, the event will be a stimulating occasion both scientifically and socially. Undoubtedly, it will be a great opportunity to see other colleagues and friends.

The EPNS continues to grow from strength to strength. For more details about the EPNS, please visit our website at www.epns.info, follow us on twitter @EPNSnews or e-mail at info@epns.info.

The EPNS Congress 2019 is a wonderful forum for you to refresh your knowledge base and explore the innovations in Paediatric Neurology. The Congress will offer plenty of networking opportunities, providing you with the opportunity to meet and interact with the leading scientists and researchers, friends and colleagues.

Sincerely, I thank you for joining us for a symphony of outstanding science.

Sameer Zuberi
EPNS President
13th European Paediatric Neurology Society (EPNS) Congress
ABSTRACT BOOK

http://www.epns.info/

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17-21 September ATHENS, GREECE
MAICC Megaron Athens International Conference Centre
ORAL PRESENTATIONS
OC001 Epidemiology, aetiology and genomics of drug-resistant epilepsies of early childhood: a national population-based prospective cohort study

Joseph Symonds1, Katherine Elliott1, Andreas Brunklaus1, Alice Jollands2, Shelagh Joss4, Martin Kirkpatrick2, Stewart MacLeod2, Ailsa McLellan3, Daniela Pilz4, Jay Shetty1, Kirsty Stewart1, Louise Diver5, Sarah Gardiner5, Julian Knight5, Sameer Zuberi1

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Objectives: To prospectively identify all patients with drug resistant epilepsy (DRE) presenting <3y of age in a population-based cohort and define the incidence of DRE. Using the latest technology including MRI, metabolic investigation, gene panels and whole genome sequencing (WGS) to determine aetiology and syndromes within the cohort.

Methods: Participants were recruited as part of a prospective national cohort study from May ’14 to May ’17. All children presenting with epilepsy before their 3rd birthday were eligible. Patients with DRE – ongoing seizures despite adequate trials of 2 anti-epileptic drug regimens – were identified through prospective follow-up. Patients without known aetiology after neuroimaging were tested using chromosomal microarray and 104 gene epilepsy panel. Those without known aetiology after these genetic tests had WGS.

Results: There were 125,000 births during the recruitment period. The incidence of DRE was 1 per 1,230 live births (32% of all epilepsy). 99 patients had DRE. Aetiology was identified in 82/99 (83%). 58 (59%) had a genetic aetiology of whom: 4 had trisomy, 12 had pathogenic copy number variants (CNVs) and 34 had single gene variants. Recurringly implicated single genes were: SCN1A (n = 5), KCNQ2 (n = 3), CDKL5 (n = 2), and TSC2 (n = 2). 21 patients (21%) had a primarily structural cause.

Factors associated with the development of drug-resistance were genetic aetiology (OR = 3.7, 95% CI 1.8-7.4) and presence of global developmental delay (OR = 9.1, 95% CI 4.3-19.0).

Conclusions: Early childhood DRE affects 1 per 1,230. With the latest imaging and genomic technologies aetiology can be identified in 83%.

Disclosure: No potential conflict stated.

OC002 Electrical Status Epilepticus in Sleep (ESES): A review of 59 paediatric patients

Ruben Rocho, Joana Martins, Cristina Garrido, Inês Carrilho, Rui Chorão, Manuela Santos, Teresa Temudo, Sónia Figueiró Centro Materno-Infantil do Norte, Porto, Portugal

Introduction: Electrical status epilepticus in sleep (ESES) is a rare, age-related electrographic pattern characterized by nearly continuous spike-wave discharges in slow wave sleep, usually with a frequency of 1.5-3 Hz. The aim of the study was to review the clinical electrophysiological findings and treatment modalities and outcome of children with ESES.

Materials and Methods: Electroencephalographic reports of children followed in our hospital since 2006 were analyzed and the patients with ESES were selected. Demographic, clinical and electroencephalographic and outcome variables were evaluated.

Results: Fifty-nine patients (54% males) were included. The median of age for the diagnosis of epilepsy was 5 years and for ESES was 7 years. The etiology of epilepsy was presumed to be genetic in 42 patients, structural in 11 patients, infectious in two and unknown in four patients.

Fifty-two patients had focal epilepsy (21 with epilepsy of childhood with centrotemporal spikes), four had generalized epilepsy and in 3 cases was not possible to classify.

Among the 59 patients, 36 of them had normal neurodevelopment before ESES. Seventy-six percent revealed cognitive impairment and decline in school performance during ESES. After ESES, 67% had cognitive impairment in different severity. Steroids and clobazam were the mostly frequently and effective used drugs to terminate ESES. There was at least some clinical improvement with treatment in 98% of cases and in 87% there was an improvement of the EEG epileptic activity during non-REM sleep.

Conclusion: ESES should be kept in mind in children with focal epilepsy with unexplained regression or stagnation of development. Despite the diagnosis and treatment, the majority of children with ESES will have cognitive impairment.

Disclosure: No potential conflict stated.
**OC003**

**First symptoms and presentation at diagnosis of paediatric onset neuronal ceroid lipofuscinoses**

Blandine Dozières-Puyravel1, Hala Nasser1, Monique Elmaleh-Berges1, Elisa Lopez Hernandez2, Catherine Caillaud2, Antoinette Gelot1, Samia Pichard1, Stéphane Auvin1

1Robert Debré Hospital, Paris, France, 2Necker Hospital, Paris, France, 3Armand Trousseau Hospital, Paris, France

Introduction: Neuronal ceroid lipofuscinoses (NCLs) are autosomal recessive paediatric neurodegenerative disorders. There are 14 different diseases classified as NCLs, designated CLN1 disease through CLN14 disease. All are progressive lysosomal storage disorders affecting neurons and other cells. Our aim is to report the presenting symptoms to illustrate the differences between the subtypes of NCLs in terms of symptoms and clinical test results, in particular intermittent photic stimulation, highlighting the key features to support a rapid diagnosis.

Methods: We conducted a single-centre retrospective study, using data on initial symptoms, MRI, electrophysiology and skin biopsies. EEG recordings were reanalysed for this study.

Results: A total of 20 NCL patients were identified, including 11 cases of CLN2 disease, 2 cases each of CLN1 disease, CLN6 disease and CLN7 disease, 1 case of CLN3 disease and 2 cases that were under investigation. The mean age of suspicion of NCLs was 6 years, 7 months (4 years, 6 months for CLN2 disease). First parental concerns occurred at 4 years, 2 months (epileptic seizures), and for clinicians, the first sign was regression (cognitive, motor or both). The average time between first parental concerns and diagnosis was 2.5 years. Of 31 video-EEG recordings, all had abnormal tracing, but only 4 had spikes upon intermittent slow-frequency photic stimulation (0.5–2.0 Hz). ERG showed retinal dysfunction in 55% of cases, and VEPs were abnormal in 88%. MRI showed cerebellar atrophy in 53% of cases and cerebral atrophy in 30% of cases. Ultrastructural analyses found inclusions in 60% of skin biopsies.

Conclusion: In this population, we found no early pathognomonic signs of NCLs. The clinical picture associated with raised photic sensitivity and intermittent photic stimulation showed key features suggesting a diagnosis, with confirmation obtained by biochemical and genetic investigations.

Disclosure: Stéphane Auvin has served as a consultant or gave lectures for Eisai, GW Pharma, Novartis, Nutricia, Shire, UCB Pharma, Ultragenyx, and Zogenix. Samia Pichard had conflict of interest to declare (Biomarin).

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**OC004**

**Efficacy and safety of Fenfluramine HCl oral solution in the treatment of Dravet Syndrome: pooled analysis of two Phase 3 clinical studies**


1Department of Paediatric Neurology, University of Leuven, Leuven, Belgium, 2The Florey Institute of Neuroscience and Mental Health, Heidelberg, Australia, 3Stichting Epilepsie Instellingen Nederland, Zwolle, The Netherlands, 4Clinica Universidad de Navarra, Pediatric Neurology Unit, Pamplona, Spain, 5UCL Great Ormond Street NIHR BRC Institute of Child Health, London, United Kingdom, 6Hôpital Universitaire Necker - Enfants Malades, Service de Neurologie Pédiatrique, Centre de Référence Épilepsies Rares (CReER), Paris, France, 7Mara Hospital, Bethel Epilepsy Centre, Bielefeld, Germany, 8Anna Meyer Children’s Hospital, Florence, Italy, 9UO Neurologica, Dipartimento di Neuroscienze, Ospedale Pediatrico Bambino Gesù, IRCS, Rome, Italy, 10University of California San Francisco, San Francisco, United States of America, 11University of Colorado Denver, Children’s Hospital Colorado, Aurora, United States of America, 12Massachusetts General Hospital, Boston, United States of America, 13Mayo Clinic, Rochester, United States of America, 14Cook Children’s Medical Center, Fort Worth, United States of America, 15NYU Langone Medical Center, New York, United States of America, 16Zogenix, Inc., Emeryville, United States of America

Objective: To assess safety/efficacy of adjunctive fenfluramine (FFA) in two Phase 3 Dravet syndrome (DS) studies.

Methods: Studies enrolled DS patients 2–18 y.o. Patients with ≥6 convulsive seizures/6-week baseline were randomized to receive add-on placebo or add-on FFA (Study 1: 0.2 or 0.8 mg/kg/d; max, 30 mg/day; Study 1504, with stiripentol as a required concomitant antiepileptic drug: 0.5 mg/kg/d; max, 20 mg/d). Primary outcome was change from baseline in monthly convulsive seizure frequency (MCSF) (FFA vs placebo).

Results: In 206 patients (9±4.7 y/o; FFA, n=122, baseline MCSF=35±63; placebo, n=84, baseline MCSF=32±36), FFA treatment resulted in 54% greater reduction in mean MCSF vs placebo (primary endpoint, P<0.001). Median change in MCSF was -56% (FFA) vs -11% (placebo). Profound (≥75%) MCSF reduction was achieved by 50% (P<0.001), 35% (P<0.001), and 23% (P=0.003) after FFA (0.8, 0.5, and 0.2 mg/kg/day) vs 2% (placebo). Near-seizure freedom (≤1 seizure during entire treatment period) was observed in 25% (P<0.001), 12% (P=0.004), and 13% (P=0.003) (0.8, 0.5, and 0.2 mg/kg/day) vs 0% (placebo). Median durations of longest seizure-free interval were 25 (P<0.001), 22 (P<0.001), and 15 days (P=NS) (0.8, 0.5, and 0.2 mg/kg/day) vs 11 days (placebo). Significantly more caregivers and investigators rated patients “Much
Improved/Very Much Improved” for FFA vs placebo (caregivers, 36%–60% vs 17% [P≤0.01]; investigators, 41%–68% vs 14% [P<0.001]). Most common adverse events included decreased appetite and diarrhea. No valvular heart disease or pulmonary hypertension were observed in any patient.

Conclusions: FFA demonstrated robust efficacy and was well tolerated without development of valvular heart disease or pulmonary arterial hypertension. FFA may be an important new DS treatment option.

Funding: Zogenix, Inc.

Disclosure: LL: Research grants, Zogenix; Consultant, Brabant, LivaNova, Ovid, UCB Pharma, Zogenix; Speaker, Eisai, Shire; Patent, ZK008. LL and the KU Leuven University/Antwerp University Hospital may benefit financially from a royalty arrangement that is related to this research if Zogenix is successful in marketing its product, fenfluramine. The terms of this arrangement have been reviewed and approved by the KU Leuven University/Antwerp University Hospital. IES, RSC, FV, ET, EW: Research funding, Zogenix. GB: Research funding, GW Pharma, UCB, Zogenix; Consultant/advisor, GW Pharma, OVID/Takeda, Zogenix; Speaker, Eisai, LivaNova, UCB. JHC: Research funding, GW Pharma, Zogenix; Consultant/advisor, Eisai, GW Pharma, Shire, Zogenix; Speaker, BioMarin, GW Pharma, Shire, Zogenix. RN: Research funding, Eisai, GW Pharma, UCB, Zogenix; Consultant/advisor, Eisai, GW Pharma, Novartis, Shire, Zogenix; Speaker, Advicenne, BioMarin, GW Pharma, Novartis, Zogenix. TP: Research funding, Zogenix; Consultant and Speaker, Desitin, Shire, Novartis, UCB Pharma, Zogenix. RG: Research funding, Zogenix; Consultant, Zogenix. J5: Research grants, travel support, Zogenix; Consultant/advisor, Dravet Syndrome Foundation, Epigenix; Reviewer, Epilepsy Study Consortium. KGK: Research support, Colorado Department of Public Health and Environment, Pediatric Epilepsy Research Foundation, Zogenix; DSMB member, Greenwich Pharmaceuticals. OD: Research support, Novartis, PTC Therapeutics, Zogenix; Equity interest, Rettco, Pairnomix, Tilray, Egg Rock Holdings. MSP: Research funding, Zogenix; Consultant, Encoded Therapeutics. ML: Consultant, Zogenix. AG, CMF, BSG, AM, AA, GM: Employees, Zogenix; Ownership interest, Zogenix.

PVES (Psychology Adding Value: Epilepsy Screening) Project – Identifying and addressing mental health problems in Epilepsy clinic setting

Ailsa McLellan1, Catriona George1, Kirsten Verity1, Michelle Small1, Celia Brand1, Richard Chin1,2, Jay Shetty1
1Royal Hospital For Sick Children, Edinburgh, United Kingdom, 2University of Edinburgh, Edinburgh, United Kingdom

Objective: Mental health problems (MHP) are common in Children and Young People with Epilepsy (CYPE) and significantly impact quality of life. Child and Adolescent Mental Health Services (CAMHS) are overstretched in the UK and CYPE can have difficulty accessing these in a timely manner. A screening project was devised to identify CYPE with MHP in the clinic and provide management strategies before they left the clinic.

Methods: CYPE (aged 5–18 years) at mainstream school and not known to CAMHS completed screening questionnaires (SDQ and PEDS-QL) in the epilepsy clinic. A psychologist scored these questionnaires and a traffic light metaphor was developed to communicate level of concerns identified (green – no concern; amber – some concern; red – serious concern). This was fed back immediately to the family with the potential route through the intervention pathway (self-guided help; Psychosocial Intervention for Epilepsy (PIE) group; 3rd sector referral; parent workshop; CAMHS referral).

Results: 132 CYPE completed the screening questionnaires. 37% had serious level of concern (5% – normal population) in emotional, conduct, hyperactivity and peer relations domains. Relevant self-guided help was given to CYPE before they left the clinic and referrals made to the PIE group, parents groups, 3rd sector and CAMHS as indicated. For children referred onto CAMHS there was more robust information for a more appropriate and timely assessment. Feedback from CYPE, parents and clinicians is extremely positive.

Conclusions: Screening for MHP in the clinic setting allows for early identification and management which can improve quality of life, and would be beneficial to other chronic conditions. This is currently being translated into an electronic system to allow immediate scoring in the clinic without need for a psychologist to be present.

Disclosure: No potential conflict stated.
Clinical, radiological and genetic findings in a cohort of 65 Polymicrogyria patients

Dina Amrom, Nicolas Deconinck, Bernard Dan, Alec Aeby, Cynthia Prigogine, Anne Monier, Guillaume Smits, Ingrid Unterberger, Jacques Michaud, Jennifer Partlow, An Poduri, Maria Lehtinen, Richard Smith, William B. Dobyns, Christopher A. Walsh, Eva Andermann
Hôpital Des Enfants Reine Fabiola, Brussels, Belgium

Introduction: Polymicrogyria (PMG) is a common malformation of cortical development characterized by an excessive number of small gyri partially fused, and a disorganization of cortical lamination. Clinical features include seizures, developmental delay, oromotor dysfunction and motor disabilities. PMG is highly heterogeneous clinically, radiologically and etiologically, rendering the identification of its cause challenging in many cases.

Methods: We studied 65 patients with all types of PMG, except those definitely caused by environmental factors. This included review of medical records; conventional and molecular karyotypes; targeted gene testing and, in some patients, next generation sequencing.

Results: 65 patients were included, 61 sporadic and two families with two siblings each. One karyotype showed a reciprocal translocation 46,XY (1;8)(p23.1;p11.2). CGH anomalies included two 22q11del, one 1p36del, one 2p21del of unknown significance, one 6q25.1 del, one 2p13.3-p16.3dup, and one 2p16.1-p12 dup. We fine mapped a locus for bilateral perisylvian PMG (BPP) to 2p16.1-p16.3. Single gene mutations included TUBB2B, GPR56, IKBKG, CEP290, RAB3GAP2, and SCN3A. Affected individuals in 6 unrelated pedigrees with pathogenic SCN3A variants showed bilateral perisylvian polymicrogyria presenting with prominent speech and oral motor dysfunction, implicating SCN3A in prenatal development of cortical language areas.

Conclusions: Categorization of polymicrogyria on the basis of its topography, associated brain malformations and clinical phenotype, helps to orient the genetic testing and diagnosis. We have been able to solve 25% of the patients with an approximately equal number of chromosomal rearrangements and single gene mutations. In addition, we fine mapped a new locus for BPP to 2p13.3-p16.3. We also identified a unique developmental SCN3A channelopathy as a cause of BPP with oromotor dysfunction. Next generation sequencing is being carried out on the unsolved patients.

Disclosure: No potential conflict stated.

A new neurodegenerative disorder characterized with cystic pontine degeneration and cerebellar atrophy due to BEND4 gene mutation

Bülent Kara1, Eylül Ece İşlek1, Oya Uyguner2, Hülya Maraş Genç3, Murat Kasap1
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Introduction: BEND4 belongs to BEN-domain containing family of proteins and is strictly conserved in all eukaryotes. The protein is mainly expressed in granular layer and purkinje cells of cerebellum in the brain, and has not been associated with any existing disease. We present a new neurodegenerative disorder linked to BEND4 gene mutation.

Methods: Three siblings born to non-consanguineous Turkish parents had healthy neurologic development until the onset of an acute neurological deterioration, started at the age of 12 months to 8 years of age. Consequent loss of all the acquired motor, social and language functions, generally following infections, was associated with pontine cyst, calcification, and cerebellar atrophy.

Results: Mitochondrial genome and linkage analyses were not informative. Exome sequencing showed homozygote c.1297A>G (gly433ser) mutation in BEND4. In silico analysis indicated that this mutation might be deleterious. To attribute a putative function, we carried out an in vitro expression study using the wild type and the mutant forms (Gly433Ser) of BEND4 proteins. Immunofluorescence microscopy analysis of both the WT- and the mutant-BEND4 expressing VERO cells showed nuclear as well as cytoplasmic localization. A noticeable difference was observed in cytoplasmic distribution patterns. Differential proteome analysis of Vero cells expressing BEND4 revealed the presence of four differentially regulated proteins in the WT BEND4 and five differentially regulated proteins in the mutant BEND4 expressing cells. The mutant BEND4 expression especially caused selective increase in abundance of reticulocalbin-1 and ER resident protein-29. Both proteins are associated with ER and primarily involved in protein processing and folding pathways.

Conclusion: This is the first study linking a neurodegenerative disorder associated with pontine cyst and calcification to a BEND4 mutation.

Disclosure: No potential conflict stated.
Clinical and genetic spectrum of SCN2A-associated episodic Ataxia

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Background: Pathogenic variants in SCN2A are associated with various neurological disorders including epilepsy, autism spectrum disorder and intellectual disability. Few reports have recently described SCN2A-associated episodic ataxia (EA). Our study identifies its broader clinical and genetic spectrum, and describes pharmacological approaches.

Results: We report 21 patients with SCN2A-associated EA, of which 9 are unpublished cases. The large majority of patients presents with epileptic seizures (18/21, 86%), often starting within the first three months of life (12/18, 67%). In contrast, onset of episodic ataxia ranged from 10 months to 14 years of age. The frequency of EA episodes ranged from brief, daily events up to 1-2 episodes per year each lasting several weeks. Potential triggers include minor head traumas and sleep deprivation. Cognitive outcome is favorable in most patients with normal or mildly impaired cognitive development in 17/21 patients (81%). No clear genotype-phenotype correlations were identified in this cohort. However, two mutational hotspots were identified, i.e. 7/21 patients (33%) harbor the identical pathogenic variant p.A263V, whereas 5/21 (24%) carry pathogenic variants that affect the S4 segment and its cytoplasmic loop within the domain IV. In addition, we identified six novel pathogenic variants in SCN2A. While acetazolamide was previously reported as beneficial in SCN2A-associated EA in one case, our data show a conflicting response in 8 additional patients treated with acetazolamide: three of them profited from acetazolamide treatment, while 5/8 did not.

Conclusions: Our study describes the heterogeneous clinical spectrum of SCN2A-associated EA, identifies two mutational hotspots and shows positive effects of acetazolamide in about 50%.

Disclosure: No potential conflict stated.
• Patients with presence of radial migration lines (RML), and those with a higher RML/total brain volume ratio more often had clinical seizures and refractory epilepsy.
• Higher ratios of tuber and total lesion volume over total brain volume were related to lower cognitive and language indexes.
• Higher RML volume/total brain ratios and presence of tubers were related to lower cognitive indices.

**Conclusion:** In children with TSC, there is a striking association between MRI characteristics visualised in the neonatal and early infantile brain, epilepsy characteristics, and neuropsychological outcome at two years. This finding will improve our care and guidance in infants with TSC.

**Disclosure:** No potential conflict stated.

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**OC010**

**176 cases of mitochondrial diseases with mitochondrial DNA variations in Chinese children**

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**Objective:** To conclude and analyze the phenotypes and genotypes, as well as the relationship between them in mitochondrial disorders with mtDNA variations.

**Methods:** The clinical and genetic data of patients with mitochondrial disorders harbored by mtDNA variations in Beijing Children’s Hospital, Capital Medical University from January 2009 to February 2019.

**Results:** There were total 176 diagnosed cases collected in our study, involving 28 mtDNA point mutations, referring to 11 genes (MT-TL1, ATP6, ND6, ND1, ND3, ND5, TK, ND4, TI, TE, RNR1), 4 gene families (tRNA, complexI, complexII, rRNA), as well as 5 large-single scale mtDNA deletions. The top 5 genotypes were 3243A>G (n=84, 47.7%), 8993T>G or T>C (n=13, 7.4%), 8344>G (n=9, 5.1%), 9176T>C (n=9, 5.1%), 13513G>A (n=8, 4.5%). The top 6 phenotypes of 176 cases were MELAS (n=81, 46%), Leigh syndrome (n=63, 35.8%), LHON, LHON plus (n=9, 5.1%), MM (n=6, 3.4%), MERRF (n=5, 2.8%), Kearns-Sayre syndrome (n=5, 2.8%). Moreover, there were 24 death cases, in which 21 were diagnosed as Leigh syndrome, the hot point were 9176T>C and 13513G>A (respectively 6 cases).

**Conclusions:** Mitochondrial DNA variations with high heterogeneity are the important part of genetic features of mitochondrial disorders. Mitochondrial 3243A>G mutation was the most common mutation in our study, the phenotypes could include MELAS, MM, LS and MIDD, when the PCR-RFLP may be recommended firstly. There was no hot point for Leigh syndrome with mtDNA variations, so the NGS may be the first choice. Moreover, the phenotypes, genotypes and the correlation of them could give us lots of useful information for the early diagnosis, evaluation, treatment, complication management, prognosis, etc.

**Disclosure:** No potential conflict stated.
Neonatal spectral EEG and neurocognitive outcome at school age in premature infants without neurological complications

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Introduction: Prematurity is a prototype of biological risk that could affect neurocognitive outcome, however, it remains a non-specific marker. The aim of this prospective longitudinal six-year study was to evaluate the prognostic role of neonatal spectral EEG in premature infants without medical and neurological complications.

Methods: Study cohort was 26 children born between 23-34 gestational weeks; all neonates underwent multichannel EEG recordings at 35 weeks post-conception. EEG data were transformed into the frequency domain and divided into delta (0.5-4 Hz), theta (5-7 Hz), and alpha (8-13 Hz), beta (14-20 Hz) frequency bands. Children were followed long-term and as they reached six years, they performed cognitive, neuropsychological and behavioural evaluations. Continuous independent predictors (frequency bands and gestational age) were screened with a model of linear correlation among neuropsychological tests scores and significant associations with visual and auditory attention tests were found and analyzed with a multivariate regression analysis.

Results: Children showing relatively higher amount of delta power and lower amount of power in theta, alpha and beta bands performed worse to all attention outcome measures. Conclusions: We hypothesized that spectral EEG may reflect early circuitries activity in reticular ascending system and cumulative effect on ongoing development, pointing to the importance of early prognostic instruments.

Disclosure: No potential conflict stated.

The effect of fetally open, fetoscopic and postnatal Myelomeningocele closure on neuromuscular outcome in Spina Bifida Aperta

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Introduction: In spina bifida aperta (SBA), fetal myelomeningocele (MMC) closure can reduce shunt dependency and preserve segmental neuro-muscular function. Fetal MMC closure is performed by open and fetoscopic techniques. Comparative neuromuscular outcome data are incomplete. Muscle ultrasound density parameters (dMUD) can non-invasively quantify muscle damage by the MMC. We compared neuromuscular outcome parameters between fetal-open, fetoscopic and postnatal MMC surgery.

Methods: We investigated 30 age- and lesion-matched pairs: I. 17 matched-pairs of fetal open (Katowice, Poland) versus neonatal (Groningen, Netherlands) operations [median: age 2 years; MMC L1 and II. 13 matched-pairs of fetoscopic (Bonn, Germany) versus neonatal (Groningen, Netherlands) operations [median: age 1 year; MMC L1]. dMUD=[MUDcaudal-to-MMC (calf)] minus [MUDcranial-to-MMC (biceps/quadriceps)].

Results: Neuromuscular segmental difference between I. fetal-open vs postnatal operation, respectively: median: +1 dermatome (range -2.5) vs sensory function; p=0.02. Motor function and dMUD: 25 (-10-71) vs 18 (-13-61), p<0.05. II. Fetoscopic vs postnatal operation: +2 myotomes (range 0.5-4) and +2 dermatomes (range 1.5-5); dMUD: 15 (-9.68) vs 26 (5-39), shunt-dependency: 4/13 vs 12/13, all p<0.05. Fetoscopic operation seemed associated with more segmental neuroprotection (sensory and motor function) than fetal-open operation: +2 (1.5-5) vs +0.25 (-2.5-6) segments, respectively, p=0.04.

Conclusion/Discussion: In SBA, open fetal and fetoscopic MMC closure techniques are both associated with neuro-protection (compared with postnatal MMC closure), with seemingly the strongest neuroprotective effect in the fetoscopic group. Before clinical implementation, these data should be interpreted against the risk of the interventions for mother and child.

Disclosure: No potential conflict stated.
Inhibition of CD47 enhances erythrophagocytosis by modulating microglial M2 polarization after experimental neonatal intraventricular haemorrhage

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Objective: Neonatal intraventricular hemorrhage (IVH) is the most common neurological disease of premature newborns and often results in detrimental neurological sequelae. Evidence showed that faster efficient clearance of erythrocytes may limit brain injury after intracerebral hemorrhage. Cluster of differentiation 47 (CD47), which expresses on the erythrocyte surface, is known to be an important factor regulating the erythrophagocytosis. However, it is still unclear whether CD47 contributes to erythrocyte clearance after experimental neonatal IVH and the potential mechanism of it. In the current study, we investigated the role of CD47 in regulating erythrophagocytosis and brain injury after experimental neonatal IVH and the potential mechanism of it.

Methods: In vivo study, P7 Sprague Dawley rats had an intraventricular injection of 50ul saline (saline group) or autologous blood (IVH group). In addition, rats with IVH were treated with anti-CD47 blocking antibody (CD47 group) or control IgG (control group). Rats were euthanized at 3 and 28 day after T2-weighted magnetic resonance imaging and behavioral tests. Brains were used for histology, immunohistochemistry and Western blotting. Furthermore, erythrophagocytosis was evaluated in vitro by co-culture CD47 knockout (KO) or wild type (WT) erythrocytes with primary rat microglia.

Results: Intraventricular injection of CD47 antibody resulted in less ventricular wall damage, posthemorrhagic hydrocephalus, neurological dysfunction, iron accumulation and microglial activation compared with IgG group (p<0.05). Confocal microscopy in vitro showed more co-localization of M2 phenotype microglia with CD47 KO erythrocytes than with WT erythrocytes (p<0.05).

Conclusions: Our results indicated that inhibition of CD47 could enhance erythrophagocytosis by modulating microglial M2 polarization and attenuates brain injury after experimental neonatal IVH. CD47 may be a new therapeutic target for brain injury after neonatal IVH.

Disclosure: No potential conflict stated.

Protective effects of Recombinant Human Growth Hormone (rhGH) on hypoxic developmental neurons in primary cell cultures

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Objective: RhGH is suggested to upregulate neuroprotective growth factors in the developing mouse brain as demonstrated in neonatal rodent models of hypoxic brain injury. However, exact regulatory pathways as well as cell-type specific mechanisms are not fully understood. Here, we analyzed the impact of rhGH on hypoxic primary neurons to elucidate cell-type specific effect on apoptosis.

Methods: At days-in-vitro (DIV) 6, primary embryonic murine neuronal cultures were exposed to hypoxia (1% O2, 5% CO2) for 6 h followed by treatment with rhGH (5/50/200/500 ng/ml; Genotropin, Pfizer). After a reoxygenation period of 24 h, pro-apoptotic (cleaved caspase-3 (CC3), BNIP-3, DUSP-1), growth hormone regulated (IGF-1) and hypoxia-responsive cytoprotective factors (EPO, VEGF-A) were analyzed (qRT-PCR, ELISA, Western Blot) in comparison to normoxic and non-treated controls.

Results: Hypoxia significantly increased CC3 protein expression of immature neurons compared to normoxia (3.5-fold, p<0.01) indicating marked increase of apoptotic neuronal cell death. Treatment with rhGH abolished hypoxia-induced neuronal activation of CC3 protein compared to controls (p<0.05) even at lower-dose application. Interestingly, rhGH-exposed neurons dose-dependently revealed significantly higher mRNA levels of EPO under normoxic (p<0.01) as well hypoxic conditions (p<0.05). In contrast, IGF-1 mRNA levels (p<0.01) as well as VEGF-A protein concentrations were exclusively increased in hypoxic rhGH-exposed neurons compared to controls (12.9±2.1 vs 7.4±1.1 pg/mg protein, p<0.05).

Conclusion: Present in-vitro data indicate that rhGH prevents hypoxia-induced neuronal apoptosis associated with cell-type specific upregulation of EPO in immature neurons. The neuroprotective significance of rhGH activating a variety of protective and synergistic growth factors such as EPO, IGF-1, and VEGF-A remains to be determined.

Disclosure: No potential conflict stated.
Neurologic comorbidities in extremely preterm born children - Neurodevelopmental and neurological disorders

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Objectives: To describe the spectrum of neurodevelopmental function and disorders as well as neurological diseases in extremely preterm born children up to 6.5 years comprising cognition, motor function, (including cerebral palsy), neuro-behavioural difficulties (including autism spectrum (ASD) and attention deficit hyperactivity disorders), ophthalmologic disorders, hearing impairments, seizure disorders, hydrocephalus, and estimated overall severity.

Methods: All Swedish children born before 27 weeks of gestation during 2004–2007 were evaluated (the EXPRESS study). The combination of all information from the neonatal period and from clinical medical examinations, neuropsychological, motor and ophthalmological assessments at 2.5 and 6.5 years of age and, in selected patients, from medical chart reviews was used.

Results: Outcome information in 469/492 (95.3%) children alive at 1 year of age was available. At 2.5 and/or 6.5 years, a severe overall impairment and/or disorder defined as a cognitive and/or motor function <mean–3SD of matched term controls, and/or a neurological disorder in need of highly specialized medical follow-up care, was found in 32%. An at least moderate neurodevelopmental deficit (<–2SD – ≥–3SD) and/or a neurological condition in need of regular medical follow-up was seen in additional 37%. The more severe the cognitive and/or motor impairments were the higher was the risk for other and more severe neurodevelopmental and neurological disorders. Gestational age was inversely correlated with affected cognitive function, motor function, ASD, ophthalmologic disorders and overall severity.

Conclusion: Extremely preterm born children have a high risk of affected cerebral function, causing associated neurodevelopmental impairments and neurological disorders. Long-term, broad follow-up is essential.

Disclosure: No potential conflict stated.
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OC017

Felbamate for the treatment of infantile spasms: 10 years of French experience

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Introduction: Infantile spasms syndrome (ISS) have been the subject of many studies about their treatment, but there is no consensus about the therapy after the first line. In France, the first treatment used is vigabatrin and steroids combined or sequential. After this line, the strategy varies from center to center, with the use of ketogenic diet or valproate, or topiramate... During brain development, excitatory neurotransmission is facilitated. This is explained, in part, by NMDA receptor subunit composition, in particular NR2B/NR2A. Felbamate is an antiepileptic drug targeting NR1/NR2B leading our group to use it for treatment-resistant ISS. We report here our 10-years experience of felbamate use for these infants.

Methods: We conducted a retrospective study including all infants younger than 1 year treated by felbamate for EEG-recorded epileptic spasms persistent after at least vigabatrin and oral steroids administration. Clinical and EEG data have been reviewed for the study.

Results: 29 patients with infantile spasms syndrome were included. Felbamate was initiated at a median age of 11.9 months (range 4.5 - 66 months) after sequential administration or combination of vigabatrin and oral steroids, as well as a ketogenic diet for 23 of them. Nine patients (31%) became spasm-free for a mean dose of 34.6 mg/kg/day [26-45 mg/kg/day]. The mean duration of use of FLB was 19.2 months (range 1- 67 months) for the 18 patients for which the treatment has been stopped. We did not observe any severe side effects. Reversible neutropenia lead to felbamate withdrawn in 5 patients.

Conclusion: Targeting NMDA receptor using felbamate resulted in epileptic spasms control in about one third of the infants that were already resistant to first-line treatments.

Disclosure: Stéphane Auvin has served as a consultant or gave lectures for Eisai, GW Pharma, Novartis, Nutricia, Shire, UCB Pharma, Ultragenyx, and Zogenix. All the other authors have no conflicts of interest.

OC018

NARS2 is a mitochondrial gene of developmental and epileptic encephalopathy in childhood

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Objective: To stress that mitochondrial asparaginyl-tRNA synthetase NARS2 gene should be considered in epileptic encephalopathy in the absence of biochemical marker of mitochondrial dysfunction in reporting 2 unrelated children from non consanguineous parents.

Methods: Retrospective clinical, EEG, MRI and biochemical description of patients with compound heterozygous variants/ deletions of NARS2 identified by whole-exome sequencing.

Results: Patient 1 is a girl with onset of daily atypical absences at age 18 months after normal early development. Regression then occurred with loss of walking and language. Tonic-clonic seizures and episodes of focal motor status epilepticus (SE) also occurred. Seizures poorly responded to anti-epileptic drugs and ketogenic diet. At age 4 years, a hydrocortisone trial was performed considering regression and EEG pattern of continuous spike and waves during sleep, resulting in recovery of independent walking during some months. The child then regressed again, is now aged 6 years and wheelchair bound. Patient 2 is a boy with a history of psychomotor delay from birth and independent walking at 30 months. Seizures started at age 3.5 years. Epilepsy was pharmaco-resistant. Regression started after onset of first seizures. The boy is now aged 4 years and wheelchair bound. In both children, complementary exams showed profound deafness, normal MRI, normal redox cycles and normal lactate in blood and CSF. Electron transport chain activity study on fibroblasts of patient 2 was normal.

Conclusion: NARS2 is a gene of developmental and epileptic encephalopathy in childhood. Clues for diagnosis are deaf-
Disclosure: No potential conflict stated.

**OC019**

Patterns of daily activity among youth with Epilepsy

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**Objectives:** To (i) explore how youth with epilepsy (YWE) spend time on physical activity, screen-time and sleep in a 24-hour period; (ii) compare these findings to youth without epilepsy; and (iii) evaluate the findings relative to the Canadian 24-hour movement guidelines for children and youth.

**Methods:** The study is based on Canadian data from 2013-14 ‘Health Behaviour in School-aged Children Study’, a cross-sectional sample of youth ages 10-17. Three groups participated: 163 YWE, 3613 youth with non-neurological conditions and 18339 typical youth. Self-reported activity data were compared across groups.

**Results:** Demographics were similar across groups. YWE spent 5.8 hours/week on moderate-to-vigorous physical activity vs 5.6 hours/week in typical youths; 32% met the recommended ≥1 hour/day. Screen-time was 8.7 hours/day vs 7.4 hours/day in typical youths; only 5.4% met the ≤2 hr/day recommendation. Sleep duration was 10.2 hours/day vs 9.8 hours/day in typical youths, and 50.7% met the recommendation. Overall 25.7% of YWE did not meet any of the guidelines, 60.5% met one, 13.5% met two and 0.3% met all three recommendations; whereas 2.8% of typical youth and 2% of youth with non-neurological conditions met all three recommendations.

**Conclusions:** These data could inform future interventions and alert policy-makers, healthcare professionals, parents, educators and advocacy-groups to the low adherence of YWE with Canadian guideline and their risk for poor health.

Disclosure: No potential conflict stated.

**OC020**

De novo mutations in the neuronal vesicular SNARE VAMP2 affect synaptic membrane fusion and cause neurodevelopmental disorders with Epilepsy and hyperkinetic movements

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**Background:** VAMP2 encodes the vesicular-SNARE protein (synaptotubervin-2 or VAMP2), which together with its partners Syntaxin-1A and Synaptosomal-associated protein 25 (SNAP25) mediate fusion of synaptic vesicles to release neurotransmitters in the brain. VAMP2 is essential for vesicular exocytosis and activity-dependent neurotransmitter release.
Methods: We studied five children affected with axial hypotonia since birth who showed since their early infancy autistic features including flapping or flailing of the arms and hand clapping. Impairment of motor and language development was present in all cases. In three out of five affected children, a poor visual fixation was evident since the first year of life and these patients were later diagnosed with central visual impairment. Three children also exhibited a hyperkinetic movement disorder (which included the combination of dystonic posturing, moderate to severe chorea and myoclonic jerks) and developed during the first year of life refractory epilepsy or EEG anomalies (burst-suppression like).

Results: We identified two single amino acid deletions and three non-synonymous de novo variants in the VAMP2 gene. The missense mutations affected conserved residues within the C-terminus of the VAMP2 SNARE motif. The three children with the more severe phenotype (including central visual impairment, hyperkinetic movement disorders and epilepsy/EEG abnormalities) were found to carry different non-synonymous mutations affecting the C-terminal region, which has fundamental role in driving synaptic vesicle fusion. To evaluate the functional consequence of VAMP2 variants, we employed the reconstituted, lipid-mixing assay based on NBD (N-[7-nitro-2-1, 3-benzoxadiazol-4-yl])-RHO (lissamine rhodamine B) energy transfer and this assay identified impairment in vesicle fusion as a consequence of the mutations.

Conclusions: The novel genetic synaptopathy caused by VAMP2 de novo mutations highlights the key roles of this gene in human brain development and function.

Disclosure: No potential conflict stated.

Gene-replacement therapy in Spinal Muscular Atrophy Type 1 (SMA1): long-term follow-up from the Onasemnogene Abeparvovec Phase 1/2a clinical trial

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Introduction: SMA1 is a rapidly progressing disease caused by biallelic survival motor neuron 1 gene (SMN1) deletion/mutation, resulting in death/permanent ventilation by 2 years of age. Onasemnogene abeparvovec (AVXS-101) treats the genetic root cause of SMA and is designed for immediate, sustained SMN protein expression. In the phase 1/2a trial (CL-101, NCT02122952), 15 SMA1 patients received a one-time intravenous (IV) AVXS-101 infusion at low dose (cohort 1, n=3) or the proposed therapeutic dose (cohort 2, n=12). There was unprecedented event-free survival and developmental motor milestone achievement.

Methods: SMA1 patients in the phase 1/2a study could roll-over into a long-term follow-up (LTFU) study (LT-001; NCT03421977). The primary objective is long-term safety. Patients have annual visits (5 years) followed by annual phone contact (10 years). Patient record transfers from local physicians and/or neurologists are requested. Safety assessments include medical history and record review, physical examination, clinical laboratory evaluation, and pulmonary assessments. Efficacy assessments include evaluation of developmental milestones.

Results: As of December 31, 2018, 13 patients had enrolled in LT-001 and had a baseline visit; 7 patients completed a 1-year post-baseline visit. All 13 (100%) patients were alive and had no loss of developmental milestones achieved at the end of CL-101. New milestones have been achieved, further supporting the persistence of AVXS-101 efficacy. These patients ranged from 39.1–62.4 months of age (39.1–55.3 for the 10 cohort 2 patients). The time since dosing ranged from 37–56.5 months (37–49.7 for the 10 patients in cohort 2). Continuing LTFU data will be presented at the congress.

Conclusions: One-time IV administration of AVXS-101 at the proposed therapeutic dose in the CL-101 study continues to...
provide prolonged and durable efficacy with milestone development.

Disclosure: JRM has received consulting fees, research support, and served on scientific advisory boards for AveXis, Inc. LL has received personal compensation from ATOM International and license fee/royalty payments from Nationwide Children’s Hospital. LNA has received personal compensation from Acceleron Pharma and research support from Sarepta TherapeuticsFGO, EK, SS, JL, and DEF are employed by AveXis, Inc. DMS is employed by, and owns stock in, AveXis.KUL, NFM, MAI, and KC have nothing to disclose.

OC022

Longer-term assessment of Nusinersen treatment in children with later-onset spinal muscular atrophy who enrolled in CS2/CS12: an interim analysis of the SHINE Study

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Objective: Present interim results from the open-label extension study, SHINE (NCT02594124), for participants with later-onset SMA (Type II or III SMA) who first received nusinersen in the CS2 study and were eligible for CS12.

Methods: Participants in other nusinersen studies were eligible to transition to SHINE. 24 of 28 children previously dosed in CS2/CS12 received nusinersen maintenance doses in SHINE; dosing was originally every 6 months and changed to every 4 months following nusinersen approval. The study’s primary endpoint is safety and tolerability, while secondary endpoints in this population include Hammersmith Functional Motor Scale - Expanded (HFMSE), 6-Minute Walk Test (6MWT) and Upper Limb Module (ULM).

Results: In the June 30, 2017 data cut, participants with Type II SMA showed increases in HFMSE (baseline mean, 21.3 [n=11]; mean change, 9.1), 6MWT (baseline mean, 0.0m [n=11]; mean change, 150.0m) and ULM (baseline mean, 11.9 [n=11]; mean change, 3.5) from baseline to Day 1050. Participants with Type III SMA showed smaller mean changes, but had higher baseline values and either maintained or gained function which contrasts with natural history data; HFMSE: baseline mean, 48.9 (n=17), mean change, 1.1; 6MWT: baseline mean, 253.3m (n=13), mean change, 86.5m; and ULM: baseline mean, 16.9 (n=7), mean change, 0.0. No new safety concerns were identified. Information from an updated data cut (October 15, 2018) and additional outcomes will be presented.

Conclusion: Results from the June 2017 data cut demonstrate improvement or maintenance of mean motor function assessment scores among the SHINE participants who first received nusinersen in CS2 and continued treatment in CS12. The SHINE study will provide valuable information on longer-term safety, tolerability, and efficacy.

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Pharmaceuticals, Inc. for execution of clinical trial projects. JM: advisory boards for Biogen, Cytokinetics, Roche, Scholar Rock, and the SMA Foundation; consultant for Biogen and Ionis Pharmaceuticals, Inc.; research support from the Eunice Kennedy Shriver National Institute for Child Health and Human Development (1K01HD084690-01A1); conference grant from the Muscular Dystrophy Association.LM: employee of and holds stock/stock options in Ionis Pharmaceuticals, Inc., PS, IB, SG, SR, and WF: employees of and hold stock/stock options in Biogen. DCD: advisor/consultant for AveXis, Biogen, Cytokinetics, Ionis Pharmaceuticals, Inc., Metafora, Roche, Sanofi, Sarepta, and the SMA Foundation; grants from the Department of Defense, Hope for Children Research Foundation, the National Institutes of Health, and the SMA Foundation; clinical trial funding from Biogen, Mallinckrodt, PTC, Sarepta, and Ultragenyx. This study was sponsored by Biogen (Cambridge, MA, United States of America). Writing and editorial support for the preparation of this presentation was provided by Excel Scientific Solutions (Southport, United States of America): funding was provided by Biogen.

OC023

High diagnostic yield of syndromic intellectual disability by Next-Generation Sequencing techniques-NGS: whole exome sequencing and targeted NGS

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Objective: The objective of this study is to assess the diagnostic yield of next generation sequencing (NGS) techniques in our clinical setting of patients diagnosed with moderate-severe intellectual disability (ID) or global developmental delay (GDD).

Methods: We present a retrospective observational study of 154 patients with moderate to severe syndromic ID/GDD that were assessed at the Neurology and Clinical Genetics clinics from January 2012. The evaluation consisted on a complete neurological study that included brain MRI and CGH array. These patients were subsequently studied using two NGS approaches. In 23 patients a trio based whole exome sequencing (WES) study was performed. In 131 patients the molecular study was made using a custom-made panel containing 1576 genes associated with neurodevelopmental disorders (RD-Seq®V3.0).

Results: A definitive diagnosis was achieved in 84 patients. Causal variants were found in more than 50 different genes. In genes ANKRD11, MAGEL2, ASXL3, PUF60, DDR3X, KMT2D, KMT2A, KAT6A, WAC and SATB2 causal variants were found in more than one patient.

The diagnostic performance of the 2 procedures was very similar. WES achieved a molecular diagnosis explaining the phenotype of the patient in 52% of the cases, while the application of the targeted panel achieved a molecular diagnosis in 54% of the patients. Altogether, this means a diagnostic yield of 53% of the cases (95%CI 49%-57%).

Conclusions: Next generation sequencing technology using WES or a targeted panel of genes for developmental disorders demonstrates a high diagnostic performance in patients with syndromic ID/GDD. The use of a targeted panel reduces the costs derived from the technique and storage of data, and simplifies the analysis and interpretation of variants. This makes the panel a suitable tool for its application in the clinical diagnostic routine.

Disclosure: No potential conflict stated.

OC024

β-III Spectrin gene variants in non-progressive congenital Ataxias: widening the associated phenotype

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Introduction: β-III spectrin gene (SPTBN2) variants have been associated with classical ataxic phenotypes as autosomal dominant SCA5 without cognitive deficit, and recessive SCAR14 with intellectual impairment. The severe congenital ataxic phenotype has been related to recessive homozygous mutations but recent anecdotic cases with heterozygous variants have raised concern about a better delineation of the associated phenotype.

Disclosure: No potential conflict stated.
Methods: We described the clinical and neuroimaging phenotype of four unreported children with non-progressive congenital ataxia (NPCA) and likely pathogenic novel variants in the SPTBN2 gene.

Results: Three boys and a girl presented as NPCA with motor delay before 6 months of age, hypotonia, nystagmus, and slight improvement of the ataxia over the years. IQ ranged from 58 to 79 in the three boys that presented with progressive global cerebellar atrophy in consecutive cerebral MRI. In two of them, cerebellar cortex hyperintensities on FLAIR were also observed, suggesting a neurodegenerative process. The girl presented a NPCA phenotype but without intellectual impairment and normal sequential cerebral MRI. Her mother was diagnosed with a psychiatric disorder and both carried the novel p.R432H variant in SPTBN2 gene.

Conclusion: The discovery of new genes and novel variants in known genes involving ataxia is a growing scene of complexity. There is significant overlap of clinical phenotypes and neuroimaging findings usually associated to neurodegeneration. Subcellular location studies are on-going in order to determine if the detected mutations alter the proper activity of the protein, for a further insight of pathogenesis underlying these SPTBN2-associated forms.

Disclosure: No potential conflict stated.

SUPV3L1 mutation: a novel gene causing human disease

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Introduction: We present 3 patients with a characteristic neuroradiological phenotype associating abnormal white matter, anterior temporal cystic change and cerebellar atrophy in whom homozygous variants in the mitochondrial helicase gene SUPV3L1 have been identified. This is the first human disease associated with variants in this gene.

Methods: 3 patients, two sisters and a male cousin from a consanguineous family, presented with dysmorphism, microcephaly, developmental delay, motor disorder and hypopigmented skin lesions. MR imaging demonstrated diffuse white matter abnormality, cerebellar atrophy and anterior temporal lobe cysts. Extensive neuro-metabolic investigation was unremarkable and the family were referred to the Leeds Inherited White Matter Disorder MDT for further discussion.

Results: Genomic regions comprising the coding regions of 6,000+ disease genes were captured and sequenced, with variants in 98 known white matter disease genes interrogated for pathogenicity. No likely pathogenic variant was identified therefore; whole exome sequencing (Agilent SureSelectQXT, Human All Exon library V6) was performed on 3 affected family members and 3 unaffected obligate carriers. Variant analysis revealed a single variant in SUPV3L1 that segregated with the disease in all family members, which was confirmed in additional available family members by Sanger sequencing.

Conclusion: SUPV3L1 encodes SUPV3L1, a core nucleoid helicase protein involved in mitochondrial RNA metabolism that is widely expressed in all tissues. Homozygous knockout is embryonic lethal in mice, whilst ablation in adult mice leads to impaired growth, loss of muscle mass and skin abnormalities. To date human disease has not been associated with the SUPV3L1 gene. The phenotype in our patients is characteristic and adds to the growing number of genetic disorders associating leukencephalopathy with anterior temporal cystic change.

Disclosure: No potential conflict stated.
Fingolimod treatment improved quality of life in paediatric patients with Multiple Sclerosis: PARADIGMS study

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Introduction: Fingolimod demonstrated superior reduction in annualised relapse rate and magnetic resonance imaging lesions and comparable safety versus interferon (IFN) β-1a over 2 years in the Phase 3 double-blind PARADIGMS study in paediatric patients with multiple sclerosis (MS) (N=215; aged 10–<18 years). Here, we aim to report the effect of fingolimod on health-related quality of life (HRQoL) versus IFN β-1a in this paediatric population.

Methods: HRQoL was assessed using Pediatric Quality of Life (PedsQL) scores in both fingolimod and IFN β-1a treatment groups from baseline up to 2 years. The changes in patient- or parent-reported PedsQL scores such as Total Scale score, Physical Health Summary score and Psychosocial Health Summary score were preplanned and analysed using summary statistics. A post hoc analysis using inferential testing was performed to compare change in PedsQL scores between treatment groups by an analysis of covariance model adjusted by treatment, region, pubertal status, and the corresponding baseline score.

Results: Consistent numerical improvements in all PedsQL scores were observed in fingolimod-treated patients versus consistent worsening in IFN β-1a-treated patients. The post hoc inferential analysis confirmed significant improvement with fingolimod versus IFN β-1a on PedsQL in both patient- and parent-reported Total Scale score (4.55 vs. −2.16; p<0.01, and 3.22 vs. −1.65; p<0.05, respectively), Physical Health Summary score (4.19 vs. −3.22; p<0.01, and 2.26 vs. −3.73; p<0.05, respectively) and patient-reported Psychosocial Health Summary score (4.74 vs. −1.60; p<0.01). The difference in parent-reported Psychosocial Health Summary score also favoured fingolimod but did not reach statistical significance.

Conclusions: Fingolimod treatment was associated with a significant improvement in HRQoL compared with IFN β-1a as assessed by patient- and parent-reported PedsQL scores.

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The 2017 McDonald Diagnostic criteria: validation in the French Paediatric Onset Multiple Sclerosis cohort

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Objective: To compare diagnostic accuracy of McDonald 2017 vs McDonald 2010 criteria to diagnose multiple sclerosis (MS) at first attack of acquired demyelinating syndromes (ADS).
ORAL COMMUNICATIONS
PARALLEL SESSION 2B: Global Infections and Inflammatory Diseases of the CNS

OC028

Improved performance of the 2017 McDonald criteria for diagnosis of Multiple Sclerosis in children in a real-life cohort

Methods: Between May 2000 and October 2017, 265 children with incidental ADS were included in a French multicenter study. Brain and spinal MRI were performed less than 3 months after symptoms onset. Patients with a follow-up (FU) ≤1 year and normal brain MRI at onset were excluded. Sensitivity, specificity, positive predictive value, negative predictive value were compared at baseline between the 2010 and 2017 criteria.

Results: Among 152 included patients with a mean FU of 3.6±2.6 years, 71 (47%) participants including 42 (59%) girls were diagnosed with clinically definite multiple sclerosis (CDMS). Their mean age was 11.6±3.7 years with a mean FU of 4.3±2.7 years. The other 81 patients had monophasic-ADS, 47 (58%) were girls and clinical phenotype included 32 (40%) long track dysfunction, 32 (40%) ADEM, 24 (30%) rhombencephalitis, 22 (27%) transverse myelitis, 9 (11%) optic nerve. Their mean age was 7.5±4.4 years and mean FU of 3±2.3 years.

In all included patients, sensitivity was higher for the 2017 criteria than for the 2010 criteria (86% vs 56%) while specificity was lower (72% vs 86%). When excluding ADEM patients, a similar trend was observed.

Conclusion: The 2017 McDonald criteria are more efficient than 2010 criteria in identifying children with multiple sclerosis, indicating the new criteria can be used both in children and adults at first incidental ADS to diagnose MS.

Disclosure: No potential conflict stated.

OC029

Use of disease-modifying therapies in paediatric relapsing remitting Multiple Sclerosis in the UK: a multi-centre retrospective study

Methods: In this retrospective, multi-centre study, we identified children who presented with symptoms suggestive of a clinically isolated syndrome (CIS) and were followed up for at least two years or until their second attack. Cerebro-spinal fluid examination for the detection of oligoclonal bands (OCBs) and gadolinium-enhanced MRI were performed if requested by the neurologists. The performance of the 2017 and 2010 McDonald criteria for dissemination in space (DIS) and time (DIT) were evaluated.

Results: Of 156 children with CIS followed up for a median of 4.17 years, 94 (60%) were diagnosed with MS. Eighty-three (88.3%) of these fulfilled the 2010 McDonald DIS criteria at onset. Three additional children fulfilled the 2017 DIS criteria because of the inclusion of symptomatic lesions. Of the 59 children with MS who underwent post-gadolinium MRI, 43 (73%) fulfilled the 2010 DIT criteria at baseline. When the presence of OCBs was used to substitute for the requirement of fulfilling DIT, an additional 35 children (78/94, 83%) were diagnosed with MS. The 2017 criteria had higher accuracy (87.2% vs 66.7%), higher sensitivity (84.0% vs. 46.8%), but reduced specificity (91.9% vs. 96.8%) when compared to the 2010 criteria.

Conclusion: The improved performance of the 2017 McDonald criteria when compared to the 2010 criteria in children in the clinical setting was predominantly due to the inclusion of intrathecal OCBs.

Disclosure: No potential conflict stated.
with DMTs, were identified from two tertiary paediatric neurology centres between 2012-2018. Annual relapse rate (ARR) prior and on treatment were calculated.

**Results:** Of the 61 children included, 33 (54.1%) were treated with one DMT; 25 (41.0%) with two DMTs, and 3 (4.9%) with three or more sequential DMTs. The median time from initial presentation to first-line DMTs was 1.3 years (IQR: 0.6-2.1) and 1.2 years (IQR 0.6, 1.9) for second-line DMTs. Side effects were reported in 41 (67.2%) children on first-line treatment and 13 (52%) children on second-line DMTs. The most commonly reported side effects were flu-like symptoms (n=15), local reactions/bruising at injection site (n=13), headaches (n=7), myalgia and fatigue (n=6), gastrointestinal disturbance (n=4), and deranged liver function tests (n=5). In 4 patients, first-line DMTs were discontinued (n=2) or switched (n=2) due to side effects. Of the 192 clinical relapses reported in the cohort, 73 were on treatment. ARR was reduced from 1.7 to 1.5 with interferon-β/galtimer acetate (n=49, p=0.03); 1.4 to 1.0 with Dimethylfumarate (n=5, p=0.67); 2.2 to 0.4 with fingolimod (n=8, p=0.05) and 1.8 to 0.3 with natalizumab (n=10, p=<0.01). Escalation from first to second-line DMTs resulted in a reduction of ARR from 1.6 to 0.4 (n=16, p<0.001)

**Conclusions:** In this cohort, a reduction in ARR was observed with all DMTs. As expected, escalating treatment to second-line DMTs such as fingolimod and natalizumab resulted in larger reduction of ARR.

**Disclosure:** No potential conflict stated.

**OC030**

**Progress in the management of paediatric-onset Multiple Sclerosis over the last decade**

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**Objective:** To explore how recent advances in the understanding and treatment of Paediatric Onset Multiple Sclerosis (POMS) have affected patient management and outcomes.

**Methods:** A retrospective case notes review was used to examine the outcomes of POMS patients treated at three major paediatric neuroimmunology centres. Two cohorts, treated a decade apart, were compared to investigate associations between treatment approaches and outcomes.

**Results:** The study identified 30 patients treated between 2007-2010 and 44 patients in 2015-2016. Median age of all patients at initial presentation was 13.2 years (range 3.7 to 16.6 years); 73.3% and 68.2% of the 2007-2010 and 2015-2016 patients respectively were female. The increase in both availability and options of disease modifying treatments is reflected in the wider range of medications used in the 2015-2016 cohort. There is also evidence of a move towards earlier treatment, with a shorter time from diagnosis to initiation of disease-modifying treatment in 2015-2016 patients (median 5 months vs. 9 months, p=0.048).

Annualised relapse rates were 41.8% lower in 2015-2016 patients (1.000 vs. 0.582, p=0.043), and a 39-month longer time to first relapse on treatment was observed in 2015-2016 patients compared to those treated in 2007-2010 (47.0 vs. 8.0, p=0.060). When analysing neurocognitive performance on routine tests, 44.5% fewer 2015-2016 patients were categorised as cognitively impaired (13.8% vs. 58.3%, p<0.0005).

**Conclusions:** The improved outcomes observed in patients treated in the later years provides evidence that treatment approaches have increased in effectiveness over a decade. Further research is needed both to confirm this and to determine if these improvements translate into better long-term outcomes in these patients.

**Disclosure:** No potential conflict stated.
Exposure and response prevention in a large Danish clinical cohort of children and adolescents with Tourette Syndrome

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Background: Historically, Tourette syndrome (TS) has been managed with pharmacological therapies, but recent years' behavioral therapy (BT), such as exposure response prevention (ERP) and habit reversal therapy (HRT), has shown to be effective in reducing tic severity. HRT is currently the most researched and widely applied BT for TS, but both types are currently equally recommended as first-line BTs in existing guidelines. Currently no evidence regarding long-term effect has been published.

BTs were introduced in our TS-clinic in 2013. Treatment has been provided as classic treatment with physical meetings, via telemedicine or in groups.

Methods: The authors retrospectively reviewed medical charts of 95 children and adolescents with TS treated with ERP. Efficacy of the different modes of BT (classic, telemedicine, groups) was compared. Validated instruments were used to assess tics severity and quality of life as measures for efficacy of treatment. Patients were followed for one year to evaluate long-term effects.

Results and conclusion: Mean age at start ERP 13.6 years, 68.4% were boys and the mean duration of tics was 7.0 years. 63.2% received classic ERP, 32.6% telemedicine, and 4.2% group therapy. Results showed significant reduction in total tic severity and total tics with no statistically significant differences between different modes. Long-term follow-up data on 32 patients showed a continued significant decrease in tics severity one year after ERP. There were no statistically significant differences in long-term efficacy between classic ERP and telemedicine. The effect was statistically significant better after classic ERP compared with the group sessions. The results confirm ERP as an effective treatment for TS and indicates long-term effects. Results indicate that telemedical approaches could be an opportunity to facilitate wider accessibility. Further experience with group sessions is needed.

Disclosure: No potential conflict stated.

Clinical assessment of Myoclonus in a cohort of 41 patients with Myoclonus Dystonia Syndrome due to SGCE mutations

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Objective: To validate the Unified Myoclonus Rating Scale (UMRS) in patient with myoclonus dystonia syndrome (MDS) and to screen for mutations in SGCE gene.

Method: Two movement disorders experts rated MDS patients using UMRS subscales (questionnaire, functional tests, rest-, action- and stimulus sensitive-myoclonus). SGCE mutations were screened by Sanger method.

Results: 49 MDS patients (age onset 2.7±1.6; age assessment 13.2±10.8 (years)) were included, 41 of them were rated with the UMRS. Functional impairment was observed predominantly with handwriting (65%), drinking (63%), feeding (56%), dressing (35%) and walking (27%). Patients with walking difficulties were younger (8±4 vs 14±1 (p=0.002). Myoclonus severity increased with action and with stimulus elicitation (pin prick and tapping jaw). Myoclonus showed a rostro-caudal gradient (upper limbs/neck more affected than lower limbs) and asymmetric distribution, with higher scores in the non-dominant hand. UMRS subscales showed strong correlation and high internal consistency (Chronbach’s alpha: 0.80–0.83). SGCE mutations were identified in 41/49 (84%) patients (11 frameshift, 20 stop–gain, 7 splice–site, 3 missense). Genetic testing in 25/33 families identified that 80% were inherited (16 asymptomati-ic and 4 affected parents) and 20% were de novo. Patients with missense mutations obtained lower scores on action/rest myoclonus and on functional tests, although differences were non-significant.

Conclusion: The UMRS was a valid tool to assess myoclonus in MDS patients, with good clinimetric properties. We observed a strong impact in fine motor tasks (writing, drinking and eating) in most patients, while walking was impaired in younger patients. Our MDS population was genetically homogeneous for SGCE mutations.

Disclosure: No potential conflict stated.
ORAL COMMUNICATIONS
PARALLEL SESSION 2C: Movement Disorders

OC033
Patterns of baseline cerebral [18F]Fluoro-Deoxy -Glucose Positron Emission Tomography (FDG-PET) vary with Dystonia aetiology, baseline severity and Neurophysiology and Deep Brain Stimulation (DBS) Neuromodulation outcomes
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Objective: To assess if [18F]FDG-PET can assist in our effort to understand dystonia pathophysiology and also serve as a biomarker of disease severity and predictor of DBS outcome.

Methods: PET scans from 267 children with dystonia awaiting possible DBS surgery were assessed retrospectively. Scans without gross anatomical abnormality (n=240) were analysed with Statistical Parametric Mapping (SPM12). A group of 20 normal controls was used for comparison. A visualization threshold of p=0.001 was applied. Neurophysiological assessments of motor (central motor conduction time: CMCT) and sensory pathways (somatosensory evoked potentials: SEP) were obtained. Dystonia severity before and after DBS was assessed using the Burke-Fahn-Marsden Dystonia Rating Scale (BFMDRS-m) motor score.

Results: The comparison of different aetiopathological dystonic subgroups revealed some shared metabolic patterns, but also “signature” uptake characteristics for each group, including key areas of hypometabolism in the cerebellum and thalamus not expected from brain MRI. Abnormal SEPs were closely linked to thalamic hypometabolism, whereas abnormal CMCTs were associated with parietal and frontal cortex hypometabolism. Increased baseline disease severity was associated with regional hypermetabolism in the superior parietal lobule and regional hypometabolism in the frontal cortex. DBS outcome at 1 year follow-up showed a weak positive correlation with thalamic and sensorimotor FDG uptake.

Discussion: The findings offer further insights into the pathophysiology of dystonia and enhance our understanding of the correlation of regional brain glucose metabolism to dystonia subtypes and baseline neurophysiology. The PET findings also provide further evidence for a role of sensory rather than pure motor abnormalities in dystonia. Our preliminary findings linking baseline cerebral glucose uptake patterns with DBS outcome could potentially lead to more individualized prognostic counseling for DBS.

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OC034
Genetic mutations in children with Spastic-Dystonic Cerebral Palsy of cryptogenic aetiology
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Introduction: Recent reports suggest that pathogenic genomic variants may contribute to Cerebral Palsy (CP) aetiology. We aimed to examine Whole Exome Sequencing in a cohort of Greek children with spastic-dystonic CP of undetermined etiology.

Methods: Term children with spastic-dystonic CP (GMFCS I-V) and normal brain MRIs or with findings that could not explain the phenotype were selected. Genomic DNA captured from venous blood or saliva of 18 parent-child trios was processed through exome sequencing, alignment, variant calling, filtering and quality control measures.
Results: In 6/9 fully sequenced patients genomic variants were identified. One de novo deleterious variant in CACNA1E (1:181620576G>A (p.G352R) heterozygous), in a girl with epileptic encephalopathy and bilateral spastic-dystonic GMFCS V CP; two deleterious variants in TUBA1A [12:49578927A>C (p.Y408D); 12:49579735G>C (p.F138L)] in a GMFCS I boy with spastic diplegia; an AUTS2 de novo canonical splice site mutation (7:70163607G→A) in a dysmorphic girl with GMFCS III bilateral spastic CP, intellectual disability and myopia. One likely pathogenic de novo variant in GRIA3 [X:122551344 (p.S531C)] was detected in a dysmorphic female with GMFCS IV CP, intellectual disability and exaggerated startle reactions. An X-linked predicted deleterious variant in MED12 [X:70361115-70361121del_GCAGCA (p.QQ2105_2106-)] was detected in a boy with bilateral spastic GMFCS II CP, dysphagia necessitating gastrostomy and dysmorphic features suggestive of Lujan-Fryns syndrome (OMIM # 309520). A homozygous NSUN2 mutation [5:6604723G→A(p.Q580*)] was found in a male with hypotonic GMFCS II CP, intellectual disability, autism and epilepsy.

Conclusion: Deleterious genomic variants were detected in 6/9 (66.7%) children with cryptogenic spastic-dystonic CP. In this group of patients genetic investigations are important for accurate diagnosis, prognosis and perhaps treatment.

Disclosure: No potential conflict stated.

Methods: Fourteen internationally-based neuropsychiatric centres contributed patients with genetic complex childhood-onset HMD. Participating clinicians completed standardised research pro formas capturing demographic, clinical and genetic data. Two paediatric movement disorder experts reviewed available video footage and classified hyperkinetic movements according to established criteria.

Results: 143 patients with seventeen genetic defects causing HMDs, both recessive (DDC, DHPR, PTPS, SLC6A3, SPR, TH, MICU1 and PDE10A) and dominant genes (ADCY5, ATP1A3, FOXG1, GCH1, GNAO1, KMT2B, NKX2-1, SGCE, SLC2A1) were identified. In the majority, HMD were generalized (111/143, 78%) with most patients manifesting more than one type of HMD (108/143, 75%) with most patients manifesting more than one type of HMD (108/143, 75%). Parkinsonism-dystonia was characteristic of neurotransmitter defects; chorea predominated in ADCY5, ATP1A3, FOXG1, NKX2-1, SLC2A1, GNAO1 and PDE10A-related disorders; stereotypes were prominent in FOXG1 and GNAO1-related disease. Patients with generalized hyperkinesia and developmental delay had a significantly earlier onset than those with focal/segmental distribution (4.7±0.7 vs. 2.4±0.3 years, p=0.001) and normal neurodevelopment ((1.5±2.9 vs 4.7±3.8 years, p<0.001), respectively. Gene-specific effective treatments included dopaminergic agents (neurotransmitters disorders), ketogenic diet (Clu1) flunarizine (ATP1A3) tetrabenazine (GNAO1) and deep brain stimulation (SGCE, KMT2B and GNAO1-related HMD). Interpretation: This study delineates the complex movement disorder phenotype and associated features of children with HMD of genetic origin. We propose a pragmatic decision-making algorithm to guide physicians in the rational genetic investigation of patients with suspected genetic HMD, to facilitate prompt diagnosis, precise treatment and future genetic counselling.

Disclosure: No potential conflict stated.
Phase 2/3 trial to assess the safety and efficacy of Lenti-D Hematopoietic Stem Cell Gene Therapy for Cerebral Adrenoleukodystrophy

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Objective: Cerebral adrenoleukodystrophy (CALD) is characterized by inflammatory demyelination leading to progressive loss of neurologic function and death. Early diagnosis and treatment are key in ensuring optimal long-term outcomes.

Methods: Lenti-D Drug Product (DP) is an investigational gene therapy for the treatment of CALD. Boys with CALD (≤17 years) enrolled in an open-label phase 2/3 study of the safety and efficacy of Lenti-D DP underwent full myeloablative with busulfan and cyclophosphamide followed by infusion of autologous CD34+ cells transduced with elivaldogene tavalentivec (Lenti-D) lentiviral vector. Primary efficacy endpoint is the proportion of patients who are alive and free of major functional disabilities (MFD) at Month 24. Primary safety endpoint is the proportion of patients who experience acute (≥Grade 2) or chronic graft-versus-host disease (GVHD) by Month 24. Additional assessments include engraftment failure, and changes in neurologic function score and Loes score.

Results: As of April 2018, 29 patients received Lenti-D DP (median follow-up 34 months, min-max, 0.4-54.0); 17 patients had reached 24 months of follow-up and 15/17 (88%) remain alive and MFD-free with evidence of disease stabilization. Of the other 12 patients (median follow-up 4.2 months, min-max, 0.4-11.7), 11 remain in the study with no evidence of MFDs at last follow-up. No graft failure, GVHD, or transplant-related mortality were reported. There was no evidence of replication competent lentivirus or insertional oncogenesis. Most adverse events were generally consistent with myeloablative conditioning. As of February 2019, 31 patients will have received Lenti-D DP, with longest follow-up of 60 months. An updated efficacy and safety profile of Lenti-D DP will be presented.

Conclusion: These data suggest that Lenti-D DP stabilizes neurologic disease progression and appears to be a promising gene therapy for CALD.

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Effect of intrathecal recombinant human Arylsulfatase A Enzyme Replacement Therapy on structural brain MRI in children with Metachromatic Leukodystrophy

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Introduction: Metachromatic leukodystrophy (MLD) is a rare neurometabolic disorder caused by arylsulfatase A (ASA) deficiency, resulting in sulfatide accumulation, demyelination and rapid neurological deterioration. A phase 1/2 study (NCT01510028) recently assessed the safety of intrathecal (IT) recombinant human ASA (rhASA; TAK-611, formerly SHP611) in children with MLD aged 19–107 months. This retrospective analysis investigated the effect of IT rhASA on brain tissue changes in children with MLD using MRI volumetric and diffusion indices.

Methods: 170 MRIs of 24 children with MLD treated with IT rhASA (NCT01510028) were compared with 56 MRIs of 12 children with MLD treated with intravenous (IV) rhASA (NCT00418561/
OC038

Long term effect of Lentiviral (LV) Hematopoietic Stem Cell Gene Therapy (HSC-GT) on the nervous system in early-onset Metachromatic Leukodystrophy (MLD)

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Introduction: MLD, a fatal demyelinating lysosomal disease due to Arylsulfatase A (ARSA) deficiency, has no approved treatment. We report effects of HSC-GT in 29 early-onset MLD patients (pts) with ≥8 yrs post-treatment follow-up (FU).

Methods: HSC-GT consists of infused autologous HSCs transduced ex vivo with LV encoding the human ARSA gene, post busulfan conditioning. 29 early-onset MLD pts were treated (16 Late Infantile [LI], 13 Early Juvenile [EJ]): 20 per a clinical trial, 9 per compassionate use programs (CUP). Efficacy endpoints included motor and cognitive function, MR measurements of demyelination and atrophy, and electoneurographic recordings to measure nerve conduction velocity (NCV).

Results: Clinical Trial: 18/20 pts are alive with FU of 3-8 yrs; 2 EJ pts treated post-symptom onset died due to rapid disease progression. We observed durable, stable engraftment of gene-corrected cells, no treatment-related mortality and no malignancies or adverse events indicative of oncogenic transformation.

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A progressive, stable restoration of ARSA activity in the hematopoietic system and cerebrospinal fluid was noted in all. At time of GT, 8/9 LI and 4/11 EJ showed no overt manifestations of the disease. After GT, pts showed normal psychomotor development or slower progression of motor and cognitive symptoms; initial slight worsening of brain MR scores and NCV was followed by stabilization. While motor function deteriorated in pts treated after symptom onset, brain MR and IQ score stabilized in most during FU.

CUP: Results to be presented

**Conclusion:** Long-term interim clinical trial results (≤8 yrs FU) demonstrate that HSC-GT is a safe and well-tolerated treatment option with a positive benefit-risk profile. HSC-GT may prevent, stabilize or delay motor and cognitive decline and atrophy, with a greater effect in pts treated prior to symptom onset. Further research is needed to clarify the potential clinical benefit of HSC-GT on symptomatic pts.

**Disclosure:** No potential conflict stated.
characterized by seizures, language and motor function loss, blindness and early death. An open-label study demonstrated that intracerebroventricular (ICV) infusion of 300 mg cerliponase alfa, a recombinant human TPP1 enzyme, every two weeks for 96 weeks slowed deterioration in motor and language function. This study (NCT02678689) assesses safety and efficacy of cerliponase alfa in an expanded cohort including children ≤3 years old.

**Methods:** 15 pediatric subjects with CLN2 disease were planned to participate in this 144-week study. Cerliponase alfa was dosed based on age (subjects ≤2 years receive under 300 mg). Safety was assessed by adverse event (AE) frequency; efficacy was assessed by change in motor-language (ML) score (ranging from 0 to 6, with 0 representing no function and 3 representing normal function in each domain). One subject with uninterpretable language function was excluded from ML score evaluation.

**Results:** 11 subjects (7 female, 4 male; mean (SD) age 3.5 (1.3) years), including 5 aged ≤3 years at baseline, enrolled. Mean baseline ML score was 4.6 (SD=1.4). Subjects received a mean (SD) of 67 (32.5) weeks of cerliponase alfa (range 42-114). Common AEs included seizure, pyrexia, upper respiratory tract infection, and vomiting. Nine (82%) subjects experienced ≥1 serious AE with pyrexia the most frequently reported. ML score from baseline to last visit was unchanged in 7 (70%) subjects; 2 (20%) subjects had a 1-point gain and 1 (10%) had a 1-point loss. One subject with uninterpretable language function had no change in motor score.

**Conclusion:** These data suggest ICV-administered cerliponase alfa, including in children ≤3 years old, has an acceptable safety profile similar to prior studies.

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**Objective:** Literature suggests that up to 10% of children with Dravet syndrome (DS) die of Sudden Unexpected Death in Epilepsy (SUDEP) before their 20th birthday making this one of the highest SUDEP risk groups. However, the mechanisms underlying SUDEP are not well understood. We reviewed a large, mainly UK, established cohort of individuals with DS to study mortality, rate of SUDEP and examine any predisposing factors.

**Methods:** In 2008 we established a cohort of individuals with Dravet Syndrome and their families who consented to participate in a long-term prospective outcome study. Prior to re-contacting families, we communicated with the referring clinicians of 141 SCN1A positive DS patients in the UK, Ireland and Australia to identify individuals within the cohort who had died. We collected information on death and cause of death and correlated the findings with a range of clinical characteristics.

**Results:** 140 out of 141 (99%) clinicians responded. 10 patients (7%) were lost to follow up. 7/130 patients (5.4%; 4 male, 3 female) were reported to have died during the 10-year-period. Cause of death was documented as SUDEP in 57% (4/7), status epilepticus in 14% (1/7), acute respiratory distress syndrome due to an influenza infection in 14% (1/7) and the cause of death in the remaining case was unknown. Comparing the deceased group with survivors there was no significant difference between age at seizure onset, seizure precipitants, epilepsy phenotype, EEG features, degree of cognitive impairment, magnetic resonance imaging (MRI) abnormalities, mutation class (truncating vs. missense) or Grantham scores.

**Conclusions:** The mortality in DS is high with a Dravet-specific SUDEP rate of 3.8/1000-person-years which is comparable to figures for adults with drug-resistant epilepsy. No overt predisposing factors were identified.

**Disclosure:** No potential conflict stated.
OC042

Natural history of Sturge-Weber Syndrome in 21 patients and meta-correlation of 1.431 cases in the literature

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Objective: To report on the natural history of Sturge-Weber syndrome (SWS) by data analysis of (study a) children and adults referred to our Institutions; and (study b) reported cases in the literature.

Methods: In study a analysis of clinical/laboratory/imaging data obtained from patients with a confirmed clinical diagnosis of SWS. In study b, literature analysis (Medline/Scopus 2002-2019). Statistical analysis: Fisher’s z Transformed Correlation Coefficient, odds ratio, p-values.

Results: Study a= 21 SWS patients [11F, 10M; mean age: 16.8 years]; study b=1431 SWS patients [49% F, 51% M; mean age: 11.3 years]. We recorded: facial capillary malformation [89% (a) vs 93% (b)]; choroidal vascular malformation [25% (a) vs 23% (b)]; glaucoma [42% (a) vs 58% (b)]; biphthalmos [22% (a) vs 23% (b)]; seizures [90% (a) (onset = 32 months) vs 83% (b) (onset = 17 months)]; partial (a:100%; b:93%), generalized (a:12%; b:11%) or status epilepticus (a:12%; b:3%); leptomeningeal vascular malformation (a:94%; b:80%); choroid plexus involvement (a:17%; b:17%), cortical atrophy/calcifications (a:44%; b:44%) [parietal (a:90%; b:75%) and occipital (a:80%; b:69%) lobes]; hemiparesis (a:85%; b:63%), developmental delay (a:80%; b:48%) and headache/migraines (a:28%; b:63%). Anticonvulsants [94% (a) vs 91% (b)]; aspirin [72% (a) vs 61% (b)].

Statistical analysis: The correlation coefficient = 2.61[ normal: 2.26–2.95]. The main differences: study a vs b = bilateral localization of nevus flammeus, glaucoma, MRI findings, developmental delay, behavioural disorders and hemiparesis; headaches/migraines, stroke-like episodes= less represented study a vs b.

Conclusions - This is the largest meta-analysis of SWS patients (irrespective of age) and highlights the protein manifestations of this neurocutaneous disorder in the affected population.

Disclosure: No potential conflict stated.

OC043

Perinatal Thalamic Injury: MRI and diffusion tensor imaging predictors of Electrical Status Epilepticus in sleep and long-term neurodevelopmental outcome

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Objective: Perinatal thalamic injury is associated with electrical status epilepticus in sleep (ESES). The aim of this study was to quantify the risk of ESES and to assess neuroimaging predictors of neurodevelopmental outcome.

Methods: We included patients with perinatal thalamic injury, diagnosed in our center in the neonatal period (and prospectively followed), or referred during childhood. Thalamic segmentation was done manually and total brain segmentation with a semi-automatic process on MRIs at the age of 3 months. Corresponding volumes were calculated. Thalamic DTI fractional anisotropy (FA) and mean diffusivity (MD) were obtained using the 3 months and childhood scans. Sleep EEG results distinguished patients into ESES (spike wave index (SWI)>85%), ESES-spectrum (SWI 50-85%) or no ESES (SWI<50%); Intelligence Quotient (IQ) / Developmental Quotient (DQ) scores were collected.

Results: 30 patients were included. At three months, mean thalamic volume was 8.11±1.67 ml and mean total brain volume was 526.45±88.91 ml. In the prospectively followed cohort (n=23) 6 patients (26%) had classic ESES and 13 patients (57%) had ESES spectrum abnormalities after a mean follow-up of 96 months. In the univariable analysis, higher thalamic volume, higher total brain volume and lower SWI were associated with electrical status epilepticus in sleep and lower SWI were correlated with higher mean DQ after the age of 2 years.
ORAL COMMUNICATIONS
PARALLEL SESSION 3A: Epilepsy II

**EGG in infants with Tuberous Sclerosis Complex (TSC) predicts developmental outcome at the age of 2 years**

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**Aim:** To describe the predictive value of the first EEG recorded in infants with TSC for neurodevelopmental outcome at the age of 2 years.

**Methods:** 69 TSC infants enrolled in the international prospective EPISTOP trial were included. The characteristics of the first EEG were correlated with neurodevelopmental outcome at the age of 2 years using logistic regression.

**Results:** The median gestational age at first EEG was 42 weeks 4/7 (range 35 6/7-54; IQR 40 3/7-46 4/7). At the age of 2 years, 30% of the infants were diagnosed with ASD and 61% with developmental delay (developmental quotient below 70 measured by Bayley Scales).

The first EEG was abnormal in 58% of the infants. In 45% the EEGs showed interictal epileptiform discharges (IED). In 36% background activity was abnormal: focal slowing and a dysmature background were described in 17 and 14 infants, respectively. In 6 infants a subclinical seizure was recorded. An abnormal first EEG (background abnormalities and/or IED and/or subclinical seizures) was a significant predictor of ASD, both in univariate and multivariate analyses, which included preventive treatment with Vigabatrin, the TSC mutation and presence of seizures during follow-up as covariables (univariate OR 3.750 p-value 0.038, multivariate OR 3.966 p-value 0.041). On the other hand, an abnormal EEG was not a significant predictor of developmental delay.

Separate analysis of the predictive value of IED and background abnormalities showed a significant association between a dysmature EEG background and ASD (univariate OR 4.606 p-value 0.017, multivariate OR 4.941 p-value 0.026). No significant associations were found between focal slowing or IED and neurodevelopmental outcome.

**Conclusion:** In this TSC cohort, a dysmature first EEG significantly correlated with ASD at the age of 2 years.

**Disclosure:** No potential conflict stated.

**Seizure induced by cortical stimulation: is there a clinical value in the paediatric population?**

Luca De Palma1, Giusy Carfi Pavia1, Alessandro De Benedictis1, Ilaria Tondo1, Simona Cappelletti1, Alessandro Ferretti1, Maria Camilla Rossi Espagnet1, Carlo Efisio Marras1, Federico Vigevano1, Nicola Specchia1

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**Aim:** Seizure induced by direct electrical cortical stimulations are a useful tool to delineate the seizure onset zone. Till now a direct comparison of clinical stimulus induced manifestations with habitual seizures was not performed comparing adult and pediatric population.

**Methods:** We reviewed all charts of patients who performed SEEG and then operated between 2011 and 2017. Patients with a minimum post-surgical follow-up of 12 months were considered. We analyzed the different seizure pattern, spontaneous or induced, considering semiology, electrical activity, age at SEEG, pathology and surgical outcome.

**Results:** 35 patients underwent SEEG recordings, with a mean age 14 y +/- 10. The most common etiology was FCD I (13 pts)
followed by FCD II (10 pts) and non-dysplastic tissue (5 pts), 7 pts (18%) had other multiple etiologies. Eight patients (23%) had seizures induced by 1 Hz stimulation and 21 (60%) by 50 Hz. Only 2 (6%) had atypical seizures. In 18 patients (51%) subjective manifestations that were similar to habitual seizures were recorded with a wider spatial distribution than the typical induced seizure. Spasms (5/35 – 14%) were never reproduced trough cortical stimulation. Nine patients were below 5 years of age, and in 7/9 (77%) we were able to reproduce the habitual seizure. No statistical differences with the older group were found. Regarding the etiology: 7/10 (70%) FCD type II pts had seizures induced by cortical stimulations while only 8/15 (53%) with FCD I. Seizure outcome was better in the group with provoked seizure (74% vs 46% seizure free).

Conclusion: Electrical induced seizure is a useful tool to delineate the seizure onset zone independently from the age at SEEG and etiology.

Disclosure: No potential conflict stated.

The use of a patient-centric neuronal cell model of Beta-Propeller Protein-Associated Neurodegeneration (BPAN) as a drug screening platform to develop novel therapies

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Introduction: BPAN is a monogenic form of neurodegeneration, associated with brain iron accumulation and early-onset parkinsonism. It is caused by mutations in WDR45, a gene with role in early autophagy. The mechanisms linking autophagy, iron load and neurodegeneration are poorly understood, while there are no effective treatments for BPAN. We aimed to address these issues by developing a patient-derived, induced pluripotent stem cell (iPSc)-based dopaminergic neuronal cell model of the disease.

Methods: 3 paediatric patient-derived iPSc lines, 2 age-matched controls and 2 ‘isogenic controls’ (generated via CRISPR/Cas9-mediated mutation correction in 2 BPAN lines) were differentiated into dopaminergic neurons using a 70-day protocol. High content imaging assays were developed for a drug screen, looking for small molecules that reverse patient-specific cellular phenotypes.

Results: At Day 70, there is absence of WDR45 protein in patient lines, while RNA sequencing has elucidated a number of deferentially expressed genes when compared to controls. When plated on multi-well plates at low density, BPAN ventral midbrain progenitors exhibit defective autophagy, with fewer LC3 puncta per cell forming compared to controls. This assay was used to perform a drug screen using the FDA-approved Prestwick library (1,280 compounds) and a series of novel autophagy activators. Some compounds significantly enhance autophagy in all tested lines. Promising hits will be further validated in our model for their ability to correct other patient-specific phenotypic defects.

Conclusion: We have used a patient-derived dopaminergic model of BPAN for disease modelling and also as a platform...
for high content imaging-based drug screening. Our work contributes towards identifying novel, effective treatments for BPN, and increases our understanding of the link between autophagy and neurodegeneration.

Disclosure: No potential conflict stated.

Comprehensive analysis of GABA(A1R) developmental alterations in Rett Syndrome, a novel therapeutic target

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Background: Rett syndrome, a serious neurodevelopmental disorder, has been associated with an altered expression of different synaptic-related proteins and aberrant glutamatergic and GABAergic neurotransmission. Despite its severity, it lacks a therapeutic option.

Objective: Through this work we aimed to identify GABAergic neurotransmission-related therapeutic targets for Rett syndrome.

Methods: We analyzed the expression of GABA ionotropic receptor subunits in different MeCP2 gene-dosage and developmental conditions. GABA A1R subunit expression was assessed in cells lines and in primary cultured neurons, as well as in different developmental stages of Rett mouse model. Further, RNAseq and systems biology analysis was performed from post-mortem brain biopsies of Rett patients.

Results: Modulation of MeCP2 expression in cellular models (both N2A cells and primary neuronal cultures) revealed MeCP2 positive effect on GABA a1, b2 and g2 receptor subunits expression. In Mecp2+/- mouse brain, GABA subunits expression was developmentally regulated, with decreased expression during pre-symptomatic stage while expression was variable in adult symptomatic mice. Finally, the expression of GABA receptor-related synaptic proteins from postmortem brain biopsies of two Rett patients was evaluated, specifically revealing GABA A1R subunit overexpression.

Conclusion: Our results strongly support GABA A1 receptor subunit as novel potential therapeutic target for Rett syndrome. Furthermore, the identification of molecular changes along Rett syndrome prodromic stages supports the need of a neurotransmission-targeted early therapeutic intervention.

Disclosure: No potential conflict stated.

Hematopoietic Stem Cell Gene Therapy for Mucopolysaccharidosis Type I, Hurler Variant (MPS-IH)

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Introduction: MPSIHI is a lysosomal storage disease caused by α-L-iduronidase (IDUA) deficiency. Current therapeutic strategies are enzyme replacement therapy and allogeneic hematopoietic stem cell (HSC) transplantation showing limitations in preventing psychomotor decline and orthopedic complications.

Methods: A Phase I/II HSC-gene therapy (GT) trial opened in May 2018 consisting in infusion of autologous, IDUA lentiviral-transduced CD34+ cells after myeloablative conditioning. The study foresees enrollment of 6 patients, lacking a non-heterozygous HLA-matched donor, with IQ/DQ>70. Primary efficacy endpoint is IDUA activity in peripheral blood up to supraphysiologic levels at 1 year post-GT. Treatment impact on nervous system is assessed by measurement of IDUA and glycosaminoglycans (GAGs) in CSF, monitoring of motor skills, IQ, neuroradiologic and neurophysiologic parameters.

Results: By submission deadline, two patients (24 and 14 months old) were treated and have a follow-up of 6 and 1 months, respectively. HSC harvest by mobilization and hematologic recovery after GT were uneventful. Both patients reached supra-normal levels of IDUA activity in peripheral blood by day+15 post-GT. In pt. 1 IDUA levels stabilized 10 fold above the mean of the normal range; early after GT (d+90) enzyme activity was detected in CSF and GAGs showed...
1-log depletion. Six months after GT his motor functions were stable, a mild improvement of cognitive and verbal skills was recorded associated with amelioration of hearing loss. Brain and Spine MR revealed initial signs of improvement in perivascular spaces and degree of lumbar kyphosis.

Conclusion: Our preliminary results suggest an early metabolic correction of MPSIH enzyme defect in critical target tissues. Long-term follow-up and treatment of further patients are necessary to confirm that IDUA supranormal levels result in improvement of neurological outcome as compared with standard treatment options.

Disclosure: No potential conflict stated.

The MRI patterns may be an important clue in the early diagnosis of CLN2

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Objective: Neuronal ceroid lipofuscinosis type 2 (CLN2) disease is a rare potential treatable lysosomal storage disorder that results from deficient activity of the lysosomal tripeptidyl peptidase 1 (TPP1) enzyme caused by mutations in the TPP1/CLN2 gene. Early diagnosis is important but delays are common. In this study, the role of MRI patterns were described in the early diagnosis of CLN2.

Methods: We evaluated the clinical features and MRI patterns of children diagnosed with CLN2 according to enzyme or genetic results. Initial, early and late MRI patterns of 12 children diagnosed with CLN2 were described.

Results: Twelve children aged between 2 and 7 years, 8 female and 4 male, were diagnosed with CLN2. The mean age at onset of symptoms was 3 years and 4 months, and the mean age at diagnosis was 4 years and 6 months. Seizure, the most important prominent symptom, was seen in all cases. First MRI reports of 6 children were normal, the others had nonspecific mild cerebral and/or cerebellar atrophy. When we saw these patients in first examination, we suspected and diagnosed CLN2 according to MRI patterns of 10 children. In addition to cerebral and cerebellar atrophy, linear hyperintensity of central white matter and thin corpus callosum were described in all patients. These findings of MRI are seen even in the initial phase, and suggest the early diagnosis of CLN2 in children with seizure, ataxia and/or developmental delay.

Conclusion: We think that the MRI patterns of children diagnosed with CLN2 are highly selective and suggestive. Although these patterns are not specific, they may be an important clue in the early diagnosis of CLN2.

Brain white matter abnormalities associated with copy number variants

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Introduction: White matter signal abnormalities can be demonstrated in various neurodevelopmental disorders on brain magnetic resonance imaging (MRI). The pattern of white matter abnormalities can aid in the diagnostic process. This study aims to characterize the white matter changes found in microdeletion/microduplication syndromes.

Methods: Fourteen patients with neurodevelopmental disorders due to copy number variations (CNVs) were collected from a cohort of children with evidence of white matter abnormalities on brain MRI, from white matter clinics in two medical centers. A pediatric neuroradiologist blindly interpreted the MRI scans. Clinical and genetic findings were retrospectively extracted from the medical records.

Results: Twelve different microdeletion/microduplication syndromes were diagnosed: 1p36 deletion, 14q32 duplication with mosaicism, 5q14.3 deletion, 15q13.3 deletion, 18q23 deletion (3), 18 ring chromosome, 19q13 duplication (2), 18p11 deletion, 4p16 deletion (Wolf-Hirschhorn syndrome; WHS), 1q43q44 deletion, 21q22 deletion, 5p15 deletion (Cri du chat syndrome). White matter changes included: multifocal (10/14) periventricular (13/14) and subcortical (5/14) signal abnormalities and white matter volume loss (6/14). Dysgenesis of the corpus callosum was depicted in 13/14. The main clinical features were: global developmental delay (14/14), hypotonia (13/14), epilepsy (10/14), dysmorphic features (8/14), microcephaly (7/14), low growth parameters (6/14) and systemic involvement (6/14).
**Conclusion:** We showed that different chromosomal micro-rearrangement syndromes share similar MRI patterns—nonspecific multifocal periventricular and subcortical WM changes associated with corpus callosum dysgenesis. Hence, the presence of these features in a patient evaluated for global developmental delay/intellectual disability suggests a chromosomal micro rearrangement syndrome and therefore a chromosomal microarray analysis (CMA) should be performed.

**Disclosure:** No potential conflict stated.

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**Genotype-phenotype correlations in Italian patients with KCNQ2-related Epileptic Encephalopathy**

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**Purpose:** De novo KCNQ2 mutations have been identified as a major cause of severe developmental epileptic encephalopathy (DEE) with neonatal onset. We aimed to define the clinical, neuroimaging, and electrophysiological features of KCNQ2-related DEE and provide genotype-phenotype correlations.

**Methods:** Patients with de novo KCNQ2 mutation were identified through an Italian collaboration. Their electroclinical, neuroimaging, and antiepileptic treatment data were reviewed.

**Results:** Thirty-one subjects were enrolled. Seizure onset was at 2 days (median age) mainly with focal seizures accompanied by apnoea and desaturation. EEG showed burst-suppression pattern or multifocal epileptic abnormalities. Sixteen patients (51%) showed nonspecific MRI abnormalities. During follow-up multiple seizure types, including tonic, clonic, tonic-clonic, myoclonic, and spasms, were seen. Twenty patients (65%) were seizure-free between the age of 3 days and 9 years. Eleven patients (35%) still manifested seizures at mean age of 4.2 years. Axial hypotonia was reported in 61% of patients; eight patients (26%) could walk independently and five (16%) acquired speech ability. Cognitive outcome ranged from mild (4 patients) to profound (5 patients) intellectual disability (ID), though with a predominance of a severe/profound impairment (58%). Three patients (10%) showed normal cognitive development at the last follow-up (median age: 11.6 years; range: 10–13 years). Response to sodium-channel blockers was reported in most of the patients. KCNQ2 de novo mutations identified are all missense, except for two splice-site. Five mutations occurred twice in the cohort.

**Conclusion:** Patients showed variable phenotype spectrum ranging from an epilepsy disorder with normal neurocognitive development to a severe condition with associated profound ID. Up to 10% of the patients showed a normal developmental outcome. This heterogeneous phenotype and variable outcome may be related to the different functional impairment of the channel.

**Disclosure:** No potential conflict stated.
A modified paediatric ASPECTS score above seven predicts poorer outcomes following acute symptomatic Neonatal Arterial Stroke

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Objective: There is limited reporting of neuroimaging predictors of adverse outcomes following neonatal arterial ischaemic stroke (NAIS). Our aim was to explore associations between acute MRI findings, using pedASPECTS and infarct volume, and outcomes of hemiplegic cerebral palsy, neurological impairment and epilepsy.

Methods: Cross-sectional study of consecutive newborns, with acute NAIS, prospectively recruited from two pediatric stroke registries. Two-year outcomes were assessed using the Pediatric Stroke Outcome Measure (PSOM) and GMFCS. PedASPECTS accuracy to predict outcomes was determined by receiver operator characteristic (ROC) curves, and correlation between PedASPECTS, and percentage infarct to supratentorial volume (SBV) by Spearman’s correlation coefficient.

Results: 97 children met inclusion criteria; one was lost to follow-up. Median infarct volume was 21.5 mls (IQR 10.5–49.9), percentage infarct to SBV was 6.7% (IQR 3.0–14.2%) and pedASPECTS score was 7 (IQR 4–9). At median 2.1 years follow-up, 34% developed cerebral palsy, 44% had neurological impairment and 7% developed epilepsy. PedASPECTS accuracy for predicting outcomes was good for cerebral palsy (ROC 0.811), and fair for neurological impairment (ROC 0.760) and epilepsy (ROC 0.761). Optimal pedASPECTS cut off score was ≥ 8 for all outcomes. PedASPECTS, percentage infarct to SBV, and ≥ 5% infarct volume / SBV ratio correlated with all outcomes (p<0.005). PedASPECTS correlated with percentage infarct to SBV (Spearman’s rank 0.701, p<0.0001).

Conclusions: The PedASPECTS is fair to good for prediction of long-term outcomes following NAIS and correlates with infarct volume. These findings will assist health professionals with the identification of babies at risk for cerebral palsy, neurological impairment and epilepsy, requiring close developmental surveillance.

Disclosure: No potential conflict stated.

Mineralizing Angiopathy with infantile Basal Ganglia Stroke after minor injury: case report and two cohorts

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Introduction: Basal ganglia (BG) stroke can occur following minor head trauma in infants. BG calcification and cytomegalovirus infection are risk factors. A distinct clinicoradiological entity termed mineralizing angopathy with infantile basal ganglia stroke after minor trauma (MABGS) of unknown cause was first reported from India. This condition is characterised by hemiparesis in previously healthy infants aged 6–24 months following a minor fall; acute, ipsilateral hemihypertrophy; bilateral mineralization of lenticulo-striate arteries and stroke recurrence precipitated by minor head trauma. Good neurodevelopmental outcomes were reported apart from those with recurrent stroke (5/22; 22.7%). MABGS has rarely been reported in Northern European cohorts.

Case Report: A 17-month-old boy presented to hospital with right-sided facial, upper limb and lower limb weakness occurring three hours after a fall back from sitting position. CT brain scan showed linear calcification consistent with mineralisation of lenticulo-striate arteries bilaterally. MRI confirmed an infarct in the territory of the left posterior middle cerebral artery perforators. Thrombophilia, including homocysteine, and infection screen were negative. Calcium was normal. Microcytic anaemia was treated with iron and aspirin commenced.

On day 3 the child developed ipsilateral limb spasms and hemidystonia. This settled with Lorazepam. Neurorehabilitation resulted in full functional recovery.

Cohorts: We audited local electronic child health records including the paediatric neuroradiology database. Wordsearch included ‘basal ganglia’ and ‘calcification’. No other cases were found. Of 212 patients in the Great Ormond Street cohort, 4 had calcification, of whom one had basal ganglia infarction after minor trauma.

Conclusion: MABGS is rare and has not been previously reported in the UK. CT brain as well as MRI may be considered useful in infants with BG stroke and minor head trauma. Iron deficiency may be involved in pathogenesis.

Disclosure: No potential conflict stated.
Introduction: Description of stroke-like episodes (SLEs) is heterogeneous in the literature. Underlying mechanisms are poorly understood. Our aim was to analyze the clinical, electrophysiological, and radiological features of SLEs in the acute phase to provide better understanding of the pathophysiology.

Methods and Results: We performed a monocentric retrospective analysis of 120 SLEs that occurred in 60 pediatric patients (1996–2017). Clinical presentation, early brain MRI (<48 hours) and EEG recordings (<7 days) were examined. Patients were divided into 3 groups: genetically confirmed mitochondrial disease (group 1, n=22), other genetic disorder (group 2, n=22), or unclassified (group 3, n=16). In group 1, mitochondrial and nuclear DNA abnormalities were similarly involved. In group 2, patients were diagnosed with other metabolic diseases (CDG syndrome, OTC or fatty acid oxidation deficiency) and epileptic disorders (SCN1A, SCN2A, C9orf72). Clinical presentation was uniform except age at onset which was younger in group 2. Seizures were the most common symptom, occurring in 75% of SLEs and revealed with periodic complexes and subclinical discharges in up to 36% and 24% of the cases. An infectious trigger was often reported (36%). For group 1, mitochondrial disorders and for group 2, other genetic disorders were diagnosed with other metabolic diseases (CDG syndrome, OTC or fatty acid oxidation deficiency) and epileptic disorders (SCN1A, SCN2A, C9orf72). Clinical presentation was uniform except age at onset which was younger in group 2. Seizures were the most common symptom, occurring in 75% of SLEs and revealed with periodic complexes and subclinical discharges in up to 36% and 24% of the cases, respectively. Imaging findings in the acute phase (28 MRI analyzed) showed primary grey matter pathology (100%) which manifested with cytotoxic edema. Subcortical area lesions were only observed in 18% of the cases and associated with vasogenic edema. Hyperperfusion was constant (100%).

Conclusion: Our results suggest the existence of a pathological loop involving two main mechanisms: neuronal hyperexcitability and energy failure. The entry point in this vicious spiral could differ depending on the underlying pathology, eventually leading to the common development of SLE.

Disclosure: No potential conflict stated.

OC055
Recombinant Human Growth Hormone (rhGH) and Erythropoietin (rhEPO) exert synergistic neuroprotective effects against Hypoxic Brain Injury in neonatal mice

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Objective: Cerebral anti-apoptotic, -excitotoxic, -inflammatory rhEPO effects are well characterized in-vitro and in-vivo. Human studies on its neuroprotective potential are promising, however, there are open questions concerning optimized treatment regimen. Our previous studies gave rise to the hypothesis that rhGH prolongs hypoxia-induced activation of endogenous neuroprotective growth factors. We hypothesized that combinatorial rhGH/rhEPO treatment had synergistic effects against cerebral injury due to acute hypoxia.

Methods: P7-mice were exposed to normoxia or hypoxia (8% O2, 6h, INVIVO400 hypoxia workstation, Baker Ruskin). After regeneration period of 0.12/24h, mice were treated with rhGH (4000U/kg) and/or rhEPO (5000IU/kg). After a regeneration period of 48h, expression of pro-apoptotic (BNIP-3, DUSP-1) and neuroprotective factors (EPO, VEGF-A, IGF-1/-2) as well as IGF binding proteins and receptors was analyzed by qRT-PCR, ELISA, or Western Blot. Neurotoxicity was quantified by TUNEL staining.

Results: Hypoxia increased the number of apoptotic cells in the subventricular zone of the developing mouse brain compared to controls (2.2-fold, p<0.05). This was prevented by rhGH and rhEPO treatment assessed by TUNEL staining (p<0.05). RhGH and rhEPO diminished downregulation of cerebral IGF-1 mRNA levels in hypoxic animals. There were no synergistic effects on cerebral EPO, VEGF-A, and IGF-2 mRNA expression. Notably, neither rhGH nor rhEPO exerted significant effects on the major IGF-1 binding protein IGFBP-3. However, combinatorial rhGH/rhEPO administration decreased cerebral IGFBP-3 mRNA expression compared to controls (2.6±0.1 vs 4.3±0.2, p<0.01).

Conclusions: Present data indicate synergistic neuroprotective effects of a combinatorial rhGH/rhEPO therapy against hypoxic brain injury in neonatal mice. Since IGFBP-3 limits availability of neuroprotective IGF-1 and acts pro-apoptotic in an IGF-1/IGF-1R-independent mechanism, rhGH/rhEPO-mediated IGFBP-3 downregulation may contribute to neuroprotection and might be a promising target for further research in the field of neonatal neuroprotection.

Disclosure: No potential conflict stated.
Neutrophil-to-Lymphocyte Ratio (NLR): a potential biomarker for measuring disease activity in paediatric MOG+ Relapsing Demyelination Syndrome (RDS)

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Background and Objective: Recent studies demonstrate the use of NLR as useful biomarker of disease activity in central nervous system inflammatory conditions, such as multiple sclerosis (MS) and neuromyelitis optica spectrum disorder (NMO-SD). Our objective was to evaluate the role of NLR in a paediatric MS and non-MS relapsing demyelination syndrome.

Methods: Retrospective analysis of full-blood-counts in 42 paediatric MS, 6 AQP-4 positive NMO-SD, 17 MOG-associate d RDS, and 94 healthy controls (HC). The NLR was calculated during acute demyelinating attacks (neurological deterioration lasting more than 24 hours; 32 episodes recorded) but before initiation of steroid treatment; and during remission (> 30 days neurological stability; 132 samples). Differences between various timepoints across and within groups were statistically analysed using Graph Pad Prism version 7.0; SPSS version 25 was used to draw a Receiver operating characteristic (ROC) curve.

Results: NLR appears to be significantly higher in MOG+ RDS patients during active disease compared to MS (p 0.0001). Also, NLR in MOG+ RDS is greater during relapse compared to remission (p 0.0001), and to HC (p 0.0001). During MS relapses, NLR was found to decrease compared to remission (p 0.0098); being no different to that of healthy controls. Based on ROC analysis, the optimal threshold for NLR predicting a MOG-Ab phenotype was 2.10, with 75% sensitivity and 95% specificity. Also, a NLR value of 3.04 or higher indicates relapse in MOG+ patients, with 63% sensitivity and 100% specificity.

Conclusion: NLR can distinguish between MS and other types of RDS; and appears to be correlated with disease activity in MOG+ RDS patients.

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Hypomyelinating Leukodystrophy by loss of the sphingolipid desaturase degs1: clinical profile, biomarkers and potential treatment with Fingolimod

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Introduction: A novel hypomyelinating leukodystrophy has been recently described, associated to a deficiency of DEGS1 (DEGS1-LD), a desaturase that converts dihydroceramide (DhCer) into ceramide (Cer). In this disease, a dysequilibrium of sphingolipids has been confirmed in subjects’ fibroblasts and muscle. According to our preclinical study, fingolimod is a potential therapy for these patients.

Methods: To describe the clinical and neuroimaging profile of DEGS1-LD in order to identify new patients that would benefit for potential treatment in a compassionate use, pilot, multicentric, open, single-arm clinical trial with fingolimod. We present the validation of biomarkers in plasma and CSF.

Results: To date, 20 patients have been described in our cohort. Most of the DEGS1-LD patients presented with a rapid motor regression from 5 months old (0.5-24) with dystonia, spasticity, nystagmus, seizures and progressive failure to thrive. A subgroup of subjects (21%) presented a later onset of progressive spasticity, with previous normal development and without growing deficits. Cerebral MRI showed a hypomyelinating pattern that slightly improved with age. Corpus callosum thinning and vermian atrophy are frequently observed from 2 years old. Among different biochemical findings, the DhCer/Cer ratio in plasma and CSF has been validated as biomarker. Our main efficacy evaluation criterion is a reasonable degree of normalization of these ratios about 50% at 2, 6 and 12 months from starting fingolimod. To date, eight patients have been recruited for the open clinical trial.
Conclusions: DEGS1-LD is a devastating disease with an early and progressive clinical deterioration. Fingolimod is a potential therapy for these patients. The identification and validation of DihCer/Cer ratio as biomarker will allow for monitoring the biological impact of the treatment.

Disclosure: No potential conflict stated.

**ORAL COMMUNICATIONS**

**PARALLEL SESSION 3D: White matter**

**OC058**

Leukoencephalopathy with Brainstem and Spinal cord involvement and Lactate elevation (LBSL): atypical MRI patterns in early severe forms

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Introduction: LBSL, caused by DARS2 mutations, is regarded as a relatively mild, homogeneous leukoencephalopathy, diagnosed by characteristic MRI abnormalities. A few severely affected patients, still fulfilling the diagnostic MRI criteria, have been described. We recently noticed highly unusual MRI presentations diagnosed by whole exome sequencing (WES). We reviewed these systematically.

Methods: Cases were collected where WES had revealed DARS2 mutations in patients with a severe clinical presentation and atypical MRI abnormalities. MRIs of these patients were analyzed retrospectively.

Results: 19 MRI scans of 9 patients (age at first scan: median 0.7 years, range 0.0-2.5 years) were evaluated. They revealed two patterns, one dominated by early cerebral hypoplasia and rapid, severe atrophy (n=4), and one dominated by white matter abnormalities (n=5). In the 4 patients with rapid cerebral atrophy, the presence of numerous abnormal tortuous blood vessels was striking. By contrast, volume of cerebellum, brain stem and basal ganglia was unaffected. Of note, typical brain stem abnormalities of LBSL were present in 3 of the 4 patients. In the 5 patients with white matter involvement, rarefaction was prominent. Diffusion restriction was present in non-rarefied abnormal white matter. 4 of these patients lacked the typical brain stem abnormalities.

Conclusion: This series indicate that DARS2 mutations are associated with a more heterogeneous phenotype than currently known. Thus far, severe white matter rarefaction and cerebral hypoplasia followed by rapid atrophy have not been described in LBSL. Our findings have implications for diagnosis and for understanding disease mechanisms, pointing at dominant neuronal / axonal involvement in severe cases. This is substantiated by the finding that activation of biallelic DARS2 null alleles in conditional transgenic mice leads to massive neuronal apoptosis.

Disclosure: No potential conflict stated.

**OC059**

Neurofilament light chain is a useful biomarker in paediatric patients with Multiple Sclerosis

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Introduction: Serum neurofilament light chain (sNfL) is a promising biomarker of neuroaxonal injury in adult multiple sclerosis (MS). Data for paediatric MS are limited. We aimed to determine the potential of sNfL as a biomarker for disease activity and treatment response in paediatric patients with MS.

Methods: The study comprised 55 paediatric patients with MS. Twenty-seven patients received interferon (IFN) as IFN β-1a or IFN β-1b (IFN group) and 28 patients switched from IFN, glatiramer acetate, natalizumab or untreated to fingolimod (fingolimod group). sNfL levels were compared with 301 healthy controls (age range: 3 months to 17.9 years). The sNfL levels were quantified using a high-sensitivity single molecule array (SIMOA™). The association between sNfL levels and IFN, glatiramer acetate, natalizumab or untreated to fingolimod activity and treatment response in paediatric patients with MS.

Results: 19 MRI scans of 9 patients (age at first scan: median 0.7 years, range 0.0-2.5 years) were evaluated. They revealed two patterns, one dominated by early cerebral hypoplasia and rapid, severe atrophy (n=4), and one dominated by white matter abnormalities (n=5). In the 4 patients with rapid cerebral atrophy, the presence of numerous abnormal tortuous blood vessels was striking. By contrast, volume of cerebellum, brain stem and basal ganglia was unaffected. Of note, typical brain stem abnormalities of LBSL were present in 3 of the 4 patients. In the 5 patients with white matter involvement, rarefaction was prominent. Diffusion restriction was present in non-rarefied abnormal white matter. 4 of these patients lacked the typical brain stem abnormalities.

Conclusion: This series indicate that DARS2 mutations are associated with a more heterogeneous phenotype than currently known. Thus far, severe white matter rarefaction and cerebral hypoplasia followed by rapid atrophy have not been described in LBSL. Our findings have implications for diagnosis and for understanding disease mechanisms, pointing at dominant neuronal / axonal involvement in severe cases. This is substantiated by the finding that activation of biallelic DARS2 null alleles in conditional transgenic mice leads to massive neuronal apoptosis.

Disclosure: No potential conflict stated.
Results: The median age of patients at disease onset was 14.9 years (range: 12.7–15.6 years) and disease duration was 1 month at baseline (follow-up duration: 12–105 months). At baseline, MS patients had significantly higher sNfL values compared to healthy controls (26.8 vs. 5.2 pg/mL; p<0.001). sNfL levels were strongly associated with the number of T2w lesions and CEL, with an average increase in sNfL of 0.6% per lesion (p=0.011) and 8.6% per lesion (p<0.001), respectively. sNfL decreased significantly from 21.3 pg/mL to 8.2 pg/mL (p<0.001) in the IFN group and from 17.7 pg/mL to 7.7 pg/mL (p<0.001) in the fingolimod group after 12±2 months of treatment.

Conclusions: Our data suggest that sNfL may be a useful biomarker for monitoring disease activity and treatment response in paediatric MS. Disease-modifying therapy such as IFN and fingolimod can significantly reduce sNfL levels in MS.

Disclosure: Jens Kuhle, Jutta Gartner and David Leppert contributed equally to this study. Marie-Christine Reinert reports no disclosures. Christian Barro received travel support from Teva and Novartis not related to this work. Jens Wuerfel is CEO of MIAC AG, Switzerland. He served on advisory boards for Actelion, Biogen, Genzyme-Sanofi, Novartis and Roche. Pascal Benkert reports no disclosures. Zuzanna Michalak reports no disclosures. Wolfgang Brück received honoraria for lectures from Bayer Vital, Biogen, Merck Serono, Teva, Genzyme, Roche and Novartis; he is a member of scientific advisory boards for Teva, Biogen, Novartis, Celgene, MedDay and Genzyme; he receives research support from Teva, Biogen, Genzyme, MedDay and Novartis. Peter Huppke received honoraria for lectures and consultancy fees from Bayer, Merck, Biogen and Novartis. Jens Kuhle received speaker fees, research support, travel support, and/or served on advisory boards from ECTRIMS, Swiss MS Society, Swiss National Research Foundation (320030_160221), University of Basel, Bayer, Biogen, Genzyme, Merck, Novartis, Protagen AG, Roche and Teva. Jutta Gartner received honoraria for lectures and consultancy fees from Bayer, Biogen, Teva and Novartis. Harald Kropshofer, Davorka Tomic are employees of Novartis Pharma AG. David Leppert was an employee of Novartis Pharma AG during the time of study conduct.

The integrated stress response as therapeutic target in vanishing white matter

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Introduction: Vanishing white matter (VWM) is a stress-sensitive leukodystrophy caused by mutations in eukaryotic translation initiation factor eIF2B. eIF2B is conditional for the translation of mRNAs into proteins and is a central regulating factor in the integrated stress response (ISR). ISR activation by various stresses, including viral infections and fever, leads to inhibition of eIF2B activity, which downregulates protein synthesis rates and activates the ATF4 transcription response. The latter response decides on cell recovery and survival or apoptosis. In VWM, activity of mutant eIF2B is decreased, leading to constitutive activation of the downstream ISR/ATF4 transcription response. We have developed mutant VWM mice, which are representative of the human disease. In mouse and patient brain tissue we have shown that astrocytes are mainly and primarily affected in VWM and that they inhibit maturation of oligodendrocyte precursor cells into mature, functional oligodendrocytes by secreted factors. We have also shown that the ISR is selectively activated in astrocytes.

Objective: To investigate whether modulation of the ISR impacts VWM disease severity.

Methods: We treated VWM mice with Guanabenz, an old FDA-approved a2-adrenergic antihypertensive drug. Guanabenz targets the ISR at the level of GADD34-eIF2-eIF2B. We also treated VWM mice with ISRIB, a small compound that activates eIF2B and thus reduces the ISR.

Results: The VWM mice treated with Guanabenz between 2 and 10 months showed improved brain white matter pathology with improved astrocytes and more myelin. The VWM mice treated for several months with ISRIB had improved or normalized motor skills and ameliorated brain white matter pathology with reduced ISR activation, improved astrocyte abnormality and more myelin. Neither drug had significant side-effects.

Conclusion: The ISR is a viable target for drug therapy in VWM.

Disclosure: No potential conflict stated.
OC061 Proteomic study on neurotransmitter defects find several biomarkers pointing towards neurodevelopment dysregulation

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Introduction: Inborn errors of monoamines are rare mono- genetic diseases caused by defects in the synthesis, catabolism and transport of catecholamines and serotonin. Neurological manifestations include movement disorders, developmental delay and complex encephalopathies. Low levels of CSF monoamine metabolites are related to severe phenotypes, however no other biomarkers of neuronal dysfunction have been described so far. Our aim is to define new biomarkers to better understand the pathophysiology and the diverse response to treatment.

Methods: 92 CSF samples have been recruited from 9 centres from different countries belonging to the international group I-NTD. The population comprises the following disorders: TH, GTPCH, DHPR, PTPS, SR & one DAT (age range from newborn to 30 years).

Results: A total of 1188 proteins have been detected in the CSF of patients, 385 proteins being common in 80/92. Regardless the specific disorder, we found that around 10% of the pool of 385 proteins are related with nervous system development including glutamate receptors, axon guidance and neurexins.

After performing an specific analysis we found different proteins with differential expression between groups (dendritic, postsynaptic markers and plasmatic factors) that could be used as a biomarkers for prognosis and diagnostic (that could characterize and differentiate each enzymatic defect).

Conclusion: This is the first proteomic study performed in a large cohort of patients with monoamine defects that show evidence of neurodevelopmental dysfunction markers in in-born errors of neurotransmission. We can therefore consider these diseases as neurodevelopmental disorders. Future studies will focus on the use of these biomarkers for the clinical phenotype characterization and the response to treatment.

Disclosure: No potential conflict stated.

OC062 Neurotransmitter depletion in early Epileptic Encephalopathies and possible therapeutic options

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Introduction: 40% of seizures occurring during first three years of life are due to an epileptic encephalopathy (EE). Patients with EE may have secondary low levels of neurotransmitters (NTs): Homovanillic acid (HVA) and 5-Hydroxyindoleacetic acid (5HIAA) and their replacement with L-Dopa and/or 5-hydroxytryptophan (5-HTP) may be of benefit in epilepsy control and neurodevelopmental skills.

Methods: Clinical data and levels of neurotransmitters in cerebrospinal fluid (CSF) of 200 patients with EE followed in HSJD, Barcelona, were recruited. Data about neurological features, EEG, genetic studies, brain MRI and extensive metabolic screening were collected. We described 10 patients with treatment with L-dopa/carbidopa and 5-HTP.

Results: The series was composed by 93 females and 107 males with median age of 3 years at the moment of lumbar puncture and 0.9 years at the epilepsy onset. 79(39.5%) had abnormal levels of biogenic amines. 39(49%) had low isolated levels of 5-HIAA, 6(7.5%) isolated HVA and 21(26.5%) a combined HVA+5-HIAA decrease. 32 patients had a positive genetic diagnosis. Refractory epilepsy (78% vs 60%; p<0.05) and
abnormalities in the brain MRI (p<0.05 were related to higher probability of NT depletion. So far 10 patients with low CSF NT levels have been treated (four with 5-HTP and 6 with combined L-dopa+carbidopa and 5-HTP). All of them showed an improvement in frequency of seizures, attention span and behavior (decrease of irritability).

Conclusions: Although this is an ongoing study and requires further analysis, biogenic amines seem to be importantly affected in EE, in particular 5-HIAA. Studies about therapeutic replacement in long series of patients are badly needed to establish formal treatment recommendations, but these preliminary results are promising.

Disclosure: No potential conflict stated.

OC063

Characterization of the first whole-body KO mouse model for BPAN

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Introduction: De novo heterozygous or hemizygous variants in the WDR45 gene on chromosome Xp11 are the genetic cause of a rare neurologic disorder characterized by increased iron deposition in the basal ganglia. As WDR45 encodes a beta-propeller scaffold protein with a putative role in autophagy, the disease has been renamed Beta-Propeller Protein-Associated Neurodegeneration (BPAN). With 68 published cases, BPAN represents one of the most common forms of Neurodegeneration with Brain Iron Accumulation (NBIA).

Aim: To advance our understanding of the pathomechanism leading to BPAN, and provide a model to test future treatment options, we generated and characterized the first whole-body Wdr45 KO mouse.

Methods: The mouse line was generated using a TALEN-approach, which created a homo/hemizygous 20bp deletion in exon 2 of Wdr45. A large scale, standardized, and comprehensive phenotypic analysis of the line was performed at the German Mouse Clinic.

Results: Investigation of brains from 9 months-old mice revealed numerous degenerated neurons and large axonal spheroids with clear signs of neurodegeneration in the medulla oblon-gata, cerebral cortex and thalamus. This is consistent with the appearance of the substantia nigra of BPAN patients. Around the same age, mutants underwent a neurological screen that strongly indicated motor impairment. The phenotype worsened over time. The role of mitochondria in the development and progression of the disease was also investigated. Data revealed that Wdr45 KO mice presented with an increased mitochondrial mass in the brain, as pointed out by the higher citrate synthase activity compared to wild-type littermates, and a brain-specific decrease of complex I activity (CI). Mitochondrial mass and CI activity were instead normal in the heart. Those data suggested that altered autophagy due to WDR45 impairment leads to CI dysfunction, and that the brain is more susceptible than other tissues to WDR45-dependent damage.

Disclosure: No potential conflict stated.

OC064

The natural history of Polymerase Gamma (POLG) Disease: a study of 155 cases

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Objective: POLG gene variants are the most common cause of inherited mitochondrial disease. The current clinical classification is complicated and difficult to implement in everyday practice. To improve early recognition and simplify the classi-
ORAL COMMUNICATIONS
PARALLEL SESSION 4B: Neuromuscular

Unrevealing the molecular diagnosis and Magnetic Resonance Imaging abnormalities of a multicentre-based cohort of children with Leigh Syndrome

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Objective: To perform a genetic and radiological assessment in children fulfilling criteria of Leigh Syndrome (LS).

Methods: We performed molecular analysis in 35 LS patients through next generation sequencing techniques, and a systematically analysis of brain MRIs.

Results: We confirmed molecular diagnosis through customized panel (13), exome sequencing (10) and mtDNA sequencing (6) in all cases. Patients were classified in two groups (a) genetic defects linked to mitochondrial disorders (MD group) (29/35; 82.9%): ATPase6, MTND1, MTND6, ECHS1, HIBCH, NDUFAF6, NDUFAF5, NDUFS4, MCR, PDHA1, SLC25A19, SUCLG1; and (b) genetic variants not related to mitochondrial disorders (non-MD group) (6/35; 17.1%): SNCA, GNAO1, ADAR and PKRKA. Disease onset in the non-MD group (8.8 ± 7.59 (0-18) months) and (20.4 ± 23.3 (0-96) months) in the MD group. Elevated lactate was observed in blood (MD 48% non-MD 33%) and CSF (MD, 31%). Neurological regression, dystonia and acute encephalopathy were common in both groups, but optic atrophy was mostly related to MD diagnosis. Brain MRI showed atrophy/cavitation of putamen (77%), caudate (76%) and globus pallidus (GP) (40%). Cavitation was a common sign in the MD group and, when located in GP, it was exclusively related to HIBCH and ECHS1 variants (p=0.018). Cerebellar atrophy was observed in 9 patients. Dentate T2W HI were significantly related to HIBCH (p=0.033). Other affected structures were thalamus (20%) and white matter (26%).

Conclusion: We identified a wide genetic variability in our cohort of LS patients. However, we also identified a number of patients with mutations in epilepsy and movement disorders genes, suggesting that established criteria for LS are not completely specific. Basal ganglia neurodegeneration with cavi-
Onasemogene Abeparvovec Gene-Replacement Therapy in presymptomatic Spinal Muscular Atrophy (SMA)

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Introduction: SMA results in motor and respiratory function loss; the genetic root cause is biallelic survival motor neuron 1 gene (SMN1) deletion/mutation. Genomic copies of a similar gene (SMN2) modify disease severity. In a phase 1/2a study, onasemogene abeparvovec (AVXS-101), an SMN gene-replacement therapy, improved outcomes of symptomatic SMA type 1 patients (2xSMN2) dosed ≤6 months. This study evaluated AVXS-101 for the treatment of presymptomatic newborns with SMA.

Methods: SPR1NT is a multicenter, open-label, phase 3 study enrolling ≥27 SMA patients (2xSMN2 or 3xSMN2). Asymptomatic infants ≤6 weeks receive a one-time intravenous AVXS-101 infusion (1.1x1014 vg/kg). Safety and efficacy are assessed through study end (18/24 months for patients with 2x/3x-SMN2). Primary outcomes are independent sitting ≥30 seconds (2xSMN2) or standing with assistance (3xSMN2). Exploratory outcomes include motor function improvement (CHOP INTEND, Bayley-III).

Results: As of September 27, 2018, 7 infants received AVXS-101 (4 female; 6 with 2xSMN2) at age 8–37 days (median:12; mean:21). At screening, mean (range) scaled Bayley gross and fine motor scores were 9.7 (7–14) and 9.6 (7–12) points. Of those patients with 2 or more sets of scores, all had increased gross and fine motor scores compared with their baseline performance. Mean baseline CHOP INTEND score (maximum of 64) was 41.7 points, which increased by a mean of 6.8 (n=4), 11.0 (n=3), 18.0 (n=3), and 22.5 (n=2) points at 14 days, 1, 2, and 3 months; 2 patients scored ≥60 points. As of February 4, 2019, 15 patients were dosed. Additional follow-up will be presented.

Conclusion: Preliminary data from SPR1NT show rapid motor function improvements in presymptomatic SMA patients. Given that disease progression/motor neuron loss is rapid, early intervention is critical to enhance motor function.

Disclosure: MS has served as an advisory committee board member for AveXis, Inc., and Biogen, research funding as a principle investigator for AveXis, Inc.-sponsored clinical trials, and is employed by AveXis, Inc. KJS has received personal compensation for a speaking engagement from Biogen and research funding as a principle investigator for AveXis, Inc.- and Biogen-sponsored clinical trials. MFarrar has received honoraria for scientific advisory boards and research grants from Biogen. JP has received personal compensation from Biogen, AveXis, Inc., and Sarepta; and research support from Biogen, AveXis, Inc., PTC, and Sarepta. EK, MFarrow, SFGO, DEF, BEG, SAS, and JL are employed by AveXis, Inc. DMS is employed by, and owns stock in, AveXis. KAS has received personal compensation as an advisory committee board member from AveXis, Inc. and as a visiting professor from Biogen; and research funding for AveXis, Inc.- and Biogen-sponsored clinical trials. HM has nothing to disclose.

The value of AVXS-101 Gene Replacement Therapy in improving survival and motor function and decreasing ventilatory support and hospitalization contrasted to Nusinersen and natural history for Type I Spinal Muscular Atrophy

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Objective: Spinal muscular atrophy type 1 (SMA1) is a rapidly progressing, debilitating, genetic neuromuscular disease. This cross-study comparison highlights the value of onasemogene abeparvovec (AVXS-101) on survival, motor milestone achievement, ventilatory support, and hospitalizations in SMA1 patients contrasted with nusinersen and untreated patients.

Methods: SMA1 patients (two SMN2 copies) were treated with AVXS-101 (CL-101; NCT02122952; cohort 2, N=12) or nusinersen (ENDEAR; NCT02193074; N=80). Event-free survival (EFS,
Joint effect of the SMN2 and SERF1A genes on early onset Spinal Muscular Atrophy patients

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Objectives: Despite genetic homogeneity, SMA has broad phenotypic variability that indicates involvement of disease modifiers. Sq13 SMA locus not only harbours the disease causing SMN1 gene, but is also enriched in other genes (SMN2, SERF1A and NAIP), repeated sequences and pseudogenes. We aimed to examine the main and joint effect of SMN2, SERF1A and NAIP gene copy number on phenotypic variability of early-onset SMA.

Methods: MLPA was used to assess copy number of the SMN2, SERF1A and NAIP genes in genetically confirmed Serbian SMA patients.

Results: 23 were diagnosed with severe type I, 37 with intermediate type II and 39 with type III). Inverse correlation was observed between the copy number of each individually examined gene and SMA type (Spearman rank test, SMN2 \( p=2.2 \times 10^{-16} \), SERF1A \( p=6.6 \times 10^{-15} \), NAIP \( p=1.4 \times 10^{-08} \)). Generalised linear models and backward selection, starting with a full model including SMN2, SERF1A and NAIP copy number and their interactions, revealed that the best minimal model describing the phenotypic variability in early-onset SMA included the main effect of SMN2 \( (p<2 \times 10^{-16}) \) and SERF1A \( (p<2 \times 10^{-16}) \) copy number and interaction of these two genes \( (p=0.02628) \).

Conclusion: SMN2 and SERF1A gene copy number, as a consequence of complex rearrangements at Sq13 region, modifies the early-onset SMA clinical outcome among Serbian patients as independent variables and through their joint effect. We will also try to analyse gene copy number not only on SMA types but also on subtypes within type 1, type 2 and type 3 SMA.

Disclosure: No potential conflict stated.

Clinical and radiological characterization of FIG4 related Neuronopathy

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Background: Variants in the FIG4 gene which encodes a PI(3,5)P25-phosphatase may lead to obstruction of endocytic trafficking, causing accumulation of enlarged vesicles in peripheral neurons and fibroblasts in murine and in vitro models. Autosomal recessive variations in this gene are associated with neurological disorders including Charcot-Marie-Tooth disease type-4J (CMT4J) and Yunis-Varon syndrome (YVS).

Disclosure: OD, DEF, FGO, MM, MD, FK, and RA are employed by AveXis; DMS is employed by, and owns stock in, AveXis; BM has received consulting fees from AveXis.

Results: The proportion of patients achieving EFS at ≥14 months was 30% in PNCR, 50% in NN101, 66% in nusinersen-treated patients, and 100% in AVXS-101-treated patients. No patient in either natural history study achieved motor milestones. In nusinersen-treated patients, 8% sat independently and 1% stood; 92% of AVXS-101-treated patients sat unassisted, 17% stood with assistance, and 17% walked independently. The proportion of patients requiring permanent assisted ventilation was 57% in PNCR, 19% in nusinersen-treated patients, and 0% in AVXS-101-treated patients. The mean unadjusted annualized rate of hospitalizations (total hospitalizations/total number of subject-years followed) was 4.3 for the ENDEAR control, 4.5 for nusinersen-treated patients, and 2.1 for AVXS-101-treated patients.

Conclusion: A single dose of AVXS-101 resulted in dramatic survival and motor milestone achievements with reduced healthcare utilization, which could decrease cost and alleviate patient, caregiver, and societal burden, suggesting an overall improved quality of life compared to nusinersen.

Disclosure: OD, DEF, FGO, MM, MD, FK, and RA are employed by AveXis; DMS is employed by, and owns stock in, AveXis; BM has received consulting fees from AveXis.

Disclosure: No potential conflict stated.
Method: We present four children with homozygosity for the FIG4 missense variant c.506A>C (p.Tyr169Ser) with a distinct clinico-radiological phenotype.

Results: Four children aged 3, 11, 11 and 12y are described, from three South Asian consanguineous families. Three presented with infant onset dystonia and one with hypotonia. All have depressed lower limb reflexes; two have nerve conduction studies consistent with severe sensorimotor neuropathy. All have moderate-severe cognitive and severe motor impairment with a static course. All have swallowing difficulties and three are gastrostomy fed. MRI brain showed mild cerebellar atrophy and bilateral T2 hyperintense swelling of the olivary nuclei/anteriorolateral medulla in all four patients. None had any other lesion in the triangle of Guillain-Mollaret. One child also had abnormal signal in the internal capsule and cerebral white matter suggestive of hypomyelination. Homozygosity for the FIG4 missense variant c.506A>C in was detected in all four cases.

Conclusion: These children represent a novel phenotype associated with a FIG4 variant, with features of CMT4J and some of YVS, suggestive of a degenerative (neuronopathic) rather than a neuropathic process, characterised by both central and peripheral signs, intellectual disability, and MRI changes of cerebellar atrophy and bilateral medullary hyperintensities. FIG4 analysis should be considered in patients with central and peripheral nervous system signs and medullary radiological changes, providing earlier diagnosis, prognostic value, and informing reproductive choices.

Disclosure: No potential conflict stated.

Onasemnogene Abeparvovec Gene-Replacement Therapy for Spinal Muscular Atrophy Type 1: global pivotal Phase 3 study programme (STR1VE-US, STR1VE-EU, STR1VE-AP)


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Introduction: Spinal muscular atrophy type 1 (SMA1), a rapidly progressing disease caused by loss of function of the survival motor neuron 1 gene (SMN1), typically results in death/permanent ventilation by 2 years. Onasemnogene abeparvovec (AVXS-101), a one-time, intravenous, investigational gene-replacement therapy (GRT), is designed for immediate, sustained neuronal SMN expression, treating the genetic root cause of SMA. In a phase 1/2a study, AVXS-101 demonstrated exceptional improvements in survival and motor function. We report data from the global STR1VE program: phase 3 studies evaluating AVXS-101 in the United States (US; NCT03306277), European Union (EU; 2017-000266-29/NCT03461289), and Asia Pacific (AP; NCT033837184).

Methods: The STR1VE trials are multicenter, open-label, single-arm studies in symptomatic SMA1 patients ≥6 months (bi-allelic SMN1 deletion/mutations, 1–2 SMN2 copies). Primary outcomes are independent sitting ≥10 (EU, AP) or ≥30 seconds (US) at 18 months and survival (no death/permanent ventilation) at 14 months (US only; secondary outcome in EU, AP). Secondary/exploratory outcomes include independence of ventilator support and motor function improvements (Bayley-III, CHOP-INTEND).

Results: US enrollment is complete (N=22, as of 8 June, 2018). As of 31 December, 2018, 8/22 enrolled patients achieved sitting without support for ≥30 seconds and 20/21 surviving patients are alive without permanent ventilation (aged 8–16.3 months, 6.5–14.1 months post-dose). Eighteen of 21 surviving patients

Disclosure: No potential conflict stated.

http://www.epns.info/
used no non-invasive ventilation support. As of 19 February, 2019, 21 patients were enrolled in the EU (30 planned). The AP region is currently enrolling patients (6 planned). Updated data, pooled from intent to treat populations across studies, will be presented.

**Conclusion:** These data indicate that AVXS-101 has significant therapeutic benefit in prolonging survival and improving motor function in symptomatic infants with SMA1.

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Correlation of ACC MRI scoring and neurodevelopmental outcomes in children with prenatally diagnosed Isolated Corpus Callosal Agenesis

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Objectives: Predicting neurodevelopmental outcome in children with agenesis of the corpus callosum (ACC) remains a challenge. Even in isolated ACC 20% of patients have significant developmental and/or cognitive delays, that are not predictable prenatally. The aim of our study was to apply a new scoring system in prenatal MRI to attempt to predict outcomes in isolated ACC.

Methods: We evaluated long-term neurodevelopmental outcome in 20 children with isolated ACC, who underwent fetal MRI between 01/01/2014 and 31/12/2018. MRI features were scored independently by two neuroradiologists, using morphologic brain characteristics on standard fetal MRI protocol (T2, T1, DWI, EPI). Neurodevelopmental outcome was tested with the Bayley Scales of Infant and Toddler Development – Third Edition (BSID-III). Correlation between ACC-MRI Score and neurodevelopmental outcome has been conducted.

Results: Neurodevelopmental outcome was favorable and within normal range in nearly 90%. Average gestational age at MRI was 28 weeks. Average age at evaluation was 24.5 months (range 7-42 months). Normal development by the BSID-III was defined as a development quotient (DQ) score ≥85, moderate to severe developmental delay was defined as a DQ score <70. A significant negative correlation has been found between ACC-MRI Score and neurodevelopmental outcome for children with isolated ACC. Additionally, we observed lower scores in verbal comprehension, social judgment and executive functions correlating with specific MRI features. All patients with moderate to severe delays presented MRI score > to 5.

Conclusions: Prenatal diagnosis still fails to detect 20% of isolated ACC that have significant neurodevelopmental delays. We present a novel MRI-Score that can be applied to standard fetal MRI protocol. High MRI scores had a good correlation with neurodevelopmental outcome in our initial sample.

Disclosure: No potential conflict stated.

Diagnostic yield and clinical impact of implementation of prenatal Exome Sequencing in fetuses with neurological abnormalities on fetal ultrasound

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Introduction: Exome sequencing (ES) is an efficient tool to diagnose genetic disorders postnatally. We report on the diagnostic yield and clinical impact of the implementation of rapid prenatal ES (pES) in fetuses with neurological abnormalities found on fetal ultrasound.

Material and methods: We analyzed the impact of pES on pregnancy outcome and pre- or perinatal management in the first 11, consecutively referred patients for pES because of one or more neurological abnormalities seen on fetal ultrasound.

Results: Cerebellar hypoplasia (n=4), callosal a/hypo/dysgenesis (n=3), microcephaly (n=1), ventriculomegaly (n=1), cysts (n=1) and lobar holoprosencephaly (n=1) were identified on fetal ultrasound. In the last patient, a 11q23.3 duplication was detected by chromosomal microarray analysis after ES counselling, which resulted in termination of pregnancy (TOP). In 8 out of 10 fetuses (80%) a pathogenic mutation was found with pES. Based on these results TOP was performed in 5 out of 10 cases (50%) before 24 weeks gestational age, the upper limit for abortion according to the Dutch law. Intrauterine fetal death occurred in 3 pregnancies; in 2 out of these 3 fetuses the diagnosis was established with pES. Two late TOPs (> 24 weeks gestation) were performed in the Netherlands after establishing a definite diagnosis; in one pregnancy, in which no mutation was found, a late TOP was performed outside the Netherlands.

Conclusion: We show that there is a high diagnostic yield and clinical impact of implementation of rapid pES in fetuses with neurological abnormalities on fetal ultrasound. Since rapid pES is feasible and affects parental decision making on pre- and perinatal management, it supports further implementation of pES in the routine prenatal setting.

Disclosure: No potential conflict stated.
Lissencephaly: molecular, radiological and clinical aspects of a single centre cohort

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Introduction: Lissencephaly is a rare malformation of cortical development due to abnormal transmantle migration resulting in absent or reduced gyration. The lissencephaly spectrum consists of agyria, pachygyria and subcortical band heterotopia. In this study we compare neuroradiology, genetic etiologies and response to antiepileptic drugs in patients with lissencephaly spectrum malformations.

Methods: From a cohort of app 1200 children with epilepsy at Astrid Lindgrens Children’s Hospital we identified 21 patients with lissencephaly spectrum malformations. The study group consisted of 14 males and 7 females, aged 18 months to 21 years at the time of data collection. All neuroradiological investigations were re-evaluated and the malformations were classified by the same neuroradiologist. Genetic testing was performed by oligonucleotide array CGH, MLPA, targeted gene panel and whole exome/genome sequencing.

Results: In eleven patients (52%) mutations in PAFAH1B1 (LIS1) or variable microdeletions of 17p13.3 including the PAFAH1B1 gene were detected. Four patients (19%) had tubulin encoding gene (TUBA1A, TUBG1 and TUBGCP6) mutations. Mutation in DCX, were detected. Four patients (19%) had tubulin encoding gene mutations in tubulin encoding genes. Radiological findings could reliably predict molecular results only in classic lissencephaly. Radiological and molecular findings did not correlate consistently with severity of clinical outcome.

Conclusion: The most common genetic etiologies in lissencephaly spectrum in our cohort were deletions or intragenic mutations in PAFAH1B1 gene or larger deletions in 17p13.3, followed by mutations in tubulin encoding genes. Radiological findings could reliably predict molecular results only in classic lissencephaly. Radiological and molecular findings did not correlate consistently with severity of clinical outcome.

Disclosure: No potential conflict stated.
**ORAL COMMUNICATIONS**

PARALLEL SESSION 4C: Fetal and Neonatal Neurology

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**OC075**

An observational study on the 2018 proposed ILAE Classification for Neonatal Seizures

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**Introduction:** A new ILAE classification for neonatal seizures was published online in 2018, as part of the ILAE public consultation process, with the aim to modify the existing 2017 ILAE classification of seizures and epilepsies, for the neonatal population. The objective of this study was to assess interobserver variability and efficacy of the latest suggested classification for neonatal seizures.

**Methods:** This was a retrospective observational study of all the neonatal cases with EEG-confirmed seizures, presenting in the neonatal, paediatric and cardiac intensive care units, over a two and a half-year period at Great Ormond Street Hospital. Primary diagnosis, semiology and duration of seizures, EEG features and brain imaging were analysed. The 2018 proposed ILAE classification for neonatal seizures was applied by two independent reviewers (MC and LL).

**Results:** A total of 41 cases were included. Median age at onset of seizures was 7 days (range: 1 day - 11 weeks; 39/40 corrected). Most infants were born at term (range: 26+4 to 42/40 gestational age). The duration of EEG recordings ranged from 1 to 53 hours; approximately 50% of the patients had at least 24 hours continuous monitoring. The median number of seizures per recording was 8 (range in duration: 18 s to 28 mins). The interobserver variability was 85%. The majority of seizures reviewed were electrographic (n=19) with the second more frequent type being clonic (n=10). Four patients were in electrographic status. No specific association between the type of seizures and neuro-imaging results was identified.

**Conclusions:** The classification appears comprehensive and applicable to the neonatal population, also supported by a high interobserver rate. The lack of clear association between type of seizures and neuroimaging could be attributed to intercurrent sedation.

**Disclosure:** No potential conflict stated.

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**OC076**

Advantages of integrated modern technology: PowerVR Programme in social deficit remediation for children with neurological disorders using multitouch–multiuser tabletops and virtual reality platform

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**Introduction:** Social competence (SC) is often impaired in children with neurological disorders (ND). Technology-based methods create effective and safe training environments. The aim was to implement combined technological platforms: multitouch-multiuser tabletops (MMT) and virtual reality (VR) software- to enhance SC in children with ND.

**Methods:** 42 children aged 8-13 years participated: 32 with ABI (epilepsy, traumatic brain injury or tic disorder) and 10 healthy controls. 12 patients (M=11.10 yrs, SD=1.543) completed 10 1-h 5-week trainings, 20 patients are in waiting-list (M=10.69 yrs, SD=1.704). All children performed in pre- and post-training assessments. Two age-matched patients trained together in the PowerVR program instructed by two clinicians. Interactive applications were implemented for paired trainings with MMT: Snowflake on Multitouch–Tabletop (MT) and NoProblem on Diamond Touch Tabletop (DTT). VR metaphors (on HTC Vive VR device) with simultaneous monitoring of vital signs (heart-rate, BP) were used in individual trainings.

**Results:** At baseline-level the patients had significant (p<0.05) deficits in executive functions on BRIEF (M=117, SD=23.594) compared to controls (M=22, SD=18.385). Impaired components of SC: cooperation, verbal/non-verbal communication, and pragmatics (FOS scores in patients 25–50% out of 100%). After the intervention executive, cooperation, communication and meta-cognitive skills improved significantly (by FOS). Trainings on VR improved social attention, emotional attitude, gestural behaviors, and decreased social anxiety. ToM skills improved in Affect Recognition (M=7, SD=5.01 vs M=10, SD=5.85), Verbal ToM (M=8, SD=3.06 vs M=10, SD=4.08), Contextual ToM (M=8, SD=3.15 vs M=11, SD=2.87), understanding Intentional Lying (M=7, SD=2.20 vs M=10, SD=0.50) and Sarcasm (M=6, SD=2.20 vs M=7, SD=2.50).

**Conclusions:** The findings suggest that the use of combined novel technological platforms in PowerVR program is a motivating and effective tool for the remediation of SC deficit in children with ND.

**Disclosure:** No potential conflict stated.
Variations in S100B levels in a population of ADHD children after a combined therapy including Methylphenidate, Melatonin and Omega-3 fatty acids

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Introduction: S100B protein may act as an indicator for brain damage, as increased serum levels have been found in diverse neurologic and psychiatric diseases. However, its role as a biomarker in attention deficit and/or hyperactivity disorder (ADHD) has not been explored yet. On the other hand, although extended-release methylphenidate (ER-MPH) is the first-line therapy for ADHD, melatonin (aMT) and omega-3 polyunsaturated fatty acids (Ω-3 PUFAs) are being tested as adjuvant therapies. Our aim is to evaluate the variations in serum S100B concentrations in a sample of ADHD children after a combined therapy with ER-MPH, aMT and Ω-3 PUFAs.

Methods: Sixty-two ADHD patients (6–15 years) were administered a combination of ER-MPH (1mg/kg/day), aMT (3mg/day) and Ω-3 PUFAs (eicosapentaenoic/docosahexaenoic acids). Blood samples to determine serum S100B levels were obtained at 3 different moments: before treatment (A), 3 months (B) and 6 months after treatment (C). Attention scores at (A), (B) and (C) were assessed by the Magallanes Scale of Visual Attention. An analysis of variance followed by a Bonferroni post hoc analysis (α=5%) were performed for comparisons.

Results: S100B values (µg/L) were: (A) 0.22±0.09, (B) 0.33±0.15 and (C) 0.35±0.16. Significant differences were found between (A)/(B) and (A)/(C) levels, but not between (B)/(C). A significant increase of attention scores was also observed when compared (A) vs. (B) and (A) vs. (C).

Conclusion: As opposed to what would be expected considering the improvement of attention, S100B levels significantly increased in our patients after treatment. This may be explained by the psychostimulant-induced neurotoxicity. More studies using different combined therapies are required to disclose the fluctuations of S100B and its function as a biomarker in children with ADHD.

Disclosure: No potential conflict stated.

Neurodevelopmental outcomes of patients with prenatally diagnosed Corpus Callosum Agenesis

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Introduction: Developmental abnormalities of the corpus callosum are one of the most common central nervous system malformations observed in humans. Corpus callosum agenesis (CCA) may be isolated, but they are frequently observed with other cerebral malformations such as neuronal migration abnormalities, white matter changes, Dandy–Walker, and Chiari II malformations. We aimed to evaluate neurodevelopmental outcomes in children with prenatally diagnosed isolated CCA.

Methods: Between January 2015 and June 2018, patients with prenatally diagnosed isolated CCA were included in the study. Corpus callosum agenesis was classified as total agenesis and partial agenesis. Developmental status of patients assessed by using the Denver Developmental Screening Test-II (DDST-II) (Turkish version). Demographic data, cranial magnetic resonance imaging and DDST-II results of the included infants were collected from the medical records and reviewed.

Results: Of the 16 patients, nine (56%) were girls and seven (44%) were boys. Their median age was 18 months (IQR: 12–27). Total CCA was detected in 12 patients and partial CCA was detected in four patients. Four patients were diagnosed with epilepsy. Chromosomal microarray were performed in four patient and normal in all of them. The results of DDST-II were normal in eight patients and abnormal in eight patients. Of eight patients, four patients severe, one patient moderate and three patients showed mild global developmental delay. There were no significant differences between total and partial CCA groups (p>0.05).

Discussion: The clinical characteristics of the patients with CCA vary from severe global developmental delay to asymptomatic patients. Neurodevelopmental outcome was favorable in most of our patients with isolated CAA. However, early identification of developmental delays among children with CAA is important in providing the appropriate care support.

Disclosure: No potential conflict stated.
Early lexical development in toddlers with Autistic Spectrum Disorder (ASD) in comparison to toddlers with Typical Development (TD)

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Objective: We aimed to study how toddlers with ASD progress in using words to communicate intentions versus TD toddlers.

Method: 24 mother-toddler dyads participated (nine ASD and fifteen TD) matched by reaching a productive lexicon of 40-70 words. Each dyad was video-recorded three times: at baseline, during naturalistic interaction and two and four months later. All productions were classified according to their resemblance to conventional words and into four communicative intentions (Declarative, Requesting, Protesting and Non-Communicative).

Results:
1. ASD toddlers were delayed in the emergence of words versus TD (31.5 months versus 17 months) with a greater within-group variability.
2. Both groups showed remarkable similarities in respect to the distribution of the different categories of conventionality, gradually progressing to word-like productions.
3. In both groups, the most common intention was Declarative. However, a higher percentage of declaratives was found among TD (F(2,21)=7.41, p<0.01).
4. In both groups, the majority of productions was directed towards the communicative partner. However, ASD used words for non-communicative purposes more often than TD (F(2,21)=14.81, p<0.01).
5. A higher frequency of approach-withdrawal, crying and self-stimulation was noted in the ASD (i.e. for withdrawal: F(1,22)=1.14, p<0.01). In the TD, a higher frequency of showing and pointing was recorded (F(1,22)=4.65, p<0.05; F(1,22)=8.39, p<0.01).

Conclusion: While both TD and ASD toddlers gradually shift from unintelligible production to conventional productions, the course may be unique in ASD. While TD toddlers begin to talk with an already-established knowledge of the main communicative functions of words, ASD seem to have only partial understanding. They improve as they expand their lexicon. These findings bear theoretical and practical implications for early intervention in ASD.

Disclosure: No potential conflict stated.

Changes in motor function following Hemispherotomy: the experiences of parents, children and young people

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Aims: Hemispherotomy is an accepted treatment for diffuse hemispheric epilepsy. This study aimed to explore experiences of patients and parents related to changes in motor function in the first year following surgery. It also sought to determine features contributing to a positive or challenging familial narrative in order to reflect on current practice and gain new insights.

Methods: This was a retrospective study, recruiting families who had undergone surgery at a single Neurosurgical centre in the United Kingdom. The sample included parents of four children and young people, aged two to seventeen years old. Two parental couples and two mothers were interviewed using semi-structured interviews. A four-year-old child participated using a creative engagement method. Thematic Analysis was used to interpret data.

Results: Three key themes and eight sub-themes emerged.

Elation and Realisation: Families described their journey from pre-operative expectations of seizure freedom, to recognising the long road ahead. They expressed that a balance exists between wanting to receive detailed information and the fear of knowing too much.

The Value of Support: Timely access to services, and community knowledge of Hemispherotomy surgery, were important for families to perceive support as beneficial. Parents sought psychological therapies and social media networks to supplement the services provided.

Adapting: Parents identified ways of coping with an emerging ‘new normal’. Self-identification as a parent versus a carer was influenced by acceptability of their child’s level of dependence.

Conclusion: An insight into the complex experiences faced by families on this elective pathway has now been described. It will help to refine the therapy led element of the pre-operative pathway at the study site and lays the foundation for more extensive research and development of tailored support resources.

Disclosure: No potential conflict stated.
OC081

Radiographic patterns of injury and risk factors in children with Hemiplegic Cerebral Palsy

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Introduction: To describe radiographic characteristics of perinatal arterial ischemic stroke (PAIS) and periventricular injury (PVI) and the associated clinical risk factors in each group.

Methods: Patients were identified through the Childhood Hemiplegic Cerebral Palsy Integrated Neuroscience Discovery Network (CP Hemi-NET) from nine clinical centres across Ontario, Canada. Lesion characteristics were determined by 2 blinded pediatric neuroradiologists. Retrospective health record review and a standardized parent interview identified pre-conception, pregnancy, and perinatal-neonatal CP risk factors.

Results: A total of 211 children with hemiplegic cerebral palsy were included (median age at diagnosis 12 months; 62% males). Cerebrovascular lesions were classified as PAIS in 101 children and as PVI in 110 children (36% with periventricular venous infarction). Males and females were equally represented (males: 60% in PAIS, 64% in PVI, p=0.5). Children with PAIS were diagnosed younger (median 9 months vs. 13 months, p<0.01), weighed more at birth (3237±801 vs 2688±1114 grams, p<0.01), and more likely to have seizures within 24 hours after birth (58% vs 25.7%, p<0.001). Children with PVI were more likely to be premature (40% vs 18%, p<0.001) and require resuscitation at birth (39% vs 25%, p=0.04). Univariate analysis demonstrated higher odds for PAIS diagnosis in the presence of a maternal history of blood clots (OR=4.9; 95% confidence interval [CI]: 1.01-23.5) or smoking (OR=2.4; 95%CI:1.5-9.9). Premature placental rupture and fertility treatments increased the odds of PVI diagnosis (OR=9; 95%CI:1.1-71 and OR=4.1; 95%CI:1.3-12.7, respectively).

Conclusion: Our study describes the neuroimaging characteristics of PAIS and PVI by neuroradiologists blinded to diagnosis in children with hemiplegic CP. Maternal history of blood clots and smoking in PAIS, and the increased odds of PVI in premature babies, those born following premature placental rupture, and fertility treatments are novel findings.

Disclosure: No potential conflict stated.

OC082

The role of Varicella Zoster Virus in Focal Cerebral Arteriopathy of childhood: results of the International “Vascular Effects of Infection in Pediatric Stroke” (VIPS) Study

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Introduction: Varicella zoster virus (VZV) reactivation after chicken pox is a postulated cause of focal cerebral arteriopathy (FCA). The VZV vaccine, using live-attenuated VZV, has reduced rates of chicken pox, but vaccine virus reactivation can cause disease like shingles. We aimed to study the role of VZV in FCA in the post-vaccination era.

Methods: The Vascular effects of Infection in Pediatric Stroke (VIPS) study prospectively enrolled and centrally classified 355 cases of arterial ischemic stroke (29 days-18 years old) and 354 stroke-free controls at 37 multinational sites, 2010-2014. We measured exposure to infections and vaccinations via parental interview, and post-stroke VZV serologies (IgM and IgG).

Results: Of 41 cases with FCA, 88% had prior exposure to VZV: 67% VZV vaccination and 33% chicken pox. Prior VZV vaccination was similar in cases of idiopathic stroke (77%, N=86) and controls (73%). Prior chicken pox was similar in idiopathic stroke (28%) but lower in controls (16%; p=0.009, chi-square vs. FCA). Of the 13 FCA cases with prior chicken pox, the infection was remote (>1 year prior to stroke) except in two whose chicken pox was 42 and 101 days prior. Those two had negative VZV IgM titers (although positive IgG titers). Overall, 5 (13%) of 40 children with FCA had positive VZV IgM titers (2 with remote chicken pox; 3 with remote vaccination), compared to 7.0% of idiopathic cases (p=0.31) and 2.6% of controls (p=0.015).

Conclusions: Although prior VZV exposure was highly prevalent, we found minimal evidence supporting VZV reactivation as a cause of FCA in this cohort. However, PCR analysis of CSF, rarely obtained in VIPS cases, would likely be more sensitive than serologies for detecting VZV reactivation in children with FCA.

Disclosure: No potential conflict stated.
OC083

Longitudinal evaluation of neurologic impairment trajectories in paediatric Arterial Ischemic Stroke (AIS)

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Objective: To evaluate the changes in pediatric stroke outcome measure (PSOM) over time in children with AIS and to characterize the predictors of neurologic recovery trajectories.

Methods: Children aged 29 days to 18 years diagnosed with AIS were prospectively enrolled in a single-centre study. Patients with ≥3 follow-up visits were included. Evolution of PSOM scores were assessed using generalized estimating equations. Predictors included sex, age group at onset (1 month–≤1 year, 1–≤4 years, >4 years), stroke laterality and location and seizure.

Results: A total of 201 children were included (median age 5.4 years; 64% males). Overall, total PSOM scores presented non-linear trajectories over time with significant improvement within the first 3 months post-stroke (β = -0.2, p < 0.01), followed by a significant increase until year 2 (β = 0.14, p < 0.01) and a subsequent slower rate of improvement afterwards (β = -0.03, p = 0.02). Compared to older children (>4 years), children ≤1 year had significant lower baseline PSOM scores (β = -0.11, p < 0.01). Significantly distinct trajectories of neurologic recovery were found among different age groups. While younger children demonstrated initial worsening (β = 0.2, p = 0.15) followed by improvement of their PSOM scores (β = -0.05, p = 0.59), older children showed a significant initial improvement, followed by a period of deterioration before they began to improve at a later age. Subcortical stroke lesions were associated with significant lower PSOM scores at baseline compared to cortical stroke (β = -0.15, p < 0.01), however, their impact on the trajectories of neurologic recovery did not vary significantly. Sex, stroke laterality and seizures had no significant effects on neurologic function trajectories.

Conclusion: A non-linear pattern of neurologic function recovery trajectories exists in children with AIS. Trajectories of recovery vary significantly based on age at stroke onset suggesting a dynamic competing effect of plasticity and recovery over time.

Disclosure: No potential conflict stated.

OC084

Retrospective study of vascular manifestations in NF1 patients: single centre experience in Northern Greece

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Introduction: Neurofibromatosis type 1 (NF1) is associated with diverse vasculopathies, mainly cerebrovascular and renal. Since neurofibromin is expressed in the smooth muscle layer of the aorta, it has been hypothesized that loss of neurofibromin expression in endothelial cells may somehow cause vascular smooth muscle cells to proliferate. Aim of this study is a retrospective review of frequency and long-term outcome of cerebral and renal vascular malformations in a pediatric cohort of NF1 patients in Northern Greece.

Methods: Data were retrieved from the medical records of 110 children with NF1 (aged 0–18 years), regularly followed–up at a tertiary hospital since 2006. Documentation of clinical and neuroimaging findings, as well as individual treatment were recorded.

Results: Seven patients (6.3%) demonstrated arterial malformations: 1) trifurcation of the posterior cerebral artery in a 9 y.o. girl, formerly not present, 2) surgically reversed midaortic syndrome in a 4 y.o. girl with stenotic double right renal arteries and secondary hypertension necessitating triple antihypertensive therapy, 3) acute-onset hemiplegia as the initial symptom of unilateral moyamoya syndrome in a 5 y.o. girl, with previously undiagnosed NF1, who underwent revascularization procedure, 4) narrowed right posterior communicating artery and double right renal artery, with extremely narrowed upper branch requiring mild antihypertensives, severe stenosis of the proximal segment of the right renal artery with co-existing milder stenosis of the superior mesenteric artery resulting in not well-controlled hypertension despite angioplasty and four-medication therapy, 6) critical stenosis of the posterior and middle cerebral arteries in a 5 and a 6 y.o. patient, respectively.

Conclusion: Increased clinical awareness for co-existing vasculopathies in pediatric patients with NF1 leads to earlier diagnosis and overall improved quality of life with less comorbidities and residual disabilities.

Disclosure: No potential conflict stated.
ORAL COMMUNICATIONS
PARALLEL SESSION 5A: Stroke

OC085
Childhood Arterial Ischaemic Stroke: results of a Germany-wide surveillance study 2015-2017

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Objective: Childhood arterial ischaemic stroke (AIS) is rare but causes significant morbidity and mortality. We aimed to investigate incidence, age-dependent clinical presentation and risk factors, and to describe the medical care situation regarding hyperacute treatment, short-time outcome and medical aftercare.

Methods: This prospective study was conducted via a hospital-based German nation-wide surveillance unit for rare paediatric diseases, called ESPED. Between January 2015 and December 2017, paediatricians of the participating children’s hospitals were asked every month to report children (age 28 days to 18 years) with a first AIS and to fill out a specific questionnaire.

Results: In the 3-year period 164 children were reported. Incidence shows peaks in infants, toddlers <2 years and adolescents with a significant male predominance only in adolescents (12-18 years). Independent of age, most children (91%) presented with focal symptoms, particularly with an acute hemiparesis. Remarkable is the occurrence of seizures in infants (57%) and more nonspecific symptoms in elder children (54%). Prothrombotic states (34%), cardiac disorders (29%) and arteriopathies (19%) were the most identified risk factors. 29 children (18%) received thrombolysis or/and mechanical thrombectomy. After acute care, the majority of children (72/131) were discharged home. At time of discharge, most common neurological symptoms were hemiparesis (42%), facial palsy (15%), and speech disturbance (12%).

Conclusion: This study provides population-based data of childhood AIS, useful for subsequent research. Besides the improvement of acute stroke management, a major interest should lie in the standardization of post-stroke care in the outpatient setting. Considering the higher stroke incidence in (male) adolescents, it is advisable to combine research activities in adolescents and young adults for a mutual exchange of knowledge of probable risk factor profiles including modifiable lifestyle risk factors.

Disclosure: No potential conflict stated.

OC086
Why can’t we achieve more recanalization treatments in the Child Stroke code? Most prevalent contraindications

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Objective: The access to recanalization therapies in stroke in children is still very scarce, being the main challenges the narrow therapeutic windows and the presence of contraindications. Our aim is to analyze the most frequent contraindications for reperfusion treatments in children diagnosed with ischemic stroke in a tertiary hospital with an established multidisciplinary pediatric stroke code.

Methods: Retrospective observational study. We include all the children aged 1 month-16 years with ICE10 diagnosis of ischaemic stroke admitted at our hospital in the period 2011-2018. We excluded in-hospital strokes. We describe time to diagnosis, etiological diagnosis, the presence of contraindications to recanalization therapies (intravenous thrombolysis-IVT or mechanical thrombectomy-MT), and outcomes at 3 months(modified Rankin Scale, mRS).

Results: A total of 13 patients were admitted with a median time from stroke onset to neuroimaging results of 206 minutes(range 65 to 1430 minutes). Recanalization techniques were performed in five patients (3 MT, 1 IVT, 1 both). The remaining 8 had formal contraindications. In five cases there was a common contraindication for MT and IVT: age below 2 years in 2 children, diagnosis of unilateral focal arteriopathy without apparent thrombus in 2 children and presenting out of therapeutic windows in 1 case. In the remaining 3 children, the contraindications for IVT were arterial dissection in 1 child and mild stroke(NIHSS <6) in 2 children; and the contraindications for MT were 2 cases of small vessel vasculitis and 1 thrombus in small vessel(PICA). The clinical evolution was favorable in all cases with a mRS at 3 months between 0-2.

Conclusion: The main contraindications for recanalization treatments were the age bellow 2 years and the diagnosis of arteriopathy(vasculitis and focal unilateral arteriopathy) with no target thrombus.

Disclosure: No potential conflict stated.
Long-term outcome in paediatric Post-Varicella Arterial Ischemic Stroke

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Disclosure: No potential conflict stated.

Conclusion: Despite a favorable evolution was initially described, our experience suggests that VZV-related AIS may result in persistent FCA and significant neurological impairment in the majority of cases.

Disclosure: No potential conflict stated.

Low haematocrit is a risk factor for acute neurological complications of cardiac bypass surgery in children with Congenital Heart Disease

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Background and Aims: Limited data are available on long-term outcome of children with VZV-related AIS. We aimed to describe the clinical, laboratory and neuroradiologic features of children affected by AIS due to post-VZV referred to our institute.

Methods: We selected 12 pediatric patients (10 males) with AIS and a virologically confirmed VZV infection or with a VZV history in the previous 12 months. Clinical, neuroimaging and laboratory data were reviewed, focusing on pediatric score outcome measure (PSOM).

Results: Average age of AIS onset, VZV primary infection and interval between infection and AIS were: 5.5 years (range: 3.9-9.9 years), 4.8 years (range 2.3-9.4 years), and 4.9 months (range 10 days- 8 months), respectively. The AIS involved the nucleo-capsular region in 10 cases, the cerebral cortex in 6 cases, the thalamus in 4 cases, and the pons in 1 subject. In one case the involvement was bilateral. Nine out of 12 patients had an inflammatory focal cerebral arteriopathy (IFCA). Virological confirmation (VZV-DNA or anti-VZV IgG in the cerebrospinal fluid) was obtained in 4 patients. Three patients were treated with rTPA/trombectomy, 6 with antiviral agents, associated with steroids in 5 cases. Prophylactic antiaggregants were administered to all patients. Mean age at last follow-up was 9 years (range 3.9-18years) with a mean follow-up of 4 years. IFCA were persistent in 7 cases and transient in 3 subjects. Another patient had a late asymptomatic iFCA. Median PSOM score was 1 (IQR 1.1-1.75).

Conclusions: Albeit a favorable evolution was initially described, our experience suggests that VZV-related AIS may result in persistent FCA and significant neurological impairment in the majority of cases.

Disclosure: No potential conflict stated.

Conclusion: In CHD, ANC appear to be associated with low pre-, intra- and post-operative haematocrits, which may be modifiable, but optimal levels require definition.

Disclosure: No potential conflict stated.
Platelet glycoprotein polymorphisms in paediatric Cerebral Sinovenous Thrombosis

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Objective: Although prothrombotic factors are increasingly recognized as an important cause of cerebral sinovenous thrombosis (CSVT) in children, specific platelet glycoprotein (GP) gene polymorphisms have not yet been investigated. Therefore, our aim was to examine the significance of eight polymorphisms, i.e. GPla C807T and G873A, GPIbα -5T>C, GPIIb/IIIa T13254C and human platelet antigens (HPA) -1, -2, -3 and -5, as well as haplotypes GPla C807T/G873A/HPA-5, GPIbα -5T>C/HPA-2 and HPA-1/HPA-2/HPA-3, in the paediatric CSVT onset.

Methods: The study was part of a project (ID HRZZ IP-2014-09-2047) and included 20 children (10 boys and 10 girls) with CSVT and 153 sex- and age-matched controls. Genotyping was performed as follows: CVD Strip assay (ViennaLab, Austria) for HPA-1, real-time PCR with TaqMan probes (Ficko T et al., 2004) for HPA-2, -3 and -5, as well as haplotypes GPla C807T/G873A/HPA-5, GPIbα -5T>C/HPA-2 and HPA-1/HPA-2/HPA-3, in the paediatric CSVT onset.

Results: Among the analyzed single polymorphisms, only the presence of at least one HPA-1b allele was found to be associated with almost 3-fold increased risk for CSVT (OR: 2.73; 95% CI: 1.06-7.04, P=0.040). Moreover, 5-9 fold increased risk for CSVT was identified in carriers of haplotypes HPA-1a/2a/3a (OR: 4.71; 95% CI: 1.42-15.64, P=0.012), HPA-1b/2a/3a (OR: 6.71; 95% CI: 3.82-13.25, P=0.019) and HPA-1b/2b/3a (OR: 8.69, 95% CI: 1.12-65.89, P=0.040).

Conclusion: Our study results reveal HPA-1 as a risk factor for paediatric CSVT not only as a single polymorphism, but also as part of three specific HPA-1/HPA-2/HPA-3 haplotypes that increase 2-3 fold the risk for CSVT onset.

Disclosure: The authors have declared no conflicting interests. This study was done as part of the project „Genetic Polymorphisms and Ischemic Stroke in Children” (ID HRZZ IP-2014-09-2047), funded by the Croatian Science Foundation. The funding source had no involvement in study design, in collection, analysis and interpretation of data, in the writing of the abstract and in the decision to submit the abstract to the conference.

Intraarterial thrombectomy in paediatric Arterial Ischemic Stroke

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Introduction: Arterial ischemic stroke (AIS) is rare in children however may cause long term neurologic deficit and mortality. Thrombectomy is a standard treatment in adults with AIS, yet a small number of cases have been reported in children.

Methods: We present five children (2girls, 3boys) aged 6-17 years (mean 13y), who underwent mechanical thrombectomy for AIS. Aspiration and/or stentriever thrombectomy were completed within 9 hours from symptom onset.

Results: All children presented with hemiparesis, one had focal seizures and loss of consciousness. Neuroimaging revealed ischemic lesions affecting the anterior circulation areas in all cases (right-sided in 3children, left-sided, and bilateral involvement each in one patient). The average NIHSS was 9.7 (4-13) in 4 children; these patients had satisfactory outcome with none to minimal deficit at the time of discharge. One patient had NIHSS>35 owing to intubation and sedation at admission; he had bilateral thromboembolic occlusions of the ICAs, supraventricular arrhythmia, and hypotension. He was a previously healthy child with dilated cardiomyopathy following presumed viral myocarditis. The clot in the right ICA was removed, but the left side couldn’t be recanalized and the patient died 4 days after the procedure. Three patients had cardiac thrombus as the underlying etiology (two dilated cardiomyopathy, one aortic valvular replacement), one had thrombophilia and one was treated for intracranial aneurysm.

Conclusion: Mechanical thrombectomy is an effective treatment in adults with AIS; for the past several years, it’s reported to be an effective and safe procedure in selected cases in childhood. Our series is significant for extending critical period for thrombectomy in childhood. The procedure resulted in satisfactory outcome in all our patients but one, who had fatal course due to cardiac thrombi and bilateral ICA occlusion.

Disclosure: No potential conflict stated.
Paediatric Optic Neuritis and anti MOG antibodies: a cohort of Italian patients, looking for prognostic factors

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Objectives: Analysis of clinical, neuroradiological and prognostic differences between seronegative and myelin oligodendrocyte glycoprotein (MOG) positive cases in a cohort of optic neuritis (ON) pediatric patients

Methods: In this Italian multicentre retrospective study, participants were identified by chart review of pediatric patients evaluated for acquired demyelinating syndromes (ADS). We selected all patients presenting with ON at the first episode of ADS. Inclusion criteria were: age 1 to 18 years at symptoms onset; presentation consistent with ON defined by occurrence of acute loss of vision detected by ophthalmological examination. We included those who were tested for MOG-IgG1 with a live cell-based assay.

Results: A total of 20 patients (10 MOG-abs and 10 seronegative) were included. Age at onset and sex ratio were similar between the two groups. Fundus oculi showed disc swelling in 9/10 in the MOG-abs cohort, with additional increased Retinal Fiber Nerve Layer (RFNL) measured by Spectral Optical Coherence Tomography (S-OCT, Spectralis Heidelberg Engineering) (5/5 performed s-OCT at baseline) and 2/10 in the seronegative group (P <0,05). Visual acuity impairment was not different between two groups, but MOG-abs cohort showed better outcome with 6/10 complete recovery versus 1/10 in the seronegative group (P 0,02). Relapse frequency was low in both groups: 2/10 MOG-abs and 1/10 seronegative cases, with a median follow up of 25 months (12-84 months).

Conclusion: Optic disc swelling and increased RFNL measured by S-OCT at baseline are strongly associated with MOG-abs positivity. MOG-abs ON more frequently show complete recovery. Relapse frequency in MOG-abs is lower in our cohort than previously reported. Relapse rate is not different between two groups that are both at risk of relapsing disease. Careful follow-up is important to address prompt immunosuppressive therapies.

Disclosure: No potential conflict stated.
rate (ARR). Other outcomes included annualised rate of new/ newly enlarged T2 (ARn/net2) lesions, number of gadolinium-enhancing (Gd+) lesions, Expanded Disability Status Scale (EDSS) score, 3-month (3m) and 6-month (6m) confirmed disability progression (CDP), and safety and tolerability.

Results: At baseline, the overall mean age and disease duration was 15.3 years and 2.1 years, respectively; mean number of relapses in the preceding 2 years was 2.4. Significant reduction in adjusted ARR was observed with fingolimod versus IFNβ-1a (0.12 vs. 0.67; risk reduction 82%, p<0.001). Fingolimod reduced the ARn/net2 lesions by 53% and number of Gd+ T1 lesions by 66% (both p<0.001) versus IFNβ-1a. The mean changes in EDSS scores from baseline were −0.23 (fingolimod) and 0.22 (IFNβ-1a). The risk of 3mCDP and 6mCDP for fingolimod versus IFNβ-1a was reduced by 77.2% (p=0.007) and 80.2% (p=0.040), respectively. Incidences of adverse events (AEs) and serious AEs were 88.8% and 16.8%, respectively, for fingolimod and 95.3% and 6.5% for IFNβ-1a.

Conclusions: Fingolimod treatment reduced relapse rate, MRI lesions and disability progression for up to 2 years versus IFNβ-1a but was associated with a higher incidence of serious AEs in patients with POMS.

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Anti-NMDA-receptor-Encephalitis leads to altered sleep-EEG-markers of neuronal plasticity

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Objective: In anti-NMDA-receptor-encephalitis auto-antibodies lead to an internalisation of NMDA-receptors. NMDA-receptors are crucial for synaptic plasticity (i.e. changes in synaptic strength) and have been related to various neurological and psychiatric disorders. Several studies suggest that synaptic strength can be measured by the slope of slow slow waves in the EEG. In healthy individuals, the slope of slow waves at sleep onset has been proposed to depend on learning related synaptic potentiation during wakefulness and decreases during sleep – a homeostatic process, important for memory consolidation.

Here, we ask whether the slopes of slow waves and their overnight changes are altered in patients with anti-NMDA-receptor-encephalitis compared to healthy controls.

Methods: 9 overnight-EEGs of 6 patients (mean age: 12,66 years, 4 female) with anti-NMDA-receptor-encephalitis and 48 healthy controls (mean age: 12,61 years, 28 female) were analysed. Slow waves (0.5-2Hz) were automatically detected within the first and last hour of NREM sleep. Slopes were calculated for each detected wave. Mean slopes and their overnight changes were compared between patients and controls using a linear model with factors disease (yes/no) and age as a known confounding factor.

Results: Slopes of the first hour of NREM sleep are lower (p=0.002) and the overnight changes (absolute/relative) are smaller (p=0.001/p=0.002) in patients compared to controls. There was no significant group difference in slopes of the last hour of NREM sleep (p=0.4).

Conclusion: As the slopes of slow waves reflect synaptic strength, we conclude that the patients’ lower slopes in the evening and smaller overnight decreases might reflect reduced synaptic potentiation during wakefulness with consequently reduced homeostatic decrease of synaptic strength during sleep. We hereby provide indications for reduced neuronal plasticity in humans with NMDA-receptor-deficiency due to anti-NMDA-receptor-encephalitis.

Disclosure: No potential conflict stated.

Nationwide survey of childhood spinal cord infarction in Japan

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Objective: We aimed to disclose epidemiology, clinical manifestations, therapies, and prognosis of spinal cord infarction in Japan.

Methods: We investigated the incidence and clinical manifestations of spinal cord infarction, by sending questionnaires to 1137 pediatric neurologists in Japan in 2016. Spinal cord infarction was defined as fulfilling five criteria as follows, sudden onset after trauma to the body, progressive paralysis, no consciousness disturbance, and differential diagnosis of acute flaccid paralysis, transverse myelitis, and GBS. This study was approved by Chiba University Ethics Committee.

Results: We have got 405 reports (46.4%) demonstrating total 22 patients (21 spinal cord infarction and 1 myelopathy). The gender ratio of male to female was 11 to 11, and mean ages were male 10.1, and female 8.0 years old. Initial etiology was diverse, i.e., lower back bruise (6), handstand (4), push up (2), cartwheel (2), and others (8). Most damaged portion was cervical (40%) and thoracic (40%), followed by lumbar lesion (20%). Damaged portion was likely to be cervical in male and thoracic in female. Urinary distention was observed in 55%. Treatments included methylprednisolone (78%), heparin (44%), edaravon (13%), intravenous immunoglobulin...
(9%), glycerin (4%), and no treatment (4%). Total recovery rate was 59%.

Conclusion: This is for the first time nationwide survey for spinal cord infarction. In our study, 41% patients still remained neurological complications, requiring early efficient therapies for this disease.

Disclosure: No potential conflict stated.

OC095<

Genetics, immunology, and outcomes of De Novo Status Epilepticus in early childhood: a national population-based prospective cohort study

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Objectives: To determine the incidence of de novo status epilepticus in children < 3 years of age. To test for genetic and immune causes in all patients. To identify risk factors for progression to epilepsy and/or developmental problems.

Methods: Participants were recruited as part of a prospective national cohort study from May '14 - May '17. All children presenting with febrile or afebrile status epilepticus were eligible. Children with a prior history of unprovoked seizures were excluded. All participants received genetic testing on a 104 gene epilepsy panel and were tested for the presence of 10 serum anti-neuronal antibodies. Follow-up was 18 months after initial presentation. Development was assessed using the Adaptive Behavioural Assessment Scale (ABAS II) parent questionnaire.

Results: 170,000 children were born during the study period. 63 presented with de novo status epilepticus < 3 years (incidence = 1 per 2,700 live births).

8/63 (13%) had a genetic cause identified, of whom 4 had a pathogenic variant in SCN1A. Other genes involved were: DEPDC5, KCNA2, POLG1, and PRRT2 (1 patient each). 8 patients (13%) had auto-antibodies detected to the following epitopes: VGKC (n = 4), GABAB-R (n = 3), and CASPR2 (n = 1). Outcomes overall were good. 41/63 (65%) had no epilepsy diagnosis and normal development at most recent follow-up. 19 patients developed epilepsy (30%). Factors significantly associated with development of epilepsy were: identification of a genetic cause (p = 0.034), afebrile status (p = 0.004), and abnormal development (p = 0.006).

Conclusions: De novo status epilepticus in the first three years of life is rare, affecting 1 per 2,700 live births. Overall, outcomes are good. Genetic cause is identified in 13% and predicts development of epilepsy.

Disclosure: No potential conflict stated.
OC096

Epilepsy surgery in the first year of life: outcome experience from a single centre in the UK

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Objective: Epilepsy surgery is an established treatment option for children with pharmacoresistant focal epilepsy. We report clinical data and outcomes of infants undergoing epilepsy surgery.

Methods: We searched our institutional electronic data base for children undergoing epilepsy surgery age≤ 12 months for retrospect case-note review.

Results: 27 cases (15 females) were identified. Most common was seizure onset in the neonatal period (17/27, 63%) and presentation with focal seizures (21/27, 78%), including 5 with generalised seizures. Epileptic spasms were seen in 6/27 (22%). Developmental impairment pre-surgery was present in 20/23, including regression in 6. Neuroimaging demonstrated cortical malformations/developmental lesions in 27: hemispheric (13/27, 48%: 12 Hemimegalencephaly, 1 Sturge Weber Syndrome[SWS]), multilobar (5/27, 19%: 2 FCD, 2 Polymicrogyria, 1 SWS), lobar (5/27, 22%: FCD), multifocal (3/27, 11%; Tubercous sclerosis), 1 hypothalamic hamartoma. Surgical procedures performed at median age 7 months (range 2-12) were: disconnections (51% hemispherotomies, 15% Temporal-parietal-occipital), cortical resections (30%). Histopathology revealed FCD in 15/20 (including 5 with hemimegalencephaly and 3 with TS), polymicrogyria in 3/20. Postoperative complications requiring surgical management occurred in 3/27 (2 hydrocephaalus, 1 subdural collection). A second surgery was undertaken in 7/27 (median interval 6 months, range 2-93).

After a median follow up of 4 years (range 0.2-11.5, 74% ≥ 2 years), 11/27 (41%) were seizure free, 7/27 (26%) had rare non-disabling seizures and 2/17 (7%) had significant seizure improvement. 18/20 had intellectual impairment, with 60% demonstrating IQ< 70 post-surgery.

Conclusion: Infants undergoing epilepsy surgery in the first year of life present commonly with hemispheric or multilobar cortical malformations and neonatal onset seizures. Whilst seizure control can be achieved in the majority, significant cognitive impairment is present at long term follow up. Further data on life quality improvement are required.

OC097

Clinical characteristics and post-surgery seizure outcomes in children with Hemimegalencephaly Spectrum

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Objective: To describe the clinical characteristics and seizure outcomes in children with hemimegalencephaly spectrum.

Methods: Retrospective case note review of children with a diagnosis of hemimegalencephaly spectrum reviewed between January 1990 and December 2018 at Great Ormond Street Hospital for Children. We collected patient demographics, clinical details, whether or not they had surgery, type of surgery and the post-surgical outcome at the last follow up.

Results: Complete clinical data with a minimum post-op follow up of 6 months was available on 58 children at the time of review. 38/58 (66%) were male. Associated syndromes were diagnosed in 9 (15.5%) children; epidermal naevus (3), linear sebaceous naevus (2), limb hypertrophy (2), and capillary haemangioma of limb (2). Median age at seizure onset was 11 days; 37/58 (64%) had their seizure onset in the neonatal period. The left hemisphere was affected in 28 (48%). 43/58 (74%) patients underwent surgery, of whom 37 had a hemispherotomy or a hemispherectomy, and 6 had a less extensive focal resection or disconnection. 11 (26%) children underwent more than one surgical procedure. Median age at first surgical procedure was 15 months. Median post-surgical follow-up was 5 years. The seizure outcomes at last follow up were, Engel class I in 23 (53.5%), Engel class II in 6 (14%), Engel class III in 12 (28%) and Engel class IV in 2 (4.5%).

Conclusion: In this large series of patients with hemimegalencephaly spectrum, the majority had a good seizure outcome (Engel class I or II) following epilepsy surgery.

Disclosure: No potential conflict stated.
Intraoperative detection of stereotactically inserted intracerebral electrodes may increase precision of resective Epilepsy surgery

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Aim: Epilepsy surgery is an effective treatment option for selected patients with focal intractable epilepsy. Long-term invasive video/EEG from intracranial electrodes is used to precisely delineate epileptogenic brain tissue in majority of surgical candidates with normal MRI or poorly defined lesion. Complete removal of this tissue represents the main predictor of postoperative seizure freedom. However, complete resection is challenging in deep brain structures such as operculo-insular cortex. Neuronavigation systems could be imprecise in such cases. We report a novel approach employing intraoperative detection of intracerebral electrodes to guide extent of surgery.

Methods: We report on 11 paediatric patients (minimal post-operative follow-up 1 year) who underwent long-term invasive video/EEG monitoring from stereotactically inserted intracerebral electrodes. Epileptogenic zone was defined using visual and quantitative analysis of intracranial EEG as well as results of multimodal neuroimaging. The length of invasive recording was 7-10 days. In contrast to other centres we proceeded to resective surgery immediately after explantation. Oblique electrodes detecting the epileptogenic zone were left in place and visually identified during resective surgery. The extent of resection was modified via detection of “epileptogenic” contacts on the electrodes.

Results: The neurosurgeon was able to intraoperatively detect electrodes in 9/11 patients. The surgery was regarded complete in 8/9 patients in whom the electrodes were detected and 6/9 of them were seizure-free at last follow-up. Resections in both patients in whom we failed to find electrodes were incomplete and they continued to have seizures.

Conclusion: Intraoperative detection of stereotactically inserted intracerebral electrodes could enhance completeness of epilepsy surgery in patients with epileptogenic zone in deep brain structures. Further studies need to elucidate effect of this procedure on long-term seizure outcome.

Disclosure: No potential conflict stated.

A randomised controlled trial of the ketogenic diet in the treatment of Epilepsy in children under the age of two years (KIWE)

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Introduction: The incidence of epilepsy is greatest in the first two years of life and this population is at risk for neurodevelopmental compromise in the long term. Little high-quality evidence is available regarding the effectiveness of ketogenic diets (KDs) in controlling seizures in infants. A multi-centre randomised controlled trial is underway to compare the effectiveness on seizure frequency of the classical KD with further anti-epileptic drug (AED) treatment in children aged 1 month to 2 years with drug-resistant epilepsy.

Methods: Eligible children undergo baseline assessment and a 1- or 2-week observation period is started with documentation of seizure frequency. Randomisation then occurs for them to receive the classical KD or a further AED. Assessments are repeated after an 8-week intervention period. Participants are followed up for 12 months from randomisation for retention, seizure outcome and neurodevelopmental status.

Results: Of 81 recruits to date, 45 were randomised to the KD arm and 36 to the AED arm. 47(58%) of recruits were male. The most common seizure type was spasms. Mean age at randomisation was 13.8±6.4 months. Eight individuals withdrew prior to 8-week follow up; nine withdrew after 8-weeks but prior to 12-months. The most common reasons for withdrawal were non-compliance with study protocol and emigration of the participants’ family.

Conclusion: Recruitment, although constant, has been challenging with this age group. Withdrawal rate has been lower than expected. We have expanded the inclusion criteria and
frequent contact is made with study personnel from all sites in order to aid sustained recruitment. The effectiveness of the KD compared to further AED treatment in this population will be reported in due course.

Disclosure: No potential conflict stated.

OC100

A novel tool to predict phenotype from genotype in SCN1A-related Epilepsies

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Objective: Mutations in the voltage-gated sodium channel gene SCN1A are associated with a spectrum of epileptic phenotypes, ranging from ‘milder’ forms such as GEFS+ to ‘severe’ Dravet syndrome (DS). Most truncating variants are associated with DS. Conversely, when a SCN1A missense variant is detected in a young child it has not been possible to predict the disease trajectory. We developed a novel method for characterising missense variants in SCN1A epilepsies and relate this tool to the clinical phenotype.

Methods: We retrospectively reviewed genetic and clinical data for 1322 SCN1A mutation-positive DS and GEFS+/FS+ patients in 6 cohorts (UK, Italy, France, Australia, Netherlands and Japan). We combined “Paralog conservation”, a measurement of the conservation of an amino acid (AA) residue at a specific position across the 10 human sodium channel \( \alpha \)-subunit gene, with the physicochemical property change of the AA substitution to generate a Paralog*Grantham (PG) score.

Results: The median PG score was significantly higher for DS missense variants (56.0, n=444) than GEFS+ missense variants (22.1, n=131) and polymorphisms (8.7, n=610, p<0.0005). 90% of GEFS+ missense variants have PG scores below 80.0, while 37% of DS missense variants have PG scores ≥ 80.0. Based on the median PG score (56.0), we divided DS missense variants into a ‘low-PG-score’ group and ‘high-PG-score’ group. DS patients with ‘high-PG-score’ missense variants (n=104) presented as early as truncating (n=361) variants (p=1.00) in keeping with greater disease severity. In comparison, ‘low-PG-score’ missense variants (n=180) were associated with later seizure onset than ‘high-score’ missense (p=0.023) or truncating (p=0.001) variants indicating a milder disease course.

Conclusion: The PG score can help to characterise the clinical significance of SCN1A missense variants, and may allow better prediction of disease trajectories.

Disclosure: No potential conflict stated.
POSTER PRESENTATIONS
Clinical features of Neurofibromatosis Type 1 in Slovenian paediatric population

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Aim: To review our pediatric patients with neurofibromatosis type 1 (NF1) and to analyze the occurrence of different clinical features among these patients.

Methods: A database on Redcap was designed on available guidelines for diagnosis of individuals with NF1. For this database patient’s demographic and clinical features, genetic testing, imaging, ophthalmological evaluation and psychological results were collected from the available medical records of patients referred to the University Children’s Hospital Ljubljana between 2000 and 2018. The charts were searched through the computer database and available data were entered.

Results: Among 146 patients included in the database 92 (63%) fulfilled either clinical or genetic criteria for diagnosis of NF1. The remaining 54 (37%) have isolated café-au-lait stains. Two or more criteria necessary for clinical diagnosis of NF1 were present in 67 pts (45, 9%). In 134 pts (91, 8%) six or more café-au-lait spots were found, 29 (19, 9%) had a first-degree relative with NF1 based criteria, 28 (19, 2%) had freckling in the axillary or inguinal regions, 24 (16, 4%) neurofibromas, 19 (13, 0%) had Lisch nodules, 12 (8, 2%) had optical glioma and 6 (4, 1%) had a distinctive bony lesion. In 37 patients additional neurological abnormalities were determined among which cognitive deficits (32pts, 21,9%) were the most common one, followed by functional disability in 8 pts (5,4%), macrocrania (5 pts, 3,4%), epilepsy 3 (2,1%) and in 17 (11,6%) hypertension.

Conclusion: During the last 2 decades, we improved clinical management of the pediatric patients with NF1 according to the published guidelines. As demonstrated severe phenotypes in our population are not so frequent. However, interdisciplinary approach and close clinical follow up is necessary for optimal management of this complex disease.

Disclosure: No potential conflict stated.

The role of Kynurenine pathway metabolites in the mechanism of ketogenic diet therapy

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Background: The present study aimed to measure blood levels of tryptophan (TRP) and its kynurenine derivatives and correlate them with seizure reduction after starting the KD in children with refractory epilepsy.

Methods: Sixteen (16) children (9 F, 7 M) with refractory epilepsy and a mean age (±SD) of 7.05 ± 5.06 years were enrolled into the study in the Department of Child Neurology at the Medical University, Lubin, Poland. Patients were treated with the classic KD or modified Atkins diet (MAD). Clinical efficacy and ketosis were monitored throughout the study. Patients’ blood levels of TRP, kynurenine (KYN), KYNA, and 3-OH-kynurenine (3-OH-KYN) were measured chromatographically at 3 months, 6 months, and 12 months on the diet; pre-KD levels served as base-line controls.

Results: Out of 16 children enrolled, 14 attained ≥ 50% reductions in seizure frequency after starting the KD. In those 14 patients, TRP levels decreased numerically (a decrease of 18-25%) but not significantly (P= 0.077) compared to the pre-KD control values at 3, 6, and 12 months on the diet. KYN levels decreased significantly (P= 0.001) compared to the pre-KD control levels (a decrease of 30-57% throughout the study). Relative to the pre-KD values, KYNA blood levels significantly increased (P< 0.001) by 39-97% throughout the study; likewise, KYN/KYA ratios significantly increased (P= 0.003) by 100-423%. In contrast, 3-OH-KYN levels (P= 0.680) and KYN/TRP ratios (P= 0.385) remained unchanged throughout the study.

Conclusions: We report a pattern of changes in the blood level of kynurenines in patients with refractory epilepsy after starting the KD.

Disclosure: No potential conflict stated.
Cerebral Sinovenous Thrombosis in a neonate with late-onset Group B Streptococcus infection

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Introduction: Cerebral sinovenous thrombosis (CSVT) is a rare, multifactorial disorders in neonates.

Methods: We report the case of CSVT in a female infant admitted with sepsis and meningitis by Group b Streptococcus (GBS).

Results: A 12-day-old female infant born at term presented with inconsolable crying, poor feeding and fever. Maternal antenatal history and delivery were uneventful. On examination, she was febrile, grunting with prolonged capillary refill time and bulging fontanel. She was screened and started on empirical intravenous antibiotics. Lumbar puncture revealed 1810 leukocytes with marked neutrophilia, low CSF glucose and raised protein. Blood and CSF cultures grew GBS 12 hours later. On day one, clonic seizures of the right arm and episodes of apnea were noted. Computed tomography showed multiple hypodense lesions in cortical and subcortical white matter of the left frontal, parietal and occipital lobes and right frontal lobe anterior to the central sulcus. Magnetic resonance imaging and venography(MRI/MRV) confirmed multiple cortical ischemic lesions, bilateral subdural empyema and extensive thrombosis of the superior sagittal sinus, right transverse sinus and bridging veins. She was commenced on low molecular weight heparin. Thrombophilia screening was negative. EEG findings were at first compatible with neuroimaging findings but gradually resolved. Repeat blood and CSF cultures were sterile. Follow-up MRI/MRV 8 weeks later showed resolution of thrombosis and residual porencephalic cortical areas. She completed an eight-week course of antibiotics and anticoagulants were gradually discontinued. The neurological evaluation on discharge revealed global hypotonia. Early rehabilitation was started with physiotherapy and close follow up was organized.

Conclusion: GBS sepsis can be a rare cause of CSVT in neonates. Early diagnosis can lead to prompt therapy and improve neurodevelopmental outcome.

Disclosure: No potential conflict stated.

Isolated Cortical Venous Thrombosis in healthy children; a case report and a literature review

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Introduction: Sinovenous thrombosis is an uncommon cause of secondary headache in children who are otherwise healthy. Cortical venous thrombosis is very rare and distinctive variant in this patients’ cohort.

Clinical case: We are reporting a healthy before 17 years old female who presented with acute bilateral throbbing headache for few days before presentation. She was presumed to have acute migraine attack but with absence of previous migraine history, urgent brain MRI and MRV were obtained after neurology consult. MRI showed isolated right cortical vein thrombosis with no extension to venous sinuses. Pt was admitted and treated with Lovenox with complete resolution of her venous thrombosis in 8 weeks. Pt continued to be asymptomatic and was transited to Xarelto which was stopped later to complete 3 months of anti-coagulation therapy.

Discussion: Isolated cortical venous thrombosis is a rare clinical and radiological disorder in pediatric age group. Most patients present with headaches, seizures or focal neurological deficits. Underlying pathophysiological mechanisms are not well understood. In adults, infections, pregnancy, and oral contraceptives are the most known risk factors. Contrasted MRI with venogram is usually diagnostic but conventional angiogram has been utilized as well. Studies have shown that risk of hemorrhagic infarction is higher compared to usual sinus venous thrombosis but odds of developing high intracranial pressure are less. Nevertheless, treatment strategies have been extrapolated from those designed for sinus venous thrombosis.

Conclusion: Isolated cortical venous thrombosis remained a rare, unique and challenging disease entity with little understanding of underlying pathophysiological processes. Our reported case is helpful to raise awareness regarding careful evaluation of children who present with acute headaches.

Disclosure: No potential conflict stated.
Subcortical Band Heterotopia (SBH), a prenatal diagnosis: case report

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Introduction: SBH also known as double-cortex is due to an abnormal neuronal migration during the fetal life. It is characterized by bilateral symmetric bands of grey matter located in the central white matter and associated in 80% with mutation in the X-linked doublecortin (DCX) gene. While mutation in the DCX gene tend to present with the classic lissencephaly phenotype in males, the SBH phenotype has been mainly described in females. Clinical manifestations include intellectual disabilities and epilepsy. The diagnosis is usually done postnatally by MRI showing SBH and genetic testing confirming DCX mutation.

Methods: We evaluated the US, MRI, genetic, and pathology data of a fetus diagnosed with SBH at 31 weeks gestational age.

Results: A 31-year old woman underwent fetal US and MRI for a CMV seroconversion during the 1st trimester. While US failed to show any abnormalities, the fetal MRI at 31 weeks showed symmetric enlarged ventricles and an abnormal neuronal migration pattern suggesting SBH. Fetal post-mortem study revealed a female with a thick and irregular cortex in the occipital and temporal lobes, enlarged ventricles and nodules of subcortical heterotopia in the white matter. CMV-PCR on the amniotic fluid was negative. Genetic testing showed a de novo pathogenic variant in the DCX gene.

Conclusion: The antenatal diagnosis of SBH usually fails because the cortex is difficult to assess by US. Although associated anomalies as enlarged ventricles can be seen by US, fetal MRI provides a better accuracy to diagnose SBH. While disturbances of the neuronal migration can occur in the context of a prenatal CMV infection, the symmetry of the lesions should orientate the diagnosis toward a disorder of neuronal migration of genetic origin.

Disclosure: No potential conflict stated.

Proposal for an epidemiological study in paediatric prolonged disorders of consciousness

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Objective: Long term care in neuro-rehabilitation is largely needed in cases of severe Acquired Brain Injury (ABI) leading to Prolonged Disorders Of Consciousness (PDOC). Few published data exist concerning the epidemiology of Paediatric PDOC. We propose to develop a study to look at the epidemiological data in this condition to help understand its evolution and for optimal planning of health resources.

Background: Severe disorders of consciousness including vegetative state (VS)/unresponsive wakefulness state (UWS) and minimally conscious state (MCS) represent successive stages in emergence of patients from coma. The umbrella term PDOC was suggested by Royal college of Physicians to encompass all patients who had impaired consciousness for over 4 weeks duration. Worldwide prevalence figures of PDOC in adults and children have been estimated based on a small number of studies, none of which focused primarily on children. Recent development of therapies for PDOC, in particular, neuro-modulatory techniques such as vagal nerve stimulation and Deep Brain Simulation, means that there is a pressing need to obtain epidemiological data in order to design definitive interventional studies.

Methods: We aim to collect data over a 12 -24-month period by prospective notification of cases by consultant Paediatricians to the BPSU. Clinical information concerning demographics, etiology, clinical state, associated co-morbidities, temporal course of condition, place and nature of care, educational and social care provision and involvement of the voluntary sector will also be obtained from responding clinicians.

Conclusion: The study results will help define the natural history of Paediatric ABI- PDOC and provide a baseline against which, to assess in future, impact of advances in paediatric intensive care in number of children surviving with PDOC.

Disclosure: No potential conflict stated.
P01-07

Narcolepsy Type 1 in paediatric patients in Slovenia

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Introduction: Narcolepsy type 1 is a rare and underdiagnosed chronic disorder of the central nervous system. With a peak onset during the second decade of life, the initial symptoms frequently reveal in the paediatric period. We reviewed clinical and neurophysiological characteristics of all childhood narcolepsy type 1 cases in Slovenia.

Methods: Retrospective study of all childhood narcolepsy patients, referred to National Sleep Disorders Centre at UMC Ljubljana and National Centre for Paediatric Sleep Disorders at GH Celje from 2000 to 2018. In all whole-night polysomnography was performed, followed by 5 multiple sleep latency tests and HLA analysis.

Results: In the observed period 7 Slovenian children (2 boys and 5 girls) have been diagnosed with narcolepsy type 1. The youngest was 7.5 and the oldest 17.5 years. The average duration of the symptoms before the diagnosis was around 26 months. All narcolepsy patients had HLA DQB1*0602. No vaccination related cases were found. Three patients were obese, however none had precocious puberty. They all presented with prominent hypersomnolence with an average MSLT of 5.18 minutes. All but one had 4 or 5 SOREM at the MSLT testing. They all reported cataplexy. Two patients were treated with stimulant medication, one with modafinil and venlafaxine and two with sodium oxybate. They all reported significant improvement of the symptoms. In two patients the parents declined any treatment.

Conclusion: 7 cases in the last 18 years confirm that narcolepsy is underdiagnosed disease in Slovenian children. Since early diagnosis and therapeutic approach are essential for promotion of cognitive development and social integration of affected children, we should focus more on preventive programs for better detection of childhood narcolepsy among laic and professional population.

Disclosure: No potential conflict stated.

P01-08

A rare cause of Stroke in childhood: Atrial Myxoma

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Introduction: Although stroke is rarely seen in childhood, early diagnosis is important because of its high morbidity and mortality. The symptoms at admission may not be as pronounced as adult patients and the diagnosis may be difficult. Ischemic stroke in children may be due to several different factors like heart disorders, blood disorders, infections or vascular disorders. The incidence of cardiac tumors, one of these causes, is very low in childhood.

Case Report: A previously healthy 16-year-old female patient with dizziness and vomiting was admitted to the emergency department. Her complaints began on the same day and progressed. The patient’s family history and past medical history were unremarkable. Her vital signs were stable; neurological examination showed diplopia and medial gaze paralysis of the left eye, stage 1 papillary edema and ataxic gait. Since cranial magnetic resonance imaging revealed multiple infarct areas in the left thalamus, pons, cerebellum, left cerebral hemisphere and bilateral posterior temporal lobes; anticoagulant therapy was initiated for ischemic stroke. Transthoracic echocardiography showed a 29x 17 mm mass which filled the left atrium completely. The patient was transported to another hospital where emergent surgical resection of the tumor was performed. Histopathological diagnosis was atrial myxoma. The patient recovered without permanent sequelae.

Results: Although cardiac myxoma is very rare in childhood, it may cause ischemic stroke. Early diagnosis and treatment of these patients can be life-saving. Cardiac tumors should be considered in the differential diagnosis of pediatric patients presenting with neurological deficits suggestive of stroke.

Disclosure: No potential conflict stated.
Auditory evoked potentials as early detectors of auditory maturation abnormalities in preterm infants with neonatal complications

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Introduction: Early brainstem auditory evoked potentials are a type of evoked potentials (EPs) which can provide functional information about the integrity of the auditory system and viability of the brainstem, contributing to the prediction of neuromaturational development later in life.

Methods: In order to detect possible differences in the maturation of the auditory system between terms and preterms, we conducted a retrospective cohort study measuring the wave V latency (in msec) in 176 infants born at term or premature. We searched for possible risk factors, which may exert a negative impact on auditory system maturation, such as infant’s gender, birth weight, percentile of head circumference, risk levels of hypoxic-ischemic encephalopathy, presence of perinatal complications or neurological complications before or shortly after birth.

Results: The maturation of the auditory system is not associated with the infant’s gender (mean difference 0.16ms, p>0.05) and the head circumference at birth but with extremely low birth weight (LBW), very-LBW (mean difference 0.06ms, p<0.05) as well as with the presence of neurological and respiratory complications shortly before or after birth (p<0.05). Moreover, neonatal neurological disorders before or after birth are associated with low APGAR score at the 10th minute of life (p<0.05). There was no significant difference in the latencies between the low HIE risk and the high HIE risk group (mean difference 0.02ms, P>0.05).

Conclusion: Low gestational age, extremely-LBW, very-LBW as well as the respiratory and neurological complications before or after birth could be considered as possible risk factors for auditory maturation abnormalities. In contrast, the infant’s gender, head circumference at birth and APGAR score in 10th minute of life do not seem to affect the maturation of auditory system.

Disclosure: No potential conflict stated.

The safety of antithrombotic therapy in paediatric Cardioembolic Arterial Ischemic Stroke

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Background: Congenital heart disease is a major cause of cardioembolic arterial ischemic stroke (CE-AIS) occurring in 25% of neonates and children. Hemorrhagic transformation (HT) rates in pediatric CE-AIS are largely unknown and adult safety data are of limited applicability.

Primary Study Aim: To determine the safety of anticoagulant treatment in infants and children with CE-AIS.

Methods: Single-center, retrospective analysis of a prospectively enrolled cohort of neonates and children with radiologically-confirmed CE-AIS from 2003 – 2017. Clinical features examined included details of cardiac anatomy and type, dose, intensity and duration of antithrombotic therapy. Radiological features examined included CE-AIS location, size and number of infarcts and hemorrhagic transformation subtype according to the European Cooperative Acute Stroke Study (ECASS). Clinical outcome was measured by the paediatric stroke outcome measure (PSOM).

Results: Ninety-three children met inclusion criteria [male 52 (55.9%); neonates 24 (25.8%); median age 0.44 (0.10 – 4.22)]. Cardiac diagnosis included 57 (61.3%) cyanotic heart disease, 14 (15.1%) acyanotic heart disease, 14 (15.1%) cardiomyopathy and 8 (8.6%) other. HT occurred in 30 of 93 children (32.3%), 6 (20.0%) of whom were symptomatic. Hemorrhage classification was HI1 in 11, HI2 in 12, PH1 in 6 and PH2 in 1. Mean total PSOM scores were different in those with and without HT (2.2 ± 2.3 vs. 1.2 ± 1.7; p=0.0463) at follow-up.

Conclusion: This study will provide crucial safety data that will translate into better care for infants and children with CE-AIS.

Disclosure: No potential conflict stated.
A rare cause of acute Vertigo
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Introduction: Ischaemic stroke is rare in paediatric patients but is increasingly recognized as a significant cause of morbidity and mortality. The etiological clarification of paediatric stroke plays an important role, since treatment directed at the primary cause may prevent event recurrence. We present a rare case of posterior circulation stroke with acute vertigo, presumably caused by a right-to-left shunting due to an isolated patent foramen ovale (PFO).

Clinical Report: A 14-year-old boy was admitted in the local hospital with a 4-hour history of sudden vertigo with severe vomiting, after defecating. His personal and family history were unremarkable. Neurological examination revealed a direction changing gaze-evoked nystagmus and a negative head-impulse test, suggesting a central vertigo. Stance and gait were impossible to evaluate due to severe symptoms. Brain-CT scan revealed an ischemic lesion in right posterior-inferior cerebellar artery territory, without significant oedema or haemorrhagic transformation. Brain-MRI and angio-MRI didn’t show any vasculopathy. Transthoracic echocardiogram was normal. Laboratory workup excluded autoimmune and thrombotic disease. Contrast-enhanced transcranial Doppler (c-TCD) showed early high-intensity transient signals with a shower pattern only during Valsalva manoeuvre, indicating a major right-to-left shunt. Cardiac investigation was then completed with transoesophageal echocardiography revealing a PFO, which was closed percutaneously. Although no obvious peripheral venous thrombosis was documented, there was a previously unreported episode of asymmetric calf pain.

Conclusion: In this case, the sudden onset of symptoms and the alterations during c-TCD, both after Valsalva, pointed to a PFO-related embolism leading to the decision of PFO closure. Recent guidelines propose PFO closure in young adults with high risk of paradoxical embolism. However, the role of an isolated PFO in childhood stroke remains unclear and the efficacy of its closure is still controversial.

Disclosure: No potential conflict stated.

Paediatric Migraine in the central region of Portugal: a primary health care–based study
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Objective: To characterize a pediatric population with a diagnosis of migraine, collecting demographic, clinical and therapeutic data, starting from the information contained in the registries of General Practitioners (GP) working in different Primary Care Units (PCU), in central Portugal.

Materials and Methods: During the first trimester of 2018, a sample of 117 individuals aged less than 18 years (from eleven PCU) with the diagnosis of migraine encoded in the informatics system of those units, was recruited. As they attended medical observations, they were interviewed according to a pre-defined script based on the International Classification of Headache Disorders (ICHD) and medical records supplemented the information collected. A descriptive analysis of the collected variables was driven.

Results: According to GP records, the estimated prevalence of pediatric migraine was 0.35% in the population served by the participating centres. It occurred mostly in females. The time elapsed between the onset of symptoms and the diagnosis had a median of 1.3 years (interquartile range 0-3 years). Only 22.2% used prophylactic drug therapy, mostly prescribed by pediatric neurologists, and 69.2% were adequately treated, considering the pharmacological class in use and 53.8% considering drugs’ dosage. The use of abortive therapy was verified in 97.2% of the cases. The most commonly used pharmacological classes were simple analgesics (65.7%) and non-steroidal anti-inflammatory drugs (50.0%). Only a minority reported using triptans (2.9%). Self-medication was reported in 12.5% of the cases. Non-pharmacological therapy was used by 66.7% of patients.

Discussion: This study was the first attempt to characterize the epidemiology of pediatric migraine in our geographic region. It still remains unrecognized and that there is a significant delay in diagnosing these patients. Optimizing clinical intervention on pediatric migraine is imperative.

Disclosure: No potential conflict stated.
**P01-13**

**Moyamoya syndrome in a child with Sickle Cell Anaemia: a cause of the rare event of childhood stroke**

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**Introduction:** Moyamoya syndrome is a rare condition in which blood vessels involved in the Circle of Willis progressively narrow in the presence of associated risks factors such as haematological disorders and its diagnosis is based on imaging angiography. Although it mostly affects Asians, it can also occur in other populations (Female predominance).

**Methods:** We report a case of a 5-year-old female child who was admitted at our hospital with complaints of fever (38.2°C), pain in tibiotalar joints and torso, fatigue and paleness.

**Results:** The child had a history of sickle thalassemia (β–S heterozygote), diagnosed during previous hospitalization (due to gastroenteritis). Clinical examination revealed arthralgia, icteric sclera, paleness and multiple Café au lait spots (under investigation for NF type 1). Blood results: WBC: 14,7x10⁹/L, CRP: 155mg/L). It was treated with IV Cefotaxime due to history of sickle thalassemia and on suspicion of bacteremia. Fundoscopy and Tibiotalar/Chest Xray did not display any pathological findings. During the first 24 hours of hospitalization progressive disturbance of gait and posture was observed. It was then transmitted to the closest tertiary hospital for further imaging investigation. Its brain MRI and MR angiography demonstrated significant thickening of arachnoid space on left hemisphere, severe occlusion of left middle cerebral artery (mild on right side), with presence of multiple prominent leptomeningeal collaterals compatible with MoyaMoya syndrome.

**Conclusion:** This case highlights that MoyaMoya syndrome is an important diagnosis to consider in children presenting with stroke symptoms especially in those with underlying blood disorder. The medical data around this condition is still limited and its optimal management continues to be debated, resulting in poor prognosis while careful long-term follow up is essential to prevent further stroke events.

**Disclosure:** No potential conflict stated.

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**P01-14**

**Transient Cerebral Arteriopathy in children and adolescents, features of clinical manifestations and course**

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**Introduction:** The problem of a pediatric stroke has become relevant in recent decades. More than 50% of children with ischemic stroke are diagnosed with arteriopathy.

**Aim:** Assessment of the clinical features and course of arteriopathy in children diagnosed with ischemic stroke.

**Materials:** 61 patients with ischemic stroke, who were treated on the basis of the Moscow City Stroke Children’s Center from 2013 to 2018. Boys vs girls – 37 vs 24, the average age 7.8 years. The observation period was from 16 months to 5 years.

**Methods:** Clinical, laboratory, radiology.

**Results:** In 35 children out of 61 were diagnosed the arteriopathy. 24/31 showed signs of unilateral focal stenosis of the distal internal carotid artery (ICA) and / or the middle cerebral artery (CMA) and / or the anterior cerebral artery (PMA) with / without occlusion, The severity of stroke by PedNIHSS in average 7,3. CT was made CT angiography 28 patients (from 7 days to 4 months from the onset of of stroke (1 patient twice), 8 - direct catheter angiography. Arteriopathies in patients with FCA were divided: vasculitis- 2, progressive arteriopathy -2, dissec- tion-1, transient cerebral arteriopathy (TCA)- 19. Dynamic MRI study (from 3 to 6 months) showed: a complete restoration of blood flow-3; increase of stenosis -4; decrease of stenosis - 9; without dynamics relatively acute period -3. MR-angiography after 9-12 months: full restoration of blood flow-9; reduction of stenosis (incomplete recovery) -7.

**Conclusion:** Modern methods of neuroimaging have significantly improved the diagnosis of childhood stroke, clarifying the nature and extent of cerebral vascular lesions, including arteriopathy, which is very important in determining the management of children and adolescents.

**Disclosure:** No potential conflict stated.
P01-15

Thrombolysis in children and adolescents with Ischemic Stroke. Experience of the Paediatric Stroke Centre of Moscow

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**Introduction:** Thrombolysis is one of the effective methods of treating ischemic stroke in adults, but the extrapolation of the method to children is impossible because of the age-related features of the hemostasis system and metabolism in children.

**Aim:** Evaluate the efficacy and safety of thrombolysis in children with ischemic stroke.

**Materials:** Six children with ischemic stroke. Criteria recommended by Thrombolysis in Pediatric Stroke were taken as criteria for selecting patients for thrombolysis. Six children from 3.5 to 16 years old (average age -10.3g) were included.

**Methods:** Clinical, laboratory, radiology.

**Results:** Patients with stroke had: thrombophilia in two, autoimmune hemolytic anemia, polyangiitis, influenza, transient nocturnal hemoglobinuria with aplastic anemia. The severity of stroke was evaluated the PedNIHSS scale and ranged from 9 to 24 points (average -15.8b). The stroke was confirmed by MRI-angiography. The time of thrombolysis: from 4 to 10 hours (average 6.3 hours). None of the patients had any complications in the form of intracranial hemorrhage. Evaluation of the clinical efficacy of thrombolysis was carried out after 6-8 hours. In three cases, the effect was pronounced: the change on the PedNIHSS scale: from 9 to 2b, from 22 to 8, from 9 to 4; in three - ineffective: 1 - with the flu, one with progressive arteriopathy, one - with polyangiitis. A child with polyangiitis and stroke in the basilar artery was thromboextracted after ineffective thrombolysis.

**Conclusion:** We need standardized inclusion / exclusion criteria, protocols for the introduction of tissue plasminogen activator and dose selection, standardized approaches to assessing the effects of the treatment. The effectiveness of thrombolysis may depend on the etiology of stroke in children.

**Disclosure:** No potential conflict stated.

P01-16

Prolonged seizures in children - Scottish population based study

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**Background:** Prolonged seizures (PS) in children carry significant risk of morbidity and mortality. Previous work has predominantly focused on status epilepticus ≥30min and a new ILAE definition has been produced following evidence that seizures ≥5min are associated with negative outcomes. We report the prevalence, and outcome of PS in children.

**Methods:** All children presented with PS between 2011-2017 from a Scottish Children’s hospital were identified. Data was collated from electronic health records; including patient demographics, clinical characteristics, acute seizure management and outcomes.

**Results:** There were 666 children (1234 seizure episodes), M:F (56.9: 43.1). These accounted for 0.38% (95% CI (0.34-0.42%)) of A+E admissions. Median age is 3.65 years, median seizure duration of 10 minutes. 45% needed learning support, 38.6% had established epilepsy diagnosis. Only 14% of the children were on phototherapy, 21% monotherapy and others were not established on regular treatment.

There was a lower likelihood of hospital admission where buccal midazolam was administered. 40% were on emergency medication plan and buccal midazolam was the commonest rescue medication. 70% needed hospital admission and 5.3% were admitted to paediatric intensive care unit.

**Conclusions:** Adverse outcomes have decreased and the use of buccal midazolam is promising. Identifying high-risk groups provides opportunity for early intervention. This data forms the basis for extensive evaluation of acute seizure management and monitoring long-term outcomes.

**Disclosure:** No potential conflict stated.
External compression of the internal carotid artery by the hyoid bone – A rare cause of Stroke

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Introduction: When investigating stroke in the young patient, a wide spectrum of possibilities should be considered. We present a patient with a partial anterior circulation stroke of the left carotid artery, presumably caused by a chronic compression of the internal carotid artery (ICA) by the hyoid bone.

Case-report: A 17-year old boy with personal history of episodic migraine presented in the emergency department with sudden onset of dysarthria and right hand numbness in the previous day. Of note, he had a recent football practice. Neurological examination revealed dysarthria, central right facial palsy and right upper limb hyposthesia. Retrospectively, a right-hand transient numbness was noted one week earlier, also after a football practice. Brain-MRI revealed a left acute frontal and lenticular ischemic lesion, and two other smaller chronic lesions in left insula, operculum and parietal-lobe. A work-up for stroke did not find any cardioembolic or atherosclerotic source, and an extensive systemic study was unremarkable. Angio-CT scan depicted a close contact from the greater horn of the hyoid bone with the left ICA, with an hypopattenuating irregularity consistent with a small thrombus. Cervical ecdodoppler showed a dynamic compression of the hyoid bone in the left ICA, without relevant alterations in transcranial doppler. He was on anticoagulation until showed resolution of thrombus, and is currently on antiplatelet and statin therapy. Surgical cervical exploration is being considered for definitive treatment.

Conclusion: We present a rare cause of ischemic stroke, which could be the cause of recurrent events if left untreated. An artery-to-artery embolism is the proposed mechanism for the ischemic lesions.

Disclosure: No potential conflict stated.

Clinico-radiological aspects and outcomes in symptomatic and incidentally diagnosed paediatric Moyamoya

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Objective: To describe characteristics of children with moyamoya disease and moyamoya syndrome and investigate the role of underlying genetic condition in diagnosis and disease management.

Methods: Retrospective review of medical records of children with a new diagnosis of moyamoya from the past 15 years was performed. Relevant demographic, clinical and radiologic data were recorded.

Results: 33 children were included. The average patient age was 7 years and the male-to-female ratio was 1.5:1. 15 children presented with arterial ischaemic stroke (AIS) and nine with transient ischaemic attacks (TIAs). 9 children who presented with ischaemic symptoms had an underlying genetic diagnosis (1 NF1, 4 Down Syndrome, 1 sickle cell disease, 1 Robinow syndrome, 1 cytochrome oxidase deficiency, 1 ACTA2 mutation). 5 children who all had an underlying genetic diagnosis (3 NF1, 1 sickle cell disease, 1 ABCC6 mutation) were asymptomatic at diagnosis and Moyamoya was an incidental finding on neuroimaging carried out for various reasons. 19 children had bilateral and 8 had unilateral arteriopathy; 8 patients had posterior circulation involvement. Surgical revascularization was undertaken in 25 children with recurrent clinical symptoms and/or evidence of progressive arteriopathy. 4 patients had recurrence of symptoms after surgery; 2 children had a TIA and 2 had AIS (one in the first week post-surgery which was fatal).

Conclusion: The findings revealed that a significant number of children with underlying genetic condition were diagnosed incidentally. New imaging techniques and signs (ASL sequences, IVY sign) in addition to standard imaging (MRA/CTA) may help identify the cases that would benefit from early neurosurgical intervention to minimize stroke morbidity.

Disclosure: No potential conflict stated.
P01-19

ABCC6 as an emerging cause of paediatric Stroke: an illustrative case and literature review

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Introduction: ABCC6 mutation is responsible for Pseudoxanthoma Elasticum (PXE), consisting in tissue ectopic calcification (mainly skin, eye and medium vessels). The phenotypic expression may range from mild to severe involvement of vessels with subsequent stenosis (Generalized Arterial Calcification of Infancy). Severe forms with paediatric onset mainly manifest with coronary and heart involvement, sometimes leading to death.

Methods: We extensively searched the literature for cases of stroke in children with ABCC6 gene mutation, and we described a new case.

Results: Stroke in patients with ABCC6 mutation is mostly described in adulthood. Only 4 paediatric cases have been published: age range was from birth to 5 years; in all internal carotid stenosis/calcification was described; in one case dual antiaggregant therapy was started and in another one bisphosphonate treatment was tried. We report a previously healthy 4-month-old boy who presented with left hemispheric stroke; 2 weeks later, another ischaemic event, interesting the right posterior cerebral territory. Neuroimaging revealed bilateral carotid syphon stenosis and temporal arteries calcification and a compensating arterial network at basilar apex. Genetic analysis revealed two heterozygous ABCC6 mutations. At 3-month follow-up, the boy has not experienced any further event, and he has microcephaly and psychomotor delay. Systemic vessels evaluation only revealed mesenteric and femoral arterial involvement.

Conclusion: ABCC6 mutation can lead to progressive arterial occlusion and calcification. Although infrequently described, stroke can be the first presentation. We suggest that in paediatric stroke, especially when associated with vessels calcification and collateral networks, genetic analysis for ABCC6 mutation should be considered. Important implications concern management, therapy and prognosis.

Disclosure: No potential conflict stated.

P01-20

Two children with Cerebral Palsy and Epilepsy due to a mutation in the COL4A1 gene

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Introduction: Mutations in the COL4A1 gene can cause a wide spectrum of malformations in the brain, the eye and the kidney. The gene encodes for the alpha 1 chain of the collagen IV alpha1,1,2 triple helix. Collagen type IV is an important component of the basement membrane. Abnormalities in collagen IV in the basement membrane surrounding the vessels can lead to hemorrhages but disturbance of the collagen network leads also to a disturbance of cell proliferation and cell migration.

Methods: We describe two children, born after an uneventful pregnancy, who developed a clinical picture of cerebral palsy and epilepsy. Brain imaging of the two patients is very different but both are caused by a (different) mutation in the COL4A1 gene. Of one of the children the father is carrying the same mutation but he is asymptomatic.

Conclusion: In children with unexpected development of cerebral palsy and epilepsy and brain MRI suggestive of a prenatal vascular accident or proliferation/migration disorder, mutations in the COL4A1 gene should be tested. Detecting parental carriers can have important clinical consequences.

Disclosure: No potential conflict stated.
**About some aspects of Hypoxic-Ischemic Encephalopathy among newborns in the Republic of Armenia**

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**Introduction:** The study of literature data shows that hypoxic-ischemic encephalopathy (HIE) in newborns is still topical. Studies on this issue are few in the Republic of Armenia, they are also incomplete, covering only some of its aspects.

**Methods:** Common statistical methods were used to study several aspects of uptake about the HIE in newborns, its specific weight among the children’s uptake of 2014-2018 years. The absolute majority of patients of this pathology are hospitalized in “Muratsan” University Hospital as a specialized neonatology center.

**Results:** The analysis shows that 34,311 children were hospitalized in “Muratsan” University Hospital in 2014-2018 years, of which newborns were 13225 (38.6%), among which HIE was diagnosed in 1472 (11.1%) patients. The results of the treatment of newborn patients in “Muratsan” University Hospital, during the period of 2014-2018 (with respect to 1000 people) shows that:
- the majority of patients have recovered, the percentage of which was 75.97-56.78%, while it’s slowing down to 56.78% in 2018,
- the “improvement” category has a conjugation of 18.59% to 39.72%, which is a fairly good indicator,
- the category of “deterioration” does not play a particular role,
- the category of “unchanged” is of no significance; the variations of the proportions are not essential
- the proportion of the category “death” from 2014 to 2018 dropped from 4.25% to 2.61%, i.e 1.6 times, which is a rather serious indicator.

**Conclusion:** It can be concluded that the problems of HIE in newborns should have their principal role and place in children’s and neonatal pathology in the healthcare system of the Republic of Armenia.

**Disclosure:** No potential conflict stated.

**Neurological presentations of Egyptian children with Silvery Hair Syndrome: single centre experience**

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**Introduction:** “Silvery hair” is a clinical manifestation of a group of rare autosomal recessive disorders including Chediak-Higashi syndrome (CHS) and Griscelli syndrome (GS). They share many common features like pigmentary dilution, silvery hair, neurological manifestations, and immunological defects. Neurological presentations are diverse, non-specific and can be classified either primary or secondary to Hemophagocytic Lymphohistiocytosis (HLH). Our aim is to highlight the diverse neurological presentations and outcome of children with silvery hair syndrome.

**Methods:** In this prospective study conducted at Alexandria University Children’s Hospital over a 4-year-period, we included all children suspected to have a silvery hair syndrome, confirmed by an abnormal trichogram and/or genetic testing. All patients were subjected to clinical examination, imaging and CSF analysis. They were classified to have either “primary” or “secondary” central nervous system (CNS) affection.

**Results:** Eleven patients with Silvery hair have been included; 8 females and 3 males. Their age at first presentation ranged from 1 week to 14 years with a median of 2.5 years. Three (27.3%) patients had a confirmed genetic disease of GS type-2, six (54.5%) had CHS and two (18.2%) patients revealed abnormal trichogram with inconclusive genetic testing. Nine (81.8%) patients had CNS affection; two patients as “primary” while seven patients had “secondary” CNS affection, referred to as “CNS-HLH”. Neurological manifestations were the initial presenting complaint in four (36.3%) patients, while two (18.2%) patients presented only due to their silvery hair, and five (45.5%) with systemic manifestations of HLH.

**Conclusion:** Neurological manifestations are common among children with silvery hair syndrome, and might be the presenting features. Recognizing the syndrome is very important for proper management and anticipation of the associated neurological complications.

**Disclosure:** No potential conflict stated.
Epilepsy and Neurofibromatosis Type 1 in children: epidemiological and clinical study in Croatian population

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Introduction: Neurofibromatosis type 1 (NF1) is the most common autosomal dominant neurocutaneous disorder. The prevalence of epileptic seizures in the general population of NF1 patients varies from 6% to 15.8%, and in pediatric population with NF1 is 3.5% - 6.7%.

Objective: To determine the frequency, clinical features and course of epileptic seizures in children with NF1.

Patients and Methods: The analysis of Croatian Neurofibromatosis Association database for period 1984–2018 included demographic and electroclinical features, neuroimaging findings as well as the course of epileptic seizures in population of 431 patients with NF1 (0-18 years).

Key Results: Between 431 children with NF1 22 (15,1%) had at least one unprovoked epileptic seizure and one girl had seizures associated with lethal meningoencephalitis. From recurrent epileptic seizures suffered 18/431 children (4.2%). The mean age at the first seizure was 6.4 years. The most common forms of seizures (15/22, 68%) were: focal with motor onset (aware/impaired awareness), and focal with progression to atrophic changes and 2 patients had hypertensive hydrocephalus. In 4 patients brain CT/MRI revealed brain tumors or other CNS complications. In 6 children, epilepsy was associated to brain tumors: 4 optical gliomas and 2 hemispheric tumors. In 4 patients brain CT/MRI revealed atrophic changes and 2 patients had hypertensive hydrocephalus. During the follow-up complete control of seizures achieved 16/18 patients. Cognitive difficulties were present in 10/18 NF1 patients with epilepsy.

Conclusion: Compared to the general population, epilepsy in children with NF1 is more common. The seizures are predominantly focal, mostly well controlled and associated to brain tumors or other CNS complications.

Disclosure: No potential conflict stated.

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Quantitative measurement of cerebrovascular reactivity and executive function in children with Moyamoya Disease

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Objective: Moyamoya is an arteriopathy of childhood, caused by progressive steno-occlusion of the arteries at the base of the brain, and cognitive difficulties are recognized even in the absence of stroke. Blood oxygen level-dependent (BOLD) MR imaging assessment of cerebrovascular reactivity (CVR), is a clinically feasible technique that allows for the prediction of ischaemic brain injury. The objective of our study was to quantitatively investigate the association between positive and negative measures of breath-hold (BH) hypercapnic challenge BOLD-MRI CVR (BH-CVR) and executive function (EF).

Methods: Twenty-one children diagnosed with Moyamoya between 2000 to 2018, over 7 years age had BH-CVR studies and studies of EF as measured by the Behavior Rating Inventory of Executive Function. After excluding post-revascularization surgery cases and technically inadequate (excessive head motion) studies 10 cases (4 males; 12.3±3.1 years) were included for the final analysis. The CVR estimates were computed and correlated with EF scores, and regression analysis performed to assess whether negative or positive CVR estimates were predictive of EF outcomes.

Results: The results demonstrated that patients’ general EF score was significantly correlated with the mean magnitude of positive CVR in whole brain (r=-0.911, p<0.01), mean magnitude of positive CVR in white matter (r=-0.913, p<0.01), the count of negative CVR voxels in white matter (r=0.793, p<0.01), and the mean magnitude of positive and negative combined CVR in white matter (r=-0.975, p<0.01). The results of the regression indicated the three predictors of white matter CVR estimates explained 77.6% of the variance (R2=0.78, F (3,10)=11.55, p<0.001).

Conclusion: These results suggested that the CVR estimates can enable cognitive prognostication in children with Moyamoya and the white matter indices may be a useful indicator for EF decline in this disease.
POSTER PRESENTATIONS > POSTER SESSION 1
Basic science, Cerebrovascular disorders, Epidemiology and follow-up, Fetal Neurology

‖ P01-25 ‖

Same-day split-bolus Acetazolamide challenge brain perfusion SPECT in paediatric neurovascular practice

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Introduction: Acetazolamide challenge brain perfusion SPECT is used in the evaluation of patients with steno-occlusive cerebrovascular disorders to identify areas of reduced cerebral perfusion or impaired autoregulatory vasodilatation. This technique uses a radioisotope scan comparing uptake at rest (basal) with uptake following a vasodilatory stimulus induced by intravenous acetazolamide. Historically, this has been performed using two scans on separate days to allow dissipation of the radioisotope, necessitating twice the scanning time and of the radioisotope, necessitating twice the scanning time and in young patients two general anaesthetics. We describe the implementation of a same-day split-bolus acetazolamide SPECT in paediatric patients at a regional paediatric neurovascular centre.

Methods: Retrospective service evaluation of children attending over a 2 year period for same-day split-bolus acetazolamide SPECT scans including review of case notes and outcomes of regional neurovascular multidisciplinary discussions.

Results: In 2 years since implementation, 7 patients have undergone same-day split-bolus acetazolamide SPECT scans at a median age of 6 years (interquartile range 4–12 years). 5 patients required general anaesthesia for the procedure. 1 procedure was unsuccessful due to IV line failure during the procedure not allowing acetazolamide administration. 5 patients had underlying moyamoya disease, 1 had fibromuscular dysplasia and 1 had unilateral focal cerebral arteriopathy. In 6 patients the scan demonstrated significant abnormalities and 4 had revascularisation surgery (3 encephal-duro-arterio-synangiosis, 1 multiple burr-holes).

Conclusion: We describe successful implementation of same-day split-dose acetazolamide SPECT in a paediatric population including general anaesthetic. This technique allows efficient use of resources, a reduction in the risk of repeated general anaesthetics, and minimises variability that may arise through either natural cerebrovascular changes or scanning equipment across several days.

Disclosure: No potential conflict stated.
Moyamoya Syndrome as a rare vasculopathy of the Central Nervous System in children with Neurofibromatosis Type 1

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Introduction: Neurofibromatosis type 1 (NF1) is a multisystem disease affecting the skin, the central nervous system and the bones. Vasculopathy, within NF1, is a significant but insufficiently recognized complication of the disease. The prevalence of Moyamoya syndrome (MMS) in patients with NF1 is estimated at 0.6%. MMS is linked to genetic factors: an abnormality was found on chromosome 17q25.2 close to the gene responsible for NF1 (17q11.2).

Case Presentation: We present two young girls. One was born as a twin who in infancy had multiple cafe-au-lait spots without other signs of NF1. At the age of 18 months right-sided hemiparesis was noticed. MRI of the brain showed bilateral optic nerve glioma, treated by chemotherapy. At the age of 5.5 years follow-up neuroradiology led to suspicion of MMS. Digital subtraction angiography (DSA) showed left-side occlusion of the middle cerebral artery (MCA), with many collaterals. The other girl was admitted to hospital at the age of 3.5 years for lethargy, dysarthria and ataxia, with suspected intoxication. In the hospital left-side transitory hemi-insufficiency was found. Physical examination revealed many cafe-au-lait spots and inguinal freckling. Given the positive family history, the criteria were met for NF1. TCCD showed pathological cerebrovascular circulation in the area of the left MCA and anterior (ACA). Magnetic angiography showed left pial angiomatosis, and a hypoplastic spheroidal and opercular segment of the left MCA, with many collaterals. DSA showed bilateral stenosis of the internal carotid artery. After a PET-CT Diamox test in both, Encephaloduroarteriosynangiosis resulted in recovery without additional symptoms or stroke.

Conclusion: Vascularopathy in NF1 is a potentially serious and under-appreciated complication. MRA screening and assessment of cerebral circulation by Doppler could help in the early detection of vascular lesions in asymptomatic patients with NF1.

Disclosure: No potential conflict stated.
**P01-29**

**Predictors of outcome of Arterial Ischemic Stroke in children**

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**Introduction:** Stroke ranks among the top 10 causes of death in children. In more than half of the surviving children who had a stroke, the risk of motor, behavioral and cognitive disorders and epilepsy results in major long-term personal, family and social consequences. Mortality rate of pediatric arterial ischemic stroke (AIS) ranges from 10-20% and may be higher in recurrent stroke. The aim of the study is to evaluate sensorimotor outcome of children with AIS and explore predictive factors that affect poor outcome.

**Patients and methods:** 50 patients (25 male/25 female) aged of 1 month to 17 years who were treated at M. Iashvili Children’s Central Hospital, with the onset of stroke from 2009 were included. Data were collected from hospital records included demographic and clinical characteristics, neurological impairments at onset, affected arteries, vascular distribution areas involved, possible causes and risk factors for stroke, presence of stroke recurrence and status at discharge. Neurologic deficit severity based on the scores of Pediatric Stroke Outcome Measure (PSOM) was assigned for each of the following 5 spheres: right sensorimotor and left sensorimotor (both including visual, hearing, motor and somatosensory function); language production; language comprehension; cognitive and behavioral performance.

**Results:** According to PSOM scores neurological outcome was favorable in 50% of patients (20 without and 5 with mild neurological deficits), and unfavorable in 50% with moderate to severe deficits.

**Conclusion:** The reported outcome after childhood stroke was variable with long-term neurological deficits or disability in half of the patients. Outcome was worse in patients with younger ages at stroke; stroke size, and combined cortical and subcortical involvement was associated with poor outcome.

**Disclosure:** No potential conflict stated.

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**P01-30**

**Epidemiological analysis of Febrile Seizure cases during 2018 in a general hospital of Central Macedonia, Greece**

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**Introduction:** Febrile seizures is the most common seizure disorder of childhood. It is very common in children under the age of 5 (Incidence= 5%). Most common age of appearance is 18 months old. In 80% of the cases the seizure is not complicated, and usually they appear in the first day of the febrile episode.

**Methods:** Retrospective analysis over a 12-month period (January 2018-January 2019) of inpatient files of all pediatric cases with febrile seizures. Categorization of them according to age of appearance, positive family history of seizure or epilepsy, temperature during the seizure etc. Statistical analysis of the results.

**Results:** 12 out of 400 hospitalized children in our clinic in one year were admitted due to febrile seizures. Median age was 32 months. None of those children had complicated seizures or needed to be transferred to a tertiary hospital. In 66,6% of the cases, seizures happened in the first 24 hours of the febrile episode. In 41,6% of the cases, positive family history of febrile seizure and in 16,6% of the cases positive family history of epilepsy was found. Most of the cases (58,3%), suffered from viral infection of the upper respiratory system. For most of the children (91,6%), the recorded episode was their first episode.

**Conclusion:** 3% of all the hospitalized children during 2018 presented febrile seizures’ episodes. However, no complications were noted and no further investigation was required in any of those children. In conclusion, febrile seizures constitute a benign febrile disorder of pre-school children, that is treated usually in our department.

**Disclosure:** No potential conflict stated.
**P01-31**

Multicystic Encephalomalacia in a twin: case report and review of the literature

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**Introduction:** Up to 20% of surviving cotwins in a monozygotic diamniotic (MCDA) twin pregnancy suffer brain insults following 2nd trimester in-utero demise of the other twin but pathologies may be diverse.

**Case report:** Mother was a healthy non-smoking primigravida with an MCDA twin pregnancy. Antenatal screening and growth scans were normal.

A baby girl was delivered at 32+0 weeks gestation by semi-elective Caesarean Section due to onset of spontaneous labour without rupture of membranes, following demise of twin 1 within 24 hours. With a birth weight of 1850g and head circumference of 30.4cm, the baby was born in good condition, not needing any resuscitation or further ventilator support. She was treated for suspected sepsis with antibiotics which were stopped following negative blood cultures at 48 hours.

The baby's initial haemoglobin was 102 g/L (normal: 140-220 g/L) with a high reticulocyte count (12.04%). Twin-to-twin transfusion or ABO incompatibility (mother’s blood group O+ and baby’s A+ but DAT negative) were considered. However, the baby was asymptomatic and remained stable without any intervention, establishing feeds well with an unremarkable Neonatal Unit stay.

Cranial ultrasound scan on day 30 (corrected 36 weeks gestation) showed bilateral periventricular cystic leukomalacia. An MRI brain scan reported extensive macrocystic, multicystic encephalomalacia with evidence of septation and some astrocytosis. Only a thin rim of periventricular white matter was visible. The basal ganglia, pituitary and optic chiasm were normal. The corpus callosum was present but reduced in bulk.

**Discussion:** Review of 75 literature cases of brain damage in MCDA twins revealed a variety of presumed vascular pathologies, including periventricular leukomalacia and venous hypertension, as well as arterial (presumed embolic) stroke as in the index case, suggesting multiple mechanisms for injury.

**Disclosure:** No potential conflict stated.

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**P01-32**

Characteristics, clinical features and prognosis of presumed Perinatal Stroke

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**Introduction:** The stroke in the newborn represents interactions among infant, maternal, and placental processes that existed the neonatal period. Presumed perinatal stroke refers to chronic infarcts, diagnosed in a delayed manner, that are presumed to have occurred in the perinatal period. These infants typically present with pathological early handedness or seizures, leading to brain imaging and the diagnosis of a remote infarction.

**Methods:** We retrospectively reviewed cases in Dr Sami Ulus Training and Research Hospital from January 2009 to January 2019. Of approximately 21 patients with neonatal or presumed perinatal stroke in our database. All cases had the history of a motor deficit in the first six months of life and the diagnosis of hemiplegic cerebral palsy.

**Results:** A total of 21 patients with 12 males (57.1%) and 9 females (42.8%) with a mean age of 8.3 were included in the study. 14 patients (66.6%) had motor problems as the main complaint at the first visit to clinic, 7 patients (33.3%) were referred after an epileptic seizure. 10 patients (47.6%) had epilepsy, all cases had focal epileptiform discharges in electroencephalogram, Cystic encephalomalacia was found in cranial MRI of 19 patients (90.4%). Seventeen patients (80%) had at least a positive thrombophilia risk factor. 10 patients (47.6%) were on aspirin and one patient (4.7%) on Clexan treatment.

**Conclusion:** We sought to characterize in detail the clinical history and to investigate cardiologic, hematologic and genetic risk factors. Identifying risk factors is important for the follow-up of these patients.

**Disclosure:** No potential conflict stated.
A paediatric case of bilateral Internal Carotid Arteries (ICA) Agenesis who presented with multiple cerebral infarctions

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Introduction: Agenesis of the internal carotid artery (ICA) is a rare congenital anomaly with a 0.01% of incidence. Although many of these cases remain asymptomatic due to sufficient collateral circulation, some may have serious symptoms. Here, we present a child who presented with multiple cerebral infarctions and was found to have bilateral ICA agenesis.

Methods: We retrospectively reviewed the medical record of the patient.

Results: A 9-year-old girl presented with acute onset vomiting and headache followed by drowsy mentality. Emergent magnetic resonance imaging (MRI) showed multifocal diffusion restrictions in left parietal cortex, bilateral centrum semiovale, and pons. Despite of supportive management with antibiotics and intravenous methylprednisolone, she experienced a focal clonic seizure at 6th day of hospitalization and follow-up MRI revealed marked increased extent of diffusion restriction lesions in the bilateral parieto-occipital lobes with gyral swelling and hemorrhage in left occipital lobe.

She was transferred to our hospital and neurologic examination at admission showed left side dominant quadriparesis, dysarthria, both side homonymous hemianopsia, right and vertical gaze palsy. Laboratory tests including metabolic and autoimmune profiles, mitochondrial gene sequencing were unremarkable. Brain MR Angiography and following direct cerebral angiography identified aplasia of bilateral ICA and focal narrowing at the distal basilar trunk.

At discharge, she showed gradual improvement of neurologic deficits with active rehabilitation and medication of low dose aspirin. Extra-intracranial arterial bypass (EIAB) surgery was done for prevention of further ischemic attacks.

Conclusion: Although agenesis of bilateral ICAs is not common, it should be differentiated one of the causes in cases of multiple cerebral infarctions in childhood.

Disclosure: No potential conflict stated.

Febrile Seizures: Scottish population based study

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Introduction: Febrile Seizures (FS) are one of the common neurological emergencies and can cause significant anxiety to parents. There are variations in management in different countries and no recent European data on FS. We aimed to calculate a population prevalence for Scotland, investigate demographic and seizure data and investigate the effects of these variables on recurrence. We also explored admission and investigations and these were necessary based on the good prognosis of FS.

Methods: This cohort study included all children (<6 years) presenting at the emergency department of the Royal Hospital for Sick Children in Edinburgh between January 2012- December 2015. A database of FS was constructed which included demographic data, seizure details, hospital admissions, investigations and follow up. Relationships between these variables were explored.

Results: 689 children (M:F 54.3%-45.7%) were diagnosed with FS (median duration 3 minutes) during the study period accounting for 0.7% emergency visits. Annual prevalence was 3.9 per 1000 for children aged 5 and under and 2.62% children had at least one FS by age 5. 86.5% of presentations were simple FS. The mean age for a first FS is 1.9 years. 40.1% of children had recurrent FS and younger (<1.9 years) children with first FS are more likely to have recurrent seizures (p<.001), receive emergency medication (p<.05), suffer from febrile status epilepticus (p<.05), be admitted to hospital (p<.001) and receive hospital follow up (p<.001). 72.6% of children were admitted and 11.0% of children received further investigations.

Conclusions: We report good short term outcome from our large cohort with majority of simple FS. Younger age is a risk factor for recurrence. This information would help in counseling parents and reduce anxiety surrounding FS.

Disclosure: No potential conflict stated.
Paediatric Stroke following Ergotamine: a case report

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Introduction: We report, to our knowledge, the first case of cerebral infarction associated with ergotamine use in a 7-year-old boy.

Methods and Results: The patient presented with acute left-sided weakness and double vision with a preceding history of acute-on-chronic headaches and lethargy, for which he had been prescribed Dihydroergotamine (2mg/ml) and given 15ml (30mg) in total. This represents a significant overdose as, although not licensed in the UK, Dihydroergotamine doses for children aged 6-9 years should not exceed a total maximum of 4.25mg (+/- 1mg) or a treatment-duration of 4 days. On examination, he had a left-sided hemiparesis alongside 4th, 5th, 6th and 7th cranial nerve palsies. MRI revealed bi-hemispheric white matter lesions localising to cerebral watershed zones, and the cerebellar hemisphere distributed in a parasagittal location (Figure 1).

Conclusions: Historically, ergotamine was the first-line agent in migraine therapy, but its use has become restricted to inpatient treatment-resistant migraine due to its side-effects, including peripheral arterial vasospasm (Demir et al., 2008; Tfelt-Hansen et al., 2000). However, the effect of ergotamine on cerebral blood flow (CBF) remains unclear, with studies reporting both reduced (Shenkin, 1951) and unchanged CBF (Hachinski et al., 1989). A single report has linked high dose, migraine-related ergotamine-use to cerebral infarction in a 50-year-old female (Lindboe et al., 1989). We believe that the combination of dehydration associated with the boy’s mild illness and the powerful vasoconstrictive effects of ergotamine (Tfelt-Hansen et al., 2000) resulted in a significant reduction in CBF and consequently cerebral infarction in our patient. We advocate that ergotamine should not be prescribed in children.

Disclosure: No potential conflict stated.

Improving the quality of life for children with Epilepsy and their caregivers in Greece: a meta-analysis of the first paediatric 24/7 epilepsy hotline (CEH) data

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Introduction: The aim of this study is to confirm and strengthen the CEH’s effectiveness in improving quality of life of the children with epilepsy and their caregivers, in relation to an earlier research, by performing a meta-analysis of CEH’s data.

Methods: A data analysis was performed on all collected call records using R language. Associations of hospitalization and successful management at home were assessed by ²-test. Correlations of the incoming number of calls with children’s ages and severity of epilepsy assessed by Pearson and Spearman types. Discriminant analysis and logistic regression used to identify the important classifiers in hospitalization and successful management at home.

Results: During 21 months study period, a total of 181 index calls were received, from 727 incoming calls. The most common epilepsy type was Primary Generalized (14.9%). Children’s ages were between 0.45 and <=5 years (40%) and 5 and <=11 years (40%). A total of 110 twice repeated calls were received (20%), while repeated calls were between 3-10 (40%). Most caregivers called to ask about first aid instructions in cases of emergency (16.3%) or less urgent epileptic crisis management (33.2%) and drug administration (30%). Hospitalization and successful management at home were significantly associated with first aid and less urgent epileptic crisis instructions, drug administration and other support (p-value<0.001). The number of incoming calls was significantly correlated with children’s ages (p-value<0.001) and severity of epilepsy (p-value<0.01). Among important classifiers in hospitalization and successful management at home were the number of incoming calls, severity of epilepsy, first aid instructions and other support (p-value<0.05).

Discussion: The results of the meta-analysis of the CEH’s data strongly confirm and strengthen its contribution in improving the patient’s management while avoiding unnecessary hospitalization.

Disclosure: No potential conflict stated.
Central Nervous System Vasculitis in a boy with Epstein–Barr virus–associated T/Natural Killer–Cell Lymphoproliferative Disorders: a case report

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Objective: Epstein–Barr virus–associated T/natural killer–cell lymphoproliferative disorders (EBV-T/NK-LPD) is a group of rare disorders resulting from EBV-infected T/NK-cell. It can develop broad clinical spectrum according to the immunologic status and viral load of host.

Methods: We described clinical and radiological presentation, laboratory results of a boy who developed central nervous system (CNS) vasculitis and myelopathy, which might be a neurologic symptom of EBV-T/NK-LPD.

Results: A 16-year-old boy came to our hospital due to necrotic skin lesion developing on the right shoulder. He had suffered from local skin reaction with fever after mosquito bite over 10 years. On the evaluation of the skin lesion, he suddenly developed left facial palsy. His brain magnetic resonance imaging (MRI) and magnetic resonance angiography (MRA) showed acute infarction on pons and middle cerebellar peduncle and irregularity on both anterior inferior cerebellar artery. On serologic test, total IgE level and anti-VCA IgG, anti-EA titer were elevated. The EBV DNA copy number from whole blood and cerebrospinal fluid (CSF) were elevated. Skin biopsy on the right side shoulder showed extranodal NK/T-cell lymphoma. According to the clinical features and laboratory findings, he was diagnosed as EBV-T/NK-LPD. He got treatment with chemotherapy and following hematopoietic stem cell transplantation, even though he developed recurrent infarction during the course of the treatment.

Conclusion: This case showed diagnostic challenging of neurologic symptom with EBV-T/NK-LPD. Neurologic symptom of EBV-T/NK-LPD is a rare, but the typical clinical spectrum of EBV-T/NK-LPD including severe mosquito bite allergy, extranodal NK/T-cell lymphoma can be an important basis for diagnosis.

Disclosure: No potential conflict stated.

Training programme for rescue treatment of seizures at school environment

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Introduction: Epilepsy affects 0.5–1% of children, more often those with mental delay, cerebral palsy and autism. Seizures consist the most often neurological disorder in childhood, with 4–10% of children presenting an epileptic episode until 16 years of age. Our purpose is to evaluate the effectiveness of training programme in recognizing and treating seizures at school.

Method: We developed a 4 hour training seminar in cooperation with health policy departments in Athens, focused on recognition and rescue treatment of seizures at school. The participants attended theoretical lectures, video-session, demonstration and practice in applying first aid medicines for seizures. A standardized questionnaire was used in order to evaluate the knowledge and practices of the participants and the effectiveness of the seminar. The questionnaire was filled in 3 phases: before the seminar, at the end of the seminar and 1 month later through mail. The 14 questions concerned demographics, theoretical knowledge in epilepsy, first aid in seizures and administration of the rescue medicines.

Results: In total, 837 teachers participated in the training programme, 524 female (62.6%), 313 (37.4%) of primary schools, 15.3 years (±6.99) of work experience. The total score before the seminar was 10.12 (±1.64) correct answers, that increased to 13.52 (±0.38) (p<0.001) right after the end of the training programme, and to 13.18 (±0.73) (p<0.001) one month later. The questions that demonstrated the greatest improvement in correct answers concerned the treatment of the epileptic event (p<0.001).

Conclusion: The training programme improved significantly the knowledge and skills of primary and high school teachers in recognizing and treating seizures. There is strong evidence that continuous training in neurologic emergencies at school within a law framework is effective and necessary.

Disclosure: No potential conflict stated.
Refractory infantile spasms in a boy with Down Syndrome and Koolen-De Vries Syndrome

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Introduction: Infantile spasms (IS) in Down syndrome usually respond well to established therapy. In case of refractory epilepsy additional etiology should be considered.

Methods: Case report

Results: A 6 month-old-boy with genetically confirmed Down syndrome, born as 1st child to healthy non-consanguinous parents after uneventful pregnancy, was admitted due to IS. Treatment with VGB, ACTH, then combination of antiepileptic drugs, due to refractory spasms and hypsarrhythmia was not efficient. Ketogenic diet and vagal nerve stimulation also did not work. A thorough diagnostic work up including metabolic and genetic investigations was unhelpful to understand this very drug resistant epilepsy. Head MRI showed wider liquor spaces, slight hypoplasia of the brain stem and leukopathy of the deep parietal white matter. Neurodevelopment was poor, with autistic features; slow growth, more than usually in patients with Down syndrome was noted. At the age of 8y repeated genetic analysis finally revealed a mutation in gene KANSL1, a frameshift variant c.1288_1289; p.Leu430Glufs*28, which is most likely the cause of the phenotypic characteristics of our patient.

Discussion and Conclusion: Koolen-de Vries syndrome (KDFS) is an autosomal dominant multisystem condition characterized by developmental delay, mild to moderate intellectual disability, hypotonia, epilepsy, characteristic facial features and congenital malformations of multiple organ systems. It is caused by genetic changes in KANSL1 gene which encodes a NSL complex involved in acetylation of histone 4. To our knowledge this is the first case of KDVS associated with Down syndrome and refractory infantile spasms. The patient’s phenotype probably results from the combination of the two genetic aberrations.

Disclosure: No potential conflict stated.

Co-existence of Type 1 Diabetes Mellitus and Periventricular Heterotopia in a child: a case report

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Objective: Type 1 diabetes mellitus is characterized by a chronic, progressive, and immune-mediated destruction of the insulin-producing beta-cells (b-cells) in the pancreatic islets of Langerhans. Heterotopias are malformations of cortical development characterized by the presence of normal brain cells in abnormal positions.

Methods: A 8-year-old boy presented with partial onset of secondarily generalized seizures. On history, the patient was followed by diabetes mellitus for two years in another hospital. On examination, vital signs, physical examination and neurological examination were normal.

Results: Interictal electroencephalography showed epileptiform abnormalities right temporal regions. Magnetic resonance imaging of the brain revealed heterotopia in posterior horn of the right lateral ventricle. Stanford-Binet test was performed and mild intellectual disability was detected.

Conclusion: We found a structural abnormality in a diabetic patient with focal seizure. Epilepsy can be a feature of diabetic patients. However, seizures should not be considered to be due solely to metabolic disorders of diabetes.

Disclosure: No potential conflict stated.
**P02-03**

**Whole Exome Sequencing (WES) limitations in diagnosis of early Infantile Encephalopathy**

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**Objective/Methods:** To report the case of a non-syndromic neonate with seizures whose WES confirmed multiple possibly pathogenic genetic changes for early infantile epileptic encephalopathy.

**Results:** A newborn male was admitted to the neonatal ICU due to severe hypertonia and repetitive jerky movements of four limbs since birth. Full-term delivery by caesarean section due to polyhydramnios. Increased fetal movements. No family history of seizures, no consanguinity either. Normal karyotype. Normal intrauterine growth and no cardiorespiratory support at birth. Soon after delivery, multiple massive repetitive myoclonias of limbs, eye blinking and facial clonic seizures that could not be stopped by restraint, coupled in some cases with changes in heart and respiratory rate were noticed. Negative infection screening. Serum glucose, electrolyte levels and metabolic screening were also normal. Neuroimaging excluded cerebral malformations and showed non-specific, bilateral, signal abnormalities in the basal ganglia. Electroencephalogram showed burst-suppression pattern. Seizures were poorly controlled despite multiple antiepileptic drugs trials. With the suspicion of vitamin dependent seizures, pyridoxine, leucovorin and biotin were also given. Despite anti-convulsive therapy, seizures remained only partially controlled and at four months of age, the infant was extremely hypertonic, fed by nasogastric tube, logging developmental milestones. WES revealed homozygous GRIN1 and TRAK1 variants and heterozygous SCN8A variant as well.

**Conclusion:** Homozygous GRIN1 and TRAK1 mutations or heterozygous SCN8A mutations can all be responsible for early infantile encephalopathy and have severe consequences in neurodevelopment very early in life. Additional genetic testing of parents is mandatory in order to clear up the clinically significant mutated gene(s) and give a solid genetic advice to this family.

**Disclosure:** No potential conflict stated.

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**P02-04**

**The clinical difference between infants with PRRT2-Positive and infants with PRRT2-Negative Cluster Epilepsy**

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**Background:** Self-limited (familial) infantile epilepsy (S(F)IE), formerly known as benign (familial) infantile convulsions (B(F)IC), is an infantile cluster epilepsy with in rule a complete recovery. This form of epilepsy is most often caused by mutations in PRRT2-gene (OMIM605751).

**Aim:** To describe the clinical difference between infants with PRRT2-positive and infants with PRRT2-negative cluster epilepsy.

**Methods:** We retrospectively revised all patients, seen between 2000 and 2018 in one university center, who presented with infantile clustered seizures and in whom genetic testing was available. We described and compared the clinical aspects of patients who were PRRT2-positive and PRRT2-negative.

**Results:** Twenty-three patients among 21 families were collected. In 12 individuals a PRRT2 mutation or deletion was identified. In 5 individuals another causal gene mutation was identified: PCDH19 (3 patients), KCNQ2 (1 patient), and ATP1A3 mutation (1 patient). PRRT2-positive patients had a lower age of seizure onset, higher family occurrence of infantile seizures, lower cluster frequency and were faster seizure free compared with PRRT2-negative patients. No notable difference was seen in mean duration of the longest cluster and for the semiology of the first seizures. PRRT2-negative patients suffered more frequently from seizures at an older age, focal to bilateral tonic-clonic seizures and difficult-to-treat seizures. There was no difference in MRI-findings and the presence of a neurodevelopmental delay.

**Conclusion:** Based on the first cluster of seizures a differentiation between PRRT2-positive and PRRT2-negative patients cannot be made. However, if during follow-up the clusters are atypical and/or if the seizures continue above one year, a non-PRRT2 mutation is more likely. Rapid diagnosis of the causal gene mutation can guide the clinicians in their therapeutic strategies and give a better idea of the prognosis of this epilepsy.

**Disclosure:** No potential conflict stated.
POSTER PRESENTATIONS > POSTER SESSION 2
Epilepsy: diagnosis and investigations

P02-05

Muscarinic Acetylcholine receptor M1 mutation causing early Infantile Epileptic Encephalopathy

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Introduction: Mutations in several potassium channel subtypes and in the voltage-gated potassium channel modulator PLCB1 have been associated with early infantile epileptic encephalopathies. Phospholipase C acts downstream of the M1 muscarinic metabotropic receptor, a G protein-coupled receptor whose activation results in slow excitatory postsynaptic potentials and decreased potassium conductance.

Methods and Results: In a young girl with early-onset refractory epilepsy, severe disability and progressive cerebral and cerebellar atrophy, trio-based whole exome sequencing analysis uncovered a de novo missense variant in CHRM1, encoding the muscarinic M1 receptor. Functional analyses proved that the p.P380L variant caused aberrant Golgi receptor glycosylation and hence impaired cellular trafficking, while it did not affect protein oligomerisation. In addition, the mutated receptor showed defective activation of intracellular signalling pathways, including cAMP generation and inositol triphosphate-dependent intracellular calcium release. Exome re-analysis of a further 80 trios with early epileptic encephalopathy did not identify any further potentially pathogenic CHRM1 variant.

Conclusion: We posit that loss-of-function mutations in the M1 muscarinic receptor are a novel cause of early infantile epileptic encephalopathy. Our data suggest that brain reduced cholinergic signalling lowers seizure threshold, plausibly by releasing M current inhibition, and severely impairs neurodevelopment.

Disclosure: No potential conflict stated.

P02-06

Mutation in the KCNQ2 ion selectivity filter causing severe Epileptic Encephalopathy responsive to Retigabine

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Introduction: A 7-year-old male with early epileptic encephalopathy with burst suppression, started having seizures in utero. By three years of age, he had more than hundred of seizures /day, highly resistant to therapy.

Methods and Results: He had severe hypotonia, optic atrophy, no developmental milestones, and progressive atrophy and hypomyelination on MRI. Whole exome sequencing trio revealed a de-novo mutation p.Gly281Arg in the KCNQ2 gene, encoding for the Kv7.2 voltage gated potassium channel. The mutation, located in the pore region, within the ion selectivity filter, was predicted to cause a non-functional channel, unaffected by the potassium channel opener retigabine. Patch clamp analysis of the mutated channel KCNQ2G281R in Xenopus revealed no currents, unchanged by administration of retigabine 5µM. However, co-expression with the wild type channel KCNQ2WT / KCNQ2G281R, mimicking the in vivo heterodimer revealed present, though reduced currents. Administration of retigabine increased currents (v50 -21.3mV vs. -38, p<0.05*). Similarly, co-expression of tetradimer of KCNQ2WT / KCNQ2G281R with KCNQ3 revealed currents improved by retigabine (v50 -30.4mV vs. -51.3mV). Following the electrophysiological studies, retigabine 15 mg/kg was administered in accordance with a named patient basis approval. A 90% reduction in seizure frequency occurred, but no cognitive improvement was noted. Unfortunately, following the discontinuation of retigabine marketing, we were forced to stop treatment, and seizure control deteriorated.

Conclusion: In conclusion, this study reinforces the importance of electrophysiologic studies in implementing personalized treatment of epilepsy.

Disclosure: No potential conflict stated.
Therapeutic drug monitoring of Fenfluramine and its metabolite Norfenfluramine in patients with Dravet Syndrome

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Introduction: Fenfluramine appears to have a good anticonvulsive effect in patients with a Dravet syndrome. Little is known about its pharmacokinetics in clinical practice. Here we describe the results of blood levels of (nor)fenfluramine and the impact of age and comedication.

Methods: A rapid, sensitive and selective analytical method was developed and validated for the determination of fenfluramine (FFA) and its main metabolite (norFFA) in human plasma. Liquid-liquid extraction was used for sample preparation followed by liquid chromatography tandem spectrometric analysis and an electrospray-ionization interface. Plasma samples were collected from June 2015 until December 2018.

Results: 190 blood samples could be collected from 36 different subjects (age: 2.2 to 43.6y) with a median FFA dose of 12.5 mg/day (0.29 mg/kg/d). Mean FFA concentration was 56.1 µg/L (range; 5.1 – 712.5 µg/L), mean norFFA concentration was 25.9 µg/L (range; 5.1 – 349.6 µg/L).

Stiripentol (STP) significantly increased the FFA concentration / dose (C/D) and FFA/norFFA ratio.

Age had no effect on the FFA/norFFA ratio although C/D ratios decreased with age, reflecting a higher clearance. Higher FFA levels (>200 µg/L) were associated with more side-effects, however without improvement of its anticonvulsive effect.

Conclusion: FFA and norFFA blood levels can be detected and are clinically relevant. A positive dose-response relation could be seen below 100 µg/L, higher levels were associated with more somnolence, fatigue and anorexia.

Already in a low dose STP inhibits the metabolization of FFA. In combination with STP, the daily FFA dose should be reduced dramatically, since levels above 200 µg/L can be seen from 0.3 mg/kg/day. This effect was not seen with other concomitant medications.

Disclosure: Dr. Schoonjans has served as a paid consultant/advisor for Brabant and Zogenix, Inc. Dr. Ceulemans has served as a paid consultant/advisor investigator for Brabant, Novartis, UCB, and Zogenix, Inc.
**P02-09**

**ALG13 de novo pathogenic mutation in a male child with Congenital Heart Disease and vertebral abnormalities**

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**Background:** ALG13 gene mutation is associated with infantile onset seizures and developmental delay. To date only one case in male patients (2017) and eleven cases in female patients of de novo hemizygous pathogenic mutation has been reported since it was first identified by exome sequencing in a male child with refractory epilepsy, multisystem involvement and abnormal glycosylation of serum transferrin, consistent with congenital disorders of glycosylation type 1 (CDG-1).

**Case Reports:** A boy was born at term to a non consanguinous parents, hypotonia was noted at birth. He was diagnosed with complex congenital heart disease at the age of six weeks of life. Echocardiography revealed ventricular septal defect, anomalous right coronary artery and hypoplasia of the pulmonary artery. He had few episodes of infantile spasms before he developed first generalised tonic-clonic seizure at 9 months of age. He had underlying global developmental delay with structural abnormalities in brain, spine and ribs revealed by MRI and skeletal survey. Examination revealed dysmorphic features with multisystem involvement of varying grades of severity. Genetic study revealed a de novo hemizygous pathogenic mutation in ALG 13 gene resulting in his typical phenotype.

**Conclusion:** Congenital heart disease has never been described in ALG13 gene mutation but its chance association can neither be ruled out at this stage. As this disease is very rare, our case would add congenital heart disease as a potential association inviting researchers worldwide to look for and report this association if found. This is the second case of ALG13 gene mutation ever reported in a male child.

**Disclosure:** No potential conflict stated.

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**P02-10**

**Diagnostic rate of targeted gene panel analysis of patients with early-infantile Epileptic Encephalopathy**

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**Introduction:** Early-infantile epileptic encephalopathies (EIEE) comprise a group of clinical entities each with a specific disease course and with EEG abnormalities that cause progressive disturbances of cerebral functions. 71 EIEE genes have been defined to date. Targeted gene panel analysis appears to be the best cost-effective diagnostic option for early-infantile epileptic encephalopathies. Here, we describe the implementation of a NGS gene panel into diagnostic routine, containing 55 EIEE genes in a EIEE cohort.

**Methods:** We retrospectively analyzed the diagnostic rate of the EIEE gene panel in 67 patients (31 males, 36 females). In this study 55 genes known to cause EIEE were analyzed by targeted WES in a cohort of EIEE between October 2017 and September 2018 (now, the study is still ongoing, and we will present the

**Results:** Pathogenic or likely pathogenic variants were identified in 17 patients (25.37%). Among these variants 7 were de novo. Pathogenic and likely-pathogenic variants were found in SCN1A (4), PCDH19 (2), PLCB1 (2), STXBP1 (2), WWOX (1), SCNA8 (1), KCNQ2 (1), SCN2A (1), NECAP1 (1), FGF12 (1) and SLC35A2 (1) genes. Variants of unknown significance (VUS) were found in 16 patients (23.88%).

**Conclusion:** The diagnostic rate of pathogenic and likely-pathogenic variants was found similar to previous studies of EIEE. Functional analysis could be performed to clarify the pathogenecity of variants classified in VUS. Targeted gene panel sequencing is an efficient tool to identify the genetic causes of EIEE and to recommend gene-specific antiepileptic drugs and alternative therapeutic approaches.

**Disclosure:** No potential conflict stated.
Alternative approaches to conventional antiepileptic drugs in early infantile Epileptic Encephalopathies: Galactose and Inositol therapies for SLC35A2 and PLCB1 gene mutations

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Introduction: The early infantile epileptic encephalopathies (EIEE) are a group of disorders characterized by early onset seizures, progressive cognitive and neuro-psychological re-impairment. In this study, we discussed three patients diagnosed by early infantile epileptic encephalopathy (EIEE) gene panel which includes 54 genes, and our alternative approach to conventional antiepileptic drugs in the management of EIEEs.

Method: Two siblings (7-year old girl and 4-year-old boy) with malign migratory partial seizures of infancy (MMPSI) and 6-year-old boy with a history of West syndrome were evaluated for refractory seizures and psycho-motor retardation. Their etiology could not be clarified by conventional investigations and EIEE gene panel which includes 54 genes were analyzed by targeted next generation sequencing technique.

Results: Targeted WES analysis showed homozygous c.1945A>G (p. Arg649Gly) variant in the PLCB1 gene in two siblings with MMPSI. Parents were heterozygous for the same variant. A heterozygous c.773C>T (p.Ser258Phe) variant was found in the SLC35A2 gene variant in other patient. This variant was not found in the parents (de novo). In silico analysis showed that all these variants were pathogenic. The task of the PLCB1 gene is encoding the phospholipase C enzyme. Inositol is thought to be metabolized to the precursor of second messenger molecules which catalyze by phospholipase C. We ordered inositol for siblings with PLCB1 mutation with prominent helpful effect.. The SLC35A2 gene encodes a UDP-galactose carrier. Galactose supplementation may increase the concentration of cytosolic UDP-galactose and thereby increase galactose transport to the golgi apparatus. We planned oral galactose supplement.

Conclusion: The genetic etiology of early infantile epileptic encephalopathies is important for alternative therapeutic approaches.

Disclosure: No potential conflict stated.

Neonatal Epilepsy and genetic testing: a new approach

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Introduction: Whereas the majority of seizures in neonates are related to acute brain injury, a substantial minority are the first symptom of a neonatal-onset epilepsy, often linked to a pathogenic genetic variant. KCNQ2-related disorders represent a continuum of overlapping neonatal epileptic phenotypes caused by a heterozygous pathogenic variant in KCNQ2.

Results: Case 1: A 10-months-old female who was born after an uneventful pregnancy presenting with seizures at 2nd day of life. She had no family history of epilepsy. She presented clonic seizures of the arms and legs. She was treated initially with phenobarbital obtaining partial response. Levetiracetam and vitamins were added. Metabolic work up, MRI and interictal EEG were normal. Genetic testing revealed de novo heterozygous mutation (c.1732A>G) in KCNQ2 gene. At 4 months she started convulsing again. Seizure control was achieved immediately after starting Carbamazepine. At 10 months of age the patient remains seizure-free on carbamazepine and her psychomotor development is normal.

Case 2: A 9 months-old male without perinatal problems. He also started with seizures at 2nd day of life consisting of tonic and apneic episodes. The ictal EEG showed brief generalized polispike i. Interictal EEG was normal. partial response to Phenytoin and Metabolic analyses, CGH-array and MRI were normal. The patient remained seizure-free following add-on oral Oxcarbamazepine. Whole-exome sequencing (WES) is pending.

Conclusions: Neonatal epilepsy is often due to identifiable genetic causes. Genetic testing is now warranted for newborns with epilepsy in order to guide management and inform discussions of prognosis. In KCNQ2-Associated Neonatal Epilepsy, Sodium channel blockers like carbamazepine (CBZ) are shown to control seizures and should be considered first-line treatment.

Disclosure: No potential conflict stated.
P02-13
Utility of gene panel testing in children with seizure onset after 2 years of age: results from a European and Middle Eastern Epilepsy genetic testing programme

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Background: Epilepsy is one of the most common childhood-onset neurological conditions with a genetic basis. Genetic diagnosis provides potential for etiologically-based management and treatment. Existing research has focused on early-onset (<2 years) epilepsies while data regarding later-onset epilepsies is limited. Program goals: Determine, in a selected pediatric epilepsy cohort, the overall and actionable molecular diagnostic (MDx) yield and the CLN2 disease MDx yield. CLN2 is a severe, rapidly progressive neurodegenerative disease with onset of seizures at/after 2 years and average age-of-diagnosis of 5 years.

Methods: Blueprint Genetics’ next-generation sequencing (NGS)-based 283-gene epilepsy panel was used. Copy number variant (CNV) detection from NGS data was included. Variant interpretation was performed according to ACMG guidelines. Program results (Oct/2017-Nov/2018) are reported from 210 patients (Europe, Middle East) with inclusion criteria: Age 24-60 months, first seizure at/after 24 months, and at least one additional finding. The program was sponsored by BioMarin Pharmaceutical Inc.

Results: Median age-at-testing: 42 months; median age-of-first-seizure-onset: 30 months; average delay from first seizure to comprehensive genetic testing: 10.3 months. Genetic diagnosis was established in 42 patients; 20.0% MDx yield. CNVs were reported in 26.2% of diagnosed patients; 27.3% of CNVs identified were intragenic. MDx included 5 CLN2 (TPP1 gene) diagnoses, 4 MECP2, 3 SCN1A, 3 Angelman syndrome, 2 each of CHD2, KCNA2, MFSD8, SCN2A and STXBP1.

Conclusion: This program demonstrates the clinical utility of a comprehensive epilepsy gene panel for patients with first seizures at/after 2 years for MDx of pediatric epilepsy and CLN2 disease to guide management and treatment.

Disclosure: KG, KA, ES, LK, JK, and T-PA are employees of Blueprint Genetics. EI and NM are employees and stockholders of BioMarin.

P02-14
Infantile spasms without Hypsarrhythmia – A distinct Epileptic Syndrome? – A series of 5 patients

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Introduction: Infantile spasms (IS) are defined as a specific seizure type. Infantile spasms without hypsarrhythmia have been described in some series of patients, occurring predominately in infancy, but also in childhood. We present a series of five patients with infantile spasms without hypsarrhythmia

Materials: Between October, 2013 and December 2018, 5 patients in our clinic, met the diagnosis criteria of clinical IS in clusters without hypsarrhythmia on EEG.

Results: All our 5 patients started having infantile spasms without hypsarrhythmia at the median age of 4.8 months. Three patients were effectively treated with a combination of Valproic Acid, Clobazam and Topiramate, or only Clobazam, or Adrenocorticotropic hormone. Three of them had refractory seizures. In all patients the EEG revealed no hypsarrhythmia in presence of clinical infantile spasms. Brain MRI was performed in 4 patients and was normal in 3 of them. Six patients had had different levels of global developmental impairment after the onset of seizures. The mean follow-up was 1,82 years due to non-compliance of some patients.

Conclusions: We observed that patients with infantile spasms without hypsarrhythmia had variable evolutions depending on their underlying conditions. Patients without structural lesions did not have severe intellectual impairment. Most cases have a presumed genetic etiology. More patients are needed to be able to better characterize the evolution and prognosis of patients with infantile spasms without hypsarrhythmia. Consensus is needed in the diagnosis and workup, including genetic testing, of these patients.

Disclosure: No potential conflict stated.
POSTER PRESENTATIONS > POSTER SESSION 2
Epilepsy: diagnosis and investigations

▶ P02-15 ◀
A case at the crossroads of Neurology and Cardiology

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Introduction: Sick sinus disease (SSD) is a dysfunction of sinoatrial node that results in sinus bradycardia or sinus pauses that may be symptomatic, usually presenting as syncope. This disease is rare in children with normal heart anatomy and the co-occurrence SSD and epileptic seizures is very rare.

Methods: Our patient underwent cardiologic evaluation, video and ambulatory EEG monitoring, psychological and psychiatric evaluations during his admission to our clinic.

Results: A 16-year-old boy with a history of multiple paroxysmal events of loss of consciousness presented to our clinic. His last three episodes were clinically suggestive of generalized tonic-clonic seizures. At that time, the ECG and Holter-ECG monitoring revealed a right bundle branch block and sinus bradycardia with minimum heart rate of 36 bpm. In November 2018 he suffered a prolonged episode of loss of consciousness of approximately 15 minutes, with normal consequent brain CT. A pacemaker (DDD) was implanted, with remission of symptoms for one month, followed by the occurrence of bilateral spike-and-wave discharges. Treatment with valproate was initiated and the patient remained long-term seizure-free.

Conclusion: The case was interpreted as multiple syncope caused by SSD which required pacemaker (DDD) implantation in a patient who subsequently presented generalized tonic-clonic seizures, accompanied by epileptiform abnormalities. Initiation of valproate led to a long-term improvement of symptoms. We emphasize the importance of long-term EEG monitoring and of a multidisciplinary team in evaluating patients with episodes of loss of consciousness in children.

Disclosure: No potential conflict stated.

▶ P02-16 ◀
Reflex seizures in “Benign Myoclonic Epilepsy in Infancy”

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Aim: Benign Myoclonic Epilepsy in Infancy (BMEI) is rare and seizures are rarely seen by the physician or captured by video-EEG monitoring. Sometimes repetitive jerking attacks can be mistaken for ‘shuddering movements’ or even as generalised tonic clonic epilepsy seizures and extensively investigated. We report a video-EEG recording of a typical seizure in a child.

Method: A fourteen month old girl presented with three weeks’ history of startle episodes appearing as shuddering movements. The infant underwent video-EEG to rule out epileptic spasms.

Results: Two habitual events were captured when awake, consisting of rhythmic head and whole body myoclonic jerking, lasting for 2-3 seconds. Both were triggered by an unexpected loud auditory stimulus. These episodes were associated with brief bursts of bilateral high amplitude sharp -slow wave discharges. Startle responses were seen on some occasions with an unexpected loud noise. This was followed by focal vertex sharp wave (SEP).

Conclusion: In view of the diagnosis, MRI brain scan was not done and child was closely monitored. Child’s developmental progress has been normal with no seizures for last 4 yrs. No treatment was given. Infrequent generalised tonic clonic seizures can develop in 10-20% of cases in early teens. Review of published case reports have shown that myoclonic astatic epilepsy, childhood absence epilepsy or Jeavons syndrome can develop 3-9 year after onset of BMEI & therefore long-term monitoring of children is recommended. Genetic factor may influence the outcome as one child with initial presentation of BMEI with mutation in the SLC2A1 gene, later developed refractory GTC, Myoclonic & absence seizures, ataxia & significant mental impairment. Although characterized as “benign”, 3-20% children may have mild cognitive, behavioural or motor deficits.

Disclosure: No potential conflict stated.
POSTER PRESENTATIONS > POSTER SESSION 2
Epilepsy: diagnosis and investigations

P02-17

Chromosome microarray in children with Epilepsy and neurological abnormalities – Our experience

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Objective: Chromosome MicroArray (CMA) has an important role in the discovery of epilepsy-associated copy number variants (CNVs) in children with epilepsy and possible additional neurodevelopmental disorders. The purpose of this study is to describe the results of performed CMA on 150 children with unexplained epilepsy associated with developmental delay, autism spectrum disorders and/or multiple congenital anomalies.

Methods: Retrospective review on clinical and genetic aspects of CNVs identified in 106 children, seen at the Department of Pediatrics, University Hospital of Rijeka, Croatia from June 2016 to January 2019. All patients had CMA performed using SurePrint G3 Unrestricted CGH ISCA v2 (Agilent Technologies, Santa Clara, California, USA).

Results: Abnormal CMA results were identified in 20 out of 106 patients with epilepsy and additionally neurodevelopmental disorder. This group included 8 patients that had CNV in genomic area predisposing to epilepsy, including 3p26.1p25.3 (n = 1), 15q11.2 (n = 2). Among others neurodevelopmental syndromes with epilepsy we found 21q22.3 deletion including S100B gene, 20q13.33 deletion with KCNQ2 and CHRNA4 genes, Xq28 duplication with MECP2 gene and Xp22.31 duplication described as variant of unknown significance (VUS). One patient had multiple pathogenic CNVs (13q22.3 duplication (CHAMP1 and NALCN genes), 20p13 deletion and 16p11.2 deletion. Diagnostic yield in our study was 18%.

Conclusions: CMA revealed pathogenic CNVs in children with epilepsy and known microdeletion syndromes. It should be the first-choice diagnostic method for patients with epilepsy with or without neurodevelopmental disorder.

Disclosure: No potential conflict stated.

P02-18

SLC6A1 variant in a child with Intractable Epilepsy

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Objective: SLC6A1 variants have recently been described in patients with generalised epilepsies, such as myoclonic-atonic epilepsy and childhood absence epilepsy, as well as in association with intellectual disability and behavioural issues. There are also reported cases of asymptomatic SLC6A1 carriers. This heterogeneity causes difficulty with diagnosis and prognosis, though there are groups that report good responses to anti-epileptic drugs (AEDs). Here we describe a severe phenotype of a patient with SLC6A1 mutation and myoclonic-atonic epilepsy intractable to multiple medications and corpus callosotomy.

Case: A 5-year old girl presented with multiple seizure types including absences, myoclonic jerks and atonic seizures. She was born at term following an uncomplicated pregnancy and had no neonatal complications. She had significant global developmental delay prior to seizure onset aged 10 months alongside concerns with autistic-type features, behavioural issues and aggression. There was a family history of infantile maternal epilepsy until 18 months. Her seizures remained refractory despite multiple AEDs and progression to corpus callosotomy.

Results: Neurometabolic investigations, MRI and CGH array were unremarkable. EEG demonstrated generalised spike/polyspike and slow waves at 2.5-3.5 Hz. SLC6A1 c.1531G>A p.(Val511Met) mutation was detected on epilepsy gene panel.

Conclusion: This case represents a more severe phenotype of SLC6A1-related epilepsy than previously described, adding to the clinical spectrum of SLC6A1-associated disorders. The case demonstrates severe pharmacoresistant epilepsy that showed no response to treatment including corpus callosotomy. Interventions now being considered include ketogenic diet and vagal nerve stimulation. This case adds to what is already known regarding phenotypic heterogeneity and may help clinicians when considering long-term prognosis for patients with SLC6A1 mutations.

Disclosure: No potential conflict stated.
P02-19

The risks of Epilepsy after the first attack in children

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Aim of study: Identify the risks of recurrence of a seizure in a two-year prospective study after the first attack in children who have not received treatment.

Materials and methods: Case-control study. 556 children after a single seizure are included in a prospective two-year study. Five subgroups were formed on the age of the children at which the first attack occurred: up to 1 year; 1-3 years; 4-5 years; 6-13 years old; 14-17 years old.

Results and discussion: Two groups were formed after a two-year study: the 1st group of children (n=447) with a recurrent attack during the two-year observation period and the diagnosis of epilepsy, the 2nd group (n=109) did not have a second attack, the diagnosis was a single seizure. A study of the risk of recurrent seizure in cohort children (n=556) showed that the risks vary significantly over time and their values with standard deviation are 0.0222±0.0015 one month after a single attack; 0.0104±0.0024 after two months; and after 6 months and one year - 0.0016±0.0008; 0.0015±0.0002, respectively. The highest initial risks of recurrence of seizure were found in children with a case of the first attack at the age of under 1 year - 0.0677±0.0160. These results are 4 times higher than in children aged 1-3 years (0.0176±0.0070), 3.5 times higher than in the subgroup of children 4-5 years (0.0190±0.0119); 4.8 times higher than in children 6-13 years old (0.0104±0.0058) and 5.6 times higher than in adolescents 14-17 years old (0.01220±0.0044), the indicators are significant differ (p log rank <0.001).

Disclosure: No potential conflict stated.

P02-20

Cerebral Palsy and Epilepsy

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Background and aims: The aims of this retrospective and hospital-based study were to describe the frequency and characteristics of epilepsy in 90 children (63 males and 27 females) with cerebral palsy (CP).

Methods: A retrospective, descriptive, hospital-based study in Child Neurology Hospital, Baku, Azerbaijan. Ninety children with CP and seizures seen in the neurology clinic during the period of 2013–2017 were studied.

Results: Epilepsy most commonly affected children with spastic tetraplegia (55.6%). Mean age of seizure onset for children with CP was 16.8 month for spastic quadriplegia, 21.6 month for hemiplegia 16.7 month for diplegic cerebral palsy. The incidence of neonatal seizures was 13% among these children. About 40% of children in the study group presented with generalized tonic clonic seizures; the electroencephalogram (EEG) showed focal epileptic discharges with or without secondary generalization in 50%. Low birth weight, neonatal seizures, seizures during the first year of life, family history of epilepsy, severity of CP and computer tomography findings were found to be related to significantly increased risk of epilepsy in children with cerebral palsy. Polytherapy was commonly used in children with spastic tetraplegia. The overall outcome of seizures in children with CP was poor needing prolonged course of anticonvulsant medications, polytherapy and higher incidence of refractory seizures and admissions for status epilepticus.

Conclusions: Epilepsy in children with cerebral palsy is characterized by earlier onset, a low frequency of generalized seizures, as well as the use of several antiepileptic drugs and intractable epilepsy. To determine the risk of epilepsy onset in children with cerebral palsy at early ages is important for optimizing its management.

Disclosure: No potential conflict stated.
**P02-21**

Evaluation of the cognitive side effects of antiepileptic treatment in children and adolescents with Epilepsy by the Test Epitrack® Junior

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**Introduction:** Children and adolescents with epilepsy are in major risk of having or developing transient or permanent cognitive defects with negative impact on their school performance and socialization. We present a pilot study that aims to evaluate the potential effect on attention and executive functions of antiepileptic drugs (AEDs) in children treated for epilepsy, using the Epitrack® Junior scale.

**Methods:** We prospectively used Epitrack® Junior in patients 6-18 years old with normal scolarisation followed at our Department for any epilepsy type (March-September 2018). Children were included either prior to initiation of the first AED or in case of treatment modification (addition of a new AED or AED discontinuation). EpiTrack was performed at inclusion and approximately 3 months later, together with clinical and VEEG reevaluation. SPSS 23.0 was used for statistical analysis.

**Results:** 32 patients [mean age: 10.6 years (SD: 2.97), male: 47%] were enrolled in the study; 25 appeared for re-evaluation. 28.1% had important and 12.5% mild impairment at baseline according to test’s categorization. Univariate analysis significantly correlated initial scores with specific antiepileptic agents (p=0.038), family or personal history of seizures (p= 0.03) and type of treatment modification (p= 0.046). Scores at follow-up were further correlated with preexisting learning difficulties (p=0.032) and number of drugs at baseline (p=0.022). Multivariate analysis for Epitrack’s score modification 3 months after intervention was correlated with EEG modification (p=0.02) and seizure’s type (p= 0.032).

**Conclusion:** Epitrack® Junior represents a quick and well-structured screening tool, sensible to certain variables involved in the management of epilepsy in childhood. We are pursuing to enroll more patients in order to confirm Epitrack’s promising role in physicians’ effort to achieve balance between therapeutic and adverse effects of antiepileptic treatment.

**Disclosure:** No potential conflict stated.

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**P02-22**

Infantile spasms – How often do we think of vitamin B12 deficiency

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**Introduction:** Vitamin B12 deficiency can present with various clinical manifestations, especially during infancy, including hematological and neurological deficits. Many infants with vitamin B12 deficiency are asymptomatic or present only with megaloblastic anemia. If present, central nervous system symptoms can start with irritability, apathy and lethargy to gross motor developmental regression and seizures unresponsive to antiepileptic medication.

**Case report:** A nine-month-old male infant presented with a two week history of head drops. His cognitive development and motor skills were normal. He was exclusively breastfed. Laboratory investigation showed hemoglobin level of 98 (range 118-149) g/L. Leukocyte, platelet count and the mean corpuscular volume were normal. The vitamin B12 level was less than 111 (range 138-652) pmol/L, and the folate level was 24,7 (range 7–46,4) nmol/L. The plasma total homocysteine concentration was normal 11,9 (< 15) umol/L. MRI of the brain was normal. Electroencephalography (EEG) showed hypsarrhythmia and he was diagnosed with Infantile spasms possibly due to vitamin B12 deficiency. Treatment with vitamin B12 was initiated and two days later he was seizure free. A week later his EEG was completely normalized. He is currently 25 months old with normal developmental milestones, seizure free and with normal findings of the EEG.

**Conclusion:** Vitamin B12 deficiency can present with severe symptoms, such as seizures and lead to apparent life-threatening events. Early diagnosis and treatment is crucial to normal infant development and avoiding unnecessary treatment with antiepileptic drugs. Vitamin B12 should always to be part of the routine investigation during the diagnosis of infantile epilepsy.

**Disclosure:** No potential conflict stated.
Successful Epilepsy surgery outcome in a child with Mesial Temporal Sclerosis whose initial EEGs were suggestive of benign Focal Epilepsy

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Introduction: Benign focal epileptiform discharges of childhood (BFEDCs) are commonly seen on electroencephalography (EEG) in children less than 15 years. Presence of these can lead to missed or delayed diagnosis and treatment of concomitant lesions.

Purpose: We report a child with a successful epilepsy surgery outcome for mesial temporal sclerosis who was initially dismissed as a suitable candidate because of frequent BFEDC with review of literature.

Methods: Medical charts of those who underwent videoEEG were analysed over a 7 year period in search of reports of temporal lobe seizures with coexistent BFEDC. Only one such case was identified whose clinical, neurophysiological and neuroimaging data were reviewed.

Results: A left handed girl with normal neurodevelopment presented with afebrile seizures at 8 years of age characterized by vacant stare, unresponsiveness followed by right sided focal motor seizures. Her seizures evolved to those where she had epigastric aura followed by unresponsiveness, pallor, pupillary dilatation, and inability to speak. Past history of two complex febrile seizures was noted in infancy. Serial EEGs revealed bilateral stereotyped sharp waves over parieto-occipital regions with fixation off sensitivity and these increased in frequency in NREM sleep. Progressively she developed pharmacoresistant epilepsy with significant cognitive and behavioral concerns which along with atypical seizure semiology prompted neuroimaging which revealed left mesial temporal sclerosis. Initially surgery was dismissed in view of BFEDCs but was contemplated only after videoEEG captured concordant seizures of left frontotemporal onset. She underwent left anterior temporal lobectomy at 14 years of age and has since been seizure free for 4 years with excellent neuropsychological outcome. Followup EEGs show absence of BFEDCs.

Conclusion: Few reports have focused upon lesional epilepsy coexistent with BFEDC. We highlight a favorable epilepsy surgery outcome in this scenario.

Disclosure: No potential conflict stated.

CLN5 mutation causing Neuronal Ceroid Lipofuscinosis: a case report

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Introduction: The neuronal ceroid lipofuscinoses (NCL) are neurodegenerative conditions that are characterized by a progressive decline of cognitive and motor capacities, retinopathy evolving into blindness, variable cerebellar atrophy, and myoclonic epilepsy, leading to significantly decreased life expectancy. CLN5 is located on the chromosome 13q21.1- q32 and encodes a soluble lysosomal glycoprotein. CLN5 neuronal ceroid lipofuscinosis typically begin between 4 and 7 years of age and present with clumsiness, progressive motor and mental deterioration, visual impairment, seizures, and early death. Here we report a patient with CLN5 NCL. The patient is a 10-year-old boy from healthy, consanguineous parents and his neonatal period was uneventful. His first symptom was visual deterioration at 6 years of age and he developed mental and motor retardation. One year later he developed generalized epileptic seizures his psychomotor regression symptoms aggravated further.

Methods and Results: His electroencephalogram (EEG) showed diffuse generalized slow spikes and slow waves. Magnetic Resonance Imaging (MRI) showed significantly decreased cerebellar volume. His epileptic seizures recurred several more times and became intractable. By the age of 7, he had lost his walking and speech ability entirely. Visual evoked potentials showed bilateral central lesion. Whole genome sequencing of DNA showed CLN5 13q22.3 c.558A>C (p.glu186Asp) mutation. CLN5 mutation is a late-onset subtype of NCL.

Conclusion: A child between ages 4 and 7 presenting with visual loss and psychomotor developmental delay should be tested for CLN5.

Disclosure: No potential conflict stated.
P02-25

Clinical and neuroimaging findings in patients with benign Focal Epileptiform Discharges of childhood

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Objective: Benign focal epileptiform discharges of childhood (BFED) are the discharges which have normal background rhythm in wake and are activated by sleep. They are independent, high amplitude, negative sharp waves, primarily occur from the centro-temporal and occipital region, less frequently from the midline are a sand frontal lobes and are accompanied with horizontal dipole. Clinical seizures and/or abnormal neuroradiological findings may be associated with these EEG findings.

Methods: Clinical features, EEG and neuroradiologic findings of 11 patients (8 males, 3 females) with BFED were evaluated retrospectively.

Results: The ages at the time of diagnosis ranged between the ages 9 years 4 months and 15 years 5 months. Neurological examination showed abnormal findings in 3 patients, one of them was diagnosed with cerebral palsy. Six patients had epileptic seizures accompanied with BFED. EEG was obtained in patients without manifest seizures due to headache and stomachache, tic disorder, head trauma, speech delay and attention deficit hyperactivity disorder, atypical autism and learning difficulties. MRI showed focal cortical displasia in 3 patients (right anterior temporal, left anteriomedial temporal, and right insular, cingulate gyrus). Left temporal glioneuronal tumor, lesions due to perinatal insult were detected each in one patient. Three patients had no specific findings and 3 patients had normal MRI. Three patients had mild intellectual disability (ID), and one had moderate ID, there maining had normal IQ. Ten patients were on anti epileptic drug (AED) treatment.

Conclusion: Clinical evaluation and neuroimaging studies of children with BFED on interictal EEG are important to recognize structural / developmental lesions and further management with AED.

Disclosure: No potential conflict stated.

P02-26

Paediatric Status Epilepticus: a retrospective overview

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Background: Convulsive Status epilepticus (SE) is the most common neurological emergency encountered in childhood; therefore, care providers need to be aware of the implications, etiology and management. Recently, two new antides; new onset refractory status epilepticus (NORSE) and febrile-induced refractory status epilepticus (FIRES) had reported as a subdimension of SE.

Method: A total of 95 children with SE were examined to evaluate clinical and prognostic datas in children diagnosed with SE from 2008 to 2018 at SBU, Dr Sami Ulus Research and Training Hospital in Ankara, Turkey, and to determine retrospectively prevalence of NORSE and FIRES.

Results: Mean age was 6.3 years, 53.3% were boys and 21 of total had priorly been diagnosed with epilepsy and followed-up under the antiepileptic drug (AED) treatment. SE were seen in epilepsy group mostly due to inappropriate intake of AEDs. The highest incidence due to etiology of SE was in acute symptomatic SE (32.4%) and the lowest incidences were detected in prolonged febrile seizures (16.6%) and remote symptomatic SE due to hipoxic ischemic encephalopathy (7.9%). Refractory SE was seen in %72.7 of patients; seven patients of them were diagnosed as a super refractory SE. 47.3% of patients refractory to anticonvulsants. General anesthesia, immunomodulatory agents and ketogenic diet was applied 6.3%, 14.7%, 2.1% of patients, respectively. NORSE and FIRES was detected in 7.3% and 4.2%, respectively. There was also a motor and intellectual disability in the total cohort, with a cumulative incidence of 3.2% for motor disability and 8.8% for intellectual disability.

Conclusion: Although it is a retrospective study, our study showed a higher incidence for refractory SE despite lower incidences for NORSE and FIRES compared to the literature.

Disclosure: No potential conflict stated.
Fatal Status Epilepticus in Dravet Syndrome: an acute Encephalopathy triggered by fever

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Purpose: Premature mortality affects Dravet syndrome (DS) patients up to 21%. Sudden unexpected death (SUDEP) and Status Epilepticus (SE) are the most common causes of death. SE occurs commonly in DS; in some cases SE can become refractory and followed by Acute Encephalopathy (AE). The pathophysiology of this entity is still poorly understood. We aim to describe retrospectively the clinical characteristics of a cohort of patients with DS who died after a SE in order to identify causal and predisposing factors.

Methods: We launched an international call through the European reference network on rare and complex epilepsies (Epinean reference network on rare and complex epilepsies (Epi-care)). A questionnaire was sent and 5 hospitals reported cases of death after SE, collecting the following information: gender, SCN1A mutation, age at death, results of cardiological screening, relevant comorbidities, previous SEs, frequency of seizures and ongoing therapies during the last 6 months before death, treatment of the SE, autopsy findings.

Results: We collected data from 6 DS patients, SCN1A+, aged 8 months-23 years (mean age 7,6 years), who died during a fever-associated SE. None had other relevant comorbidities and their previous cardiological screening with ECG were normal. Most patients (5/6) had a good seizure control and 4/6 were on therapy with association of Sodium Valproate, Clobazam and Stiripentol. Post mortem examination has been performed in only one patient without significant results.

Conclusion: Mortality in DS could be related to SE, even with a negative cardiological screening and no other relevant comorbidities. The pathogenetic mechanisms that lead to the fatal outcome are not clear. This dramatic clinical entity is likely to be unrelated to treatment, possibly triggered by high fever and ion channel dysfunction.

Disclosure: No potential conflict stated.

Bisphenol A levels in children with acute seizures

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Introduction: Bisphenol A (BPA) is a component of polycarbonate plastics and epoxy resins used in many commercial products including coatings and liners of food and drink containers. The perinatal exposure to BPA causes GABAergic disinhibition and dopaminergic enhancement, leading to an abnormal cortical-basolateral amygdala synaptic transmission and plasticity in BPA-rats. In this study, we aimed to evaluate the association of BPA with seizures in children.

Methods: This prospective study was conducted on children who were having acute seizures and BPA levels were measured from spot urine samples. Neurologically normal children, matched for age and sex, were considered as controls.

Results: In total, 70 patients and 30 controls were participated in this study. Among the case group 36 patients (51%) were male and 34 patients (49%) were female whereas 16 (53%) were male and 14 (47%) were female in control group. The median age of the patients was 3.7 years and the median age of the controls was 4.3 years. The mean of urine BPA levels in case and control groups was 0.029±0.322 and 0.067±0.057, respectively. The mean of urine BPA levels was significantly higher for controls as compared with patients (p=0.024). The mean of urine BPA levels/ body mass index in case and control groups was 0.060±0.101 and 0.160±0.203, respectively. There were no statistically significant differences between case and control groups (p=0.463).

Discussion: BPA is a common ingredient of many plastic and resin products including water bottles and baby bottles. In our study, we concluded that there was no association between BPA and seizures in children. Because of our study is based on a small sample of participants, larger sample size could provide more definitive evidence.

Disclosure: No potential conflict stated.
P02-29
A new cause of electrical Status Epilepticus in sleep: CDKL5 Disorder

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Introduction: The CDKL5 disorder is characterized by early onset epilepsy, stereotypical hand movement, absent speech, severe hypotonia and neurological impairment. Interictal electroencephalography (EEG) is often normal at early stages and is worsened during the disease course. Herein, we report ESES in a patient with CDKL5 disorder.

Case report: 7-year-old girl patient with CDKL5 disorder admitted with complaints of persistent generalized tonic and myoclonic seizures. The diagnoses was confirmed by de novo CDKL5 mutation, c.197_198delCT (p.L67QfsX23). She now has generalized tonic and myoclonic seizures several times per day while taking valproic acid, clobazam and felbamate. Interictal EEG revealed generalized spike and slow-wave activity, occurring intermittently in wakefulness but present for at least 85% of non-REM sleep, consistent with the diagnosis of ESES.

Discussion: Electrical status epilepticus in sleep has been described in a large number of genetic disorders, but to our knowledge it has never been previously described in CDKL5 disorder. Our case illustrates that ESES pattern can be seen in the course of CDKL5 disorder.

Disclosure: No potential conflict stated.

P02-30
Risk factors of Epilepsy in children with complex febrile seizures; a retrospective cohort study

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Purpose: Febrile seizure is the most common seizure that occurred in children. Some of them developed epilepsy when they are older. Multiple risk factors of epilepsy were identified in children with a history of febrile seizures. We identify risk factors of epilepsy in children with complex febrile seizures.

Methods: The study’s comprised of 248 children who were diagnosed with complex febrile seizures at Chiang Mai University Hospital. The relationship between subsequent epilepsy and risk factors were analyzed by Cox regression-survival analysis.

Results: Fifty-five patients (22.1%) had subsequent epilepsy. Factors that were found to be associated with epilepsy were prolonged seizure more than 15 mins (p=0.006; HR 2.475; 95%CI 1.294 - 4.735), developmental delay (p =0.019; HR 4.476; 95%CI 2.280-15.646), epileptiform discharges on electroencephalography (EEG) (p = 0.023; HR 1.391; 95%CI 1.174 - 1.876), and abnormal neuroimaging (CT or MRI) (p = 0.028; HR 1.355; 95%CI 1.034-1.776). Age at the onset, peak body temperature, duration between the onset of fever and the occurrence of seizures, recurrent seizures within 24 hours, focal seizures, abnormal neurological exams and family history of febrile seizures or epilepsy were not associated with subsequent epilepsy in this study.

Conclusion: Risk factors of subsequent epilepsy in children with complex febrile seizures are prolonged seizures or febrile status epilepticus, developmental delay, epileptiform discharges on EEG and abnormal neuroimaging. These children should be followed up closely to assess if they develop epilepsy.

Disclosure: No potential conflict stated.
The aetiology of Epilepsia Partialis Continua: a cautionary tale

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Introduction: The underlying causes of epilepsy partialis continua (EPC) include structural, autoimmune, vascular and neurometabolic conditions. We describe a patient with EPC presumed to be of structural origin.

Case Report: A 5 year old boy with a background of mild developmental delay presented acutely with status epilepticus and developed intractable focal seizures with EPC and left hemiparesis. Initial neuroimaging and neurometabolic investigations were normal. An epilepsy gene panel was requested. Further imaging demonstrated irregularity and thickening of an area of the medial right parietal cortex suggestive of focal cortical dysplasia (FCD). He was referred for an epilepsy surgery work-up.

In the interim, his seizures were unresponsive to multiple antiepileptic drugs including steroids. Three months after presentation he was treated with sodium valproate and became seizure free with recovery of motor function. One month after starting sodium valproate he presented with unsteady gait and lethargy considered secondary to recurrence of EPC; the dose of sodium valproate was increased. Four weeks later he became unwell and was found to have deranged liver function leading to irreversible liver failure and death, 6 months after his initial presentation with seizures.

The association of liver failure with sodium valproate led to expedition of the gene panel; he was found to be heterozygous for 2 polymerase gamma variants, one of which was a recognised pathogenic mutation. Post mortem brain examination demonstrated histological features typical of Alpers Huttenlocher syndrome. There was no evidence of FCD.

Discussion: Mitochondrial disease remains a diagnostic challenge: we propose the case for rapid genetic evaluation in patients with new onset seizure disorders.

Disclosure: No potential conflict stated.

Jeavons Syndrome: challenges in diagnosis and treatment

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Introduction: Jeavons syndrome is a rare lifelong reflex epilepsy syndrome characterized by eyelid myoclonia, with or without absence seizures, eye closure induced EEG changes and photosensitivity. It is more frequent in females. Due to brief duration and subtle eye movements, it is often confused with non epileptic disorders, thus delaying diagnosis. Some patients experience myoclonic and generalized tonic clonic seizures too. Drug resistant epilepsy is a common feature.

Methods: We present the distinctive clinical features of four patients comprising 1% of local database of 400 childhood epilepsy patients in our centre. Inclusion criteria included (a) seizure onset after 12 months (b) eyelid myoclonia with or without absence seizures, (c) EEG changes associated with eye closure (fixation-off sensitivity). We reviewed the history, diagnostic workup and anti-epileptic medications used in these cases.

Results: In our case series three were females showing female preponderance. Absence seizures with eyelid myoclonia were observed in all, while two older girls also developed generalized tonic clonic seizures. Interestingly, although one patient presented with a generalized tonic clonic seizure, she had absence seizures with eyelid myoclonia for years without earlier recognition. Another patient was diagnosed as having a tic disorder for six years. All the cases had fixation-off sensitivity on EEG, while photosensitivity was evident in younger patients. Despite trial of multiple anti-epileptic medications, patients continued to have multiple daily episodes of absences with drug resistant eyelid myoclonia.

Conclusion: Jeavons syndrome is a rare disorder and diagnosis is often missed or delayed. Despite treatment with multiple anti-epileptic medications, patients continue to experience daily events. Appropriate counselling around the nature of this syndrome is key to managing patient expectations.

Disclosure: No potential conflict stated.
Aicardi Syndrome: clinical and neuroradiological phenotype associations

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Introduction: Aicardi syndrome (AS) is a rare congenital syndrome described by J. Aicardi (1965), who defined as core features total or partial agenesis of the corpus callosum, choriorretinal “lacune” and epileptic spasms (Aicardi 1965). Because of the absence of a genetic hallmark, diagnosis is based on clinical and neuroradiological features (Aicardi 2005; Sutton et al. 2006).

Methods: We collected retrospective data of AS patients from multiple centers. Neurological outcomes were standardized using GMFCS, EDACS and MACS. We performed systematic revision of brain of MRI or TC scans and statistical analysis by chi-square test (Fisher’s exact) to find associations among neuroradiological features, epilepsy and clinical-neurological outcomes.

Results: Brain imaging was available for revision in 55/67 patients. Epileptic spasms at onset were reported in 86% of the patients 8 (mean age 75 days), in 36% of them associated with focal seizures. All these patients developed drug resistant epilepsy, with multiple daily seizures in 59%. For 93% neurological impairment was severe. At brain imaging, 98% displayed polymicrogyria and nodular heterotopias, 98.4% intracranial cysts. Posterior fossa abnormalities have been found in 71% and basal ganglia dysmorphisms in 65%.

Conclusions: Aicardi syndrome has a variable but more often severe clinical evolution. On the basis of our analysis, we reviewed the major and minor criteria necessary to confirm the diagnosis. Neuroradiological phenotype manifests with complex brain malformations, in variable combinations, whose concurrent presence is essential for the diagnosis. Posterior fossa abnormalities are a common features in Aicardi patients, but we also detected frequent and previously unreported basal ganglia abnormalities.

Disclosure: No potential conflict stated.
**POSTER PRESENTATIONS > POSTER SESSION 2**
Epilepsy: diagnosis and investigations

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**P02-34**

**A novel DEPDC5 mutation and a known pathogenic mutation in CLCN1 gene in a family with Epilepsy and a variable phenotype**

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**Objective**: Mutations in the DEPDC5 gene, a negative regulator of the mTOR pathway, are known to cause a series of dominant focal epilepsies (familial focal epilepsy with variable foci, nocturnal frontal lobe epilepsy, familial temporal lobe epilepsy, rolandic epilepsy) with variable penetrance and expressivity, while CLCN1 mutations have been associated with congenital myotonia.

**Methods**: Whole Exome Sequencing (WES) analysis was performed in a 15 year-old girl with epilepsy since the 1st month of life, presenting with tonic-clonic spasms of the upper limbs accompanied by fixed gaze. Pregnancy and perinatal period were uneventful. Her father had epilepsy at his 20s and was successfully treated for 5 years with valproic acid and lamotrigine. Brain MRI and investigation of metabolic disorders were in normal range. EEG-recording revealed spikes at the right parietal-occipital area. The patient had inadequate control of seizures despite several anticonvulsant medication used in several combinations. Neurodevelopmental and learning difficulties have been apparent since the age of 4y. Currently she has mild mental retardation and intractable epilepsy with 2-3 episodes/week, on valproic acid, perampanel, lacosamide and sultiam.

**Results**: WES analysis revealed a novel heterozygous frameshift mutation in DEPDC5 gene [c.3147delC;p.Ser1050ValfsX29] and a known pathogenic mutation in CLCN1 gene [c.2680C>T;p.Arg894Ter]. Both mutations were present in the paternal sample.

**Conclusion**: We report a girl with infantile-onset intractable epilepsy and mild psychomotor developmental delay, carrying two mutations in DEPDC5 and CLCN1 genes. Patient’s father with the same mutations had normal psychomotor development and milder phenotype of epilepsy. Our case further supports the variable penetrance of DEPDC5 mutations and extends the phenotypic spectrum which may be modified by additional mutations in other genes.

**Disclosure**: No potential conflict stated.

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**P02-35**

**Case of Focal Frontal Epilepsy in a 3 months-child with mutation of the NRPL3 gene**

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**Introduction**: The NRPL3 gene is one of the pathogenic genes of the GATOR1 complex and it is associated with the development of focal epilepsy in children, and may also be the cause of focal cortical dysplasia. It is described in 2015 by RicosM.G. et al.

**Aim of research**: To present a clinical case of focal frontal epilepsy in a child with mutation of NRPL3 gene, that was diagnosed in Ukraine for the first time.

**Material and methods**: This is second child in a family (the first child – 3 years old sister, healthy). The boy was born from healthy parents who are not relatives, healthy. At the age of 1 month, epileptic spasms and focal tonic adversive seizures appeared in the sleep, with a frequency of up to 10 per night, for a duration of 1-2 minutes. During the examination neurological changes were not detected. The child develops according to age. According to results of the interictal EEG focal changes were defined more in the frontal areas. According to results of the MRI, undiagnosed changes in the frontal and temporal lobes of the cerebral cortex were detected, and in the future we are planning to make a new examination to exclude focal cortical dysplasia or tubers. During the treatment the attacks were resistant when using valproates (aggravation with increasing dose) and 50% effect on small doses of the vigabatrin.

**Results of research**: A genetic test on epilepsy with the detection of 187 genes was performed and a pathogenic mutation of the NRPL3 gene was defined that could confirm our diagnosis.

**Conclusions**: Detection of genetic mutations can improve the diagnosis of cortical anomalies and plan treatment and prognosis of human life.

**Disclosure**: No potential conflict stated.
Electroencephalographic changes in children with Autism Spectrum Disorders

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Background: The problem of autism is relevant for modern society. The aim of our study was to study the links between changes in the bioelectrical activity of the cerebral cortex in children with autistic spectrum disorders during a routine EEG.

Method: The survey involved 258 children with a diagnosis of ASD, clinically confirmed; the control group (CG) consisted of 112 children without deviations in neuropsychological development.

Results: In 70% of children with ASD, a decrease in the amplitude of the dominant rhythm in the occipital and temporal leads was recorded. In 29%, flashes of high-amplitude slow waves were recorded in the delta range in the central leads, which was significantly different from those of the CG children. In the frontal leads, the amplitude indices were lower in children with ASD. In 29% of children with ASD, discharges of epileptiform activity were recorded, including isolated epileptic discharges in 17% of children, and in 12% generalized epileptic discharges were observed. The clinic of epilepsy was observed in 3% of the studied children with ASD, without epileptic anomaly attack was noted in 9%.

Conclusion: The revealed disorganization of cortical rhythmic activity in children with ASD can be considered as a mechanism of neuronal breakdown associated with instability and disruption of the relationship between parts of the brain. The revealed combination of RAS and epileptiform discharges may be associated with local hyper-excitability of the cortex. Since the information, communication between different parts of the cortex is extremely necessary for the normal functioning of the brain in healthy children. It should be noted that the clinical severity of autism was in direct proportion to the degree of changes detected on the EEG.

Disclosure: No potential conflict stated.

Use of SISCOM for the identification of the epileptogenic zone in children

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Objective: Role of subtraction ictal-SPECT co-registered to MRI (SISCOM) for the localization of the presumed epileptogenic zone (PEZ) in children candidate for resective surgery.

Methods: This is a retrospective study on patients <17 years with drug-resistant epilepsy screened for epilepsy surgery in the University Hospital of Leuven from January 2009 to January 2018. Forty-four patients and 51 SISCOM were included. Mean age: 9.1 years. The outcome of SISCOM was compared with the localization of the PEZ as determined by video-EEG, and analysed for multiple variables affecting feasibility and efficacy.

Results: SISCOM was feasible in terms of chronic medication management, need for rescue antiepileptic therapy during hospitalization and operative timings. Radiotracer injection occurred within 30 seconds from seizure onset in 91.4% of the patients. Ictal SPECT was performed within two hours from injection in 100% of the patients (mean: 40 minutes). SISCOM could localize the PEZ in 51% (26/51), and additionally lateralize the PEZ in 17.6% (9/51), achieving better outcomes than ictal-SPECT, PET and MRI (p<0.01). SISCOM localized the PEZ in 25% patients with non-localizing video-EEG and in 27.8% with negative MRI. Occurrence of habitual seizures during injection for ictal-SPECT and temporal localization of the PEZ both correlated with a better SISCOM outcome (p<0.05). 36.4% (16/44) patients were finally selected for surgery, with a 87.5% seizure-free rate at 12 months. A positive SISCOM outcome was correlated with seizure freedom in 66.7% and with a good final outcome in 75% of our patients.

Conclusion: SISCOM is useful to localize the epileptogenic zone in clinical practice, especially when EEG and MRI are poorly localizing. SISCOM is feasible even in young children, and adds precious non-invasive presurgical information with a potential prognostic value.

Disclosure: No potential conflict stated.
**P02-38**

**Psychogenic Non-epileptic Seizures (PNES): a retrospective study on outcomes in a general hospital paediatric service in the United Kingdom**

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**Objective:** This is a retrospective cohort study of paediatric patients under the PNES register of a district general hospital in the United Kingdom. The aim was to measure the outcomes of PNES patients at 1 year post-PNES diagnosis.

**Methods:** Patients under the age of 16 years in the paediatric epilepsy registry with confirmed diagnosis of PNES over the last 10 years were identified for this study. The diagnosis of PNES was based on history of recurrent seizures without positive findings in multiple video EEG or telemetry investigations. Burden on support systems was measured in terms of the family support, (identified as frequent contact of families with epilepsy nurse specialists of more than 1 time per week), Clinical support by the Epilepsy Nurse Specialist (Care plans and training), Social concerns, social worker involvement, CAMHS input and clinical psychology involvement. Outcomes included School attendance, social functioning, use of anti-epileptic medications at the point of PNES diagnosis and within 1 year of PNES diagnosis.

**Results:** 14 patients had a confirmed diagnosis of PNES. Mean age of first seizure was 7 years. 11 (79%) had epilepsy previously confirmed. Many children were on Anti-epileptic drugs with some on 2 anticonvulsants. Developmental disorders included ADHD, autism spectrum disorder, developmental delay, and dyspraxia. 6/14 (43%) had no developmental disorder. Social concerns (86%) and Psychological concerns (57%) were common in children with PNES and 29% required clinical psychology input. 10/12 (83%) of patients were on medication at time of PNES diagnosis and 67% remained on anti-epileptic medication 1 year post-PNES diagnosis.

**Conclusions:** PNES poses huge challenges and burden to families, school and healthcare staff. There is a need for clear pathways and access to Psychological support for affected children.

**Disclosure:** No potential conflict stated.

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**P02-39**

**Changes in background electroencephalographic activity in benign childhood Epilepsy with centrotemporal spikes after Oxcarbazepine treatment: a Standardized Low-Resolution Brain Electromagnetic Tomography (sLORETA) study**

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**Background:** Several neuroimaging studies have reported neurophysiological alterations in patients with benign childhood epilepsy with centrotemporal spikes (BCECTS). However, reported outcomes have been inconsistent, and the progression of these changes in the brain remains unresolved. Moreover, background electroencephalography (EEG) in cases of BCECTS has not been performed often.

**Methods:** We investigated background EEG activity changes after six months of oxcarbazepine treatment to better understand the neurophysiological alterations and progression that occur in BCECTS. In 18 children with BCECTS, non-parametric statistical analyses using standardized low resolution brain electromagnetic tomography (sLORETA) were performed to compare the current density distribution of four frequency bands (delta, theta, alpha, and beta) between untreated and treated conditions.

**Results:** Background EEG activity for the delta frequency band was significantly decreased in the fronto-temporal and limbic regions of the left hemisphere after oxcarbazepine treatment (threshold log-F-ratio = ±2.729, P < 0.01). The maximum current density difference was found in the parahippocampal gyrus of the left limbic lobe (Montreal Neurological Institute coordinate [x, y, z = 25, -20, -10], Brodmann area 28) (log-F-ratio = 3.081, P < 0.01).

**Conclusions:** Our results indicate the involvement of the fronto-temporal and limbic cortices in BCECTS, and limbic lobe involvement, including the parahippocampal gyrus, was noted. In addition to evidence of the involvement of the fronto-temporal and limbic cortices in BCECTS, this study also found that an antiepileptic drug could reduce the delta frequency activity of the background EEG in these regions.

**Disclosure:** No potential conflict stated.
DHX30 gene mutations: a new cause of Neurodevelopmental Disorder associated with refractory seizures

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Introduction: With the advance of New Generation Sequencing technology, new genes involved in epileptic encephalopathies were found, among them, recently was identified DHX30 gene. Epileptic encephalopathy due to mutations in the DHX30 gene consists in a rare disease characterized by cognitive and behavioral changes associated with epileptogenic process, usually refractory numerous drug therapies. So far, only 13 patients have been described harboring mutations in such gene, here we describe a new case and the first one in Latin America.

Methods: Clinical, genetic and neuroimaging retrospective data review

Results: Male patient, born to non-consanguineous parents, showed early signs of developmental delay and seizures in the first 6 months of life. Seizures have been refractory to a variety of anti-epileptic drugs and other investigations for inborn metabolic disorders turned out to be normal. Brain Magnetic Resonance Imaging had no specific findings, chromosomal array and a genetic panel for 150 genes involved in epileptic encephalopathy were also normal. Whole Exome Sequencing (WES) was performed and a de novo missense mutation was identified in the DHX30 gene. Patient showed no language development, severe motor delay, autistic-like features and developmental delay, seizures, muscular hypotonia, joint hypermobility, autistic features, sleep disturbances, strabismus and abnormal neuroimaging with diffuse cerebral atrophy. DHX30 gene mutations should be investigated in patients showing early onset seizures with autistic-like features in patients with normal or abnormal brain MRI findings.

Conclusion: Patients with DHX30 mutations often present with intellectual disability, absence of speech, significant global developmental delay, seizures, muscular hypotonia, joint hypermobility, autistic features, sleep disturbances, strabismus and abnormal neuroimaging with diffuse cerebral atrophy. DHX30 gene mutations should be investigated in patients showing early onset seizures with autistic-like features in patients with normal or abnormal brain MRI findings.

Disclosure: No potential conflict stated.

Expanding the clinical phenotype of DEAF1-Associated Neurodevelopmental Disorder (DAND) gene mutations: two new cases displaying different neurological presentations

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Introduction: Deformed epidermal autoregulatory factor-1 (DEAF1), a transcription factor essential for central nervous system and early embryonic development, has recently been implicated in cases of patients with intellectual disability (ID) and neurodevelopmental delay. So far, only eleven cases have been reported in the literature. Here, we present two new patients with DEAF1 mutations and their clinical phenotype.

Material: Clinical, genetic and neuroimaging retrospective data review.

Results: Patient 1, male, 7 years, started presenting symptoms in the first year of life with developmental delay and “autistic-like” features. Progressively, patient acquired motor milestones, but displayed no speech development. He received special education and speech therapy with slight improvement in receptive language. He never showed signs of epilepsy, but had one febrile seizure around 5 years of age. Brain MRI was unremarkable and extensive genetic investigation turned out normal.

Patient 2, male, 10 years, presented first symptoms at the age of 1 years 11 months with language regression followed by repetitive behavior and self-aggression. He stopped talking around 3 years of age. Epilepsy developed at the age of 8 years and has been refractory to several antiepileptic drugs. Brain MRI showed mild brain atrophy; comprehensive biochemical and genetic evaluation showed no abnormal findings.

Whole Exome Sequencing (WES) was performed and a de novo heterozygous DEAF1 mutation was identified in each case.

Discussion: DEAF1-associated neurodevelopmental disorder (DAND) has been used to describe patients with ID and related neurodevelopmental anomalies harboring DEAF1 mutations. Its phenotype consists of moderate to severe ID, disproportionately severely affected expressive speech (but significantly better speech comprehension and motor development) and behavioral problems. Our case reports expand its clinical phenotype to include neurological regression, refractory seizures and “autistic-like” features.

Disclosure: No potential conflict stated.
P02-42 Problems of sustainability of rendering medical assistance to patients sufficiating Epileption during transition them from the children’s network to adult practice

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Objective: To study a group of patients with epilepsy at the age of 18–20 years with the debut of epileptic seizures in childhood.

Methods: The study included 218 patients aged 18–20 years with the debut of the disease in childhood.

Results: The study showed that symptomatic (structural) focal epilepsies prevailed (41.7%) and probably symptomatic focal forms of epilepsy (20.6%). The results of the replacement of anti-epileptic therapy in adolescents during the transition from the pediatric to the adult network showed that 11% of patients experienced a breakdown of drug remission and renewed seizures, in 7.8% of cases there was a return to the original AED, in 4.1% - the introduction of an additional antiepileptic drug, in 2.3% continued attacks were observed against the background of ongoing antiepileptic therapy.

During the survey, among the problems of continuity in the transition of children from child to adult practice, patients most often noted the following factors: The purpose of treatment without taking into account the presence of a patient of various concomitant pathologies of a somatic nature. Unreasonable change in the form of epilepsy in the diagnosis without additional examination and type of drug therapy. The limited use of modern methods of examination (MRI ultrahigh resolution, VEEG). Lack of continuity in the care of the patient by specialists.

Conclusions: Multidisciplinary support programs are the ideal means of solving problems of adolescents with epilepsy. When assessing the success of the transmission, it is necessary to assess not only the level of control of seizures the but also general psychological and social aspects, indicators of quality of life and the cost of medical care.

Disclosure: No potential conflict stated.

P02-43 Investigating structural brain abnormalities on Neuroimaging in Paediatric Epilepsy

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Introduction: Focal epilepsies are common epileptic syndromes in children and neuroimaging is a common investigative practice in the paediatric population. There is no recent population based data on the correlation between clinical focal epilepsy, EEG abnormalities and abnormal MRI findings. This study aims to look at the relationship between clinical variables (such as age, sex, seizure type, EEG abnormalities) and any positive MRI findings.

Method: A study cohort was identified from Edinburgh’s Royal Hospital for Sick Children’s MRI database using a set exclusion criteria. Data on patient characteristics, epilepsy diagnosis, MRI and EEG abnormalities and anti-epileptic drug numbers was collected and compared with the significance of age, sex and clinical epilepsy diagnosis.

Results: 243 (11.1%) of all patients that underwent an MRI scan between 2017-2018 at the RHSC was due to a seizure. 40.7% were on a background of clinically diagnosed epilepsy. Of these, 35% had an MRI abnormality. Patients with focal epilepsy had the highest incidence of an MRI abnormality (57%) with frontal lobe abnormalities being the most common (37%). There was a significant association between MRI abnormalities and clinical epilepsy diagnosis (p=0.005).

Conclusion: There is a clear link between structural brain abnormalities and different epileptic diagnoses, with an apparent correlation between clinical focal epileptic diagnoses and structural brain abnormalities on neuroimaging. This pilot study forms the basis for future further evaluation of paediatric epilepsy syndromes with neuroimaging and will also be used to analyse the effectiveness of post-processing software on MRI.

Disclosure: No potential conflict stated.
**SPINAL MUSCULAR ATROPHY AND A PROGRESSIVE MYOCLONIC EPILEPSY. REPORT OF A GREEK PAEDIATRIC PATIENT**

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**Introduction:** Progressive myoclonic epilepsy (PME) is a feature of specific neurodegenerative diseases. Additional characteristics in clinical phenotype can direct to an early diagnosis of rare neurodegenerative syndromes.

**Methods:** We describe a female patient of 6.5 years-old with normal neurodevelopment the first 3 years of life. Initial symptoms appeared as clumsiness and frequent falls. She gradually progressed having myoclonic episodes, atonic crises, head drops and episodes of behavioural inhibition with fear. Her epilepsy was resistant to multiple AED, steroids and ketogenic diet. She presented with polymyoclonia, ptosis, tongue fasciculations, muscle weakness, pyramidal signs and impaired ophthalmic movements. Investigations focused on neurodegenerative, paraneoplastic and neurotransmitter disorders and a molecular genetic analysis, whole exome sequencing (WES), was ordered.

**Results:** Thorough neurometabolic workup revealed low serotonin precursors and fluoroxetine was administered with brief improvement. She developed gradual deterioration with weakness, instability and tremor. EEG showed generalised epileptic discharges that correlated with generalised myoclonic movements and behavioural episodes. Brain MRI at 6 years showed mild atrophy of cerebral and cerebellar tissue. Signs of neuronopathy (tremor, weakness and tongue fasciculations) in combination with PME led to suspicion of Spinal Muscular Atrophy (SMA) with PME. EMG showed signs of chronic denervation and motor neuronopathy.

Targeted investigation of WES revealed a heterozygous mutation in ASAH1 gene that was inherited by her father. MLPA was negative. Due to high suspicion, enzymatic activity of acid ceramidase was measured in leukocytes, which was significantly low, confirming the diagnosis of SMA-PME.

**Conclusion:** SMA-PME is an extremely rare lysosomal storage disease due to deficiency of acid ceramidase. Classical form causes Farber syndrome, for which enzymatic replacement therapy is developing. Prompt diagnosis is important as enzymatic therapy will hopefully be available in the near future.

**Disclosure:** No potential conflict stated.

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**HETEROGENEITY IN EARLY INFANTILE EPILEPTIC ENCEPHALOPATHIES OTHER THAN SCN1A – DESCRIPTION OF 21 CASES**

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**Introduction:** Early infantile epileptic encephalopathies (EIEE) reflect a broad spectrum with diverse genetic background in one of the most devastating refractory epileptic syndromes. We describe clinical, electroencephalographic (EEG), neuroimaging, genotypic features and disease-course in 21 cases with EIEE.

**Methods:** Twenty-one patients with genetically confirmed EIEE were included (14 males, 7 females). Demographic features, time of seizure-onset, seizure types, EEG patterns and MRI findings along with treatment and disease course were analyzed. Targeted therapy was administered if indicated.

**Results:** Seizure onset ranged from neonatal period to 7 months old. Genetic testing revealed channelopathies (KCNT1, KCNQ2, KCNA2, SCN2A, SCN8A) in 13 patients, synaptic proteins gene-mutations in 4 (STXBP1, GABRB3, GABRG2) and gene-mutations in intracellular signaling proteins in 4 patients (PLCB1, PIGA, CDKL5). EEG patterns included hypsarrhythmia, burst-suppression, migratory epileptic activity, focal epileptic activity and diverse degrees of background slowing. Brain MRI was normal in most cases or showed mild abnormalities. Majority of patients have profound psychomotor delay. Despite multiple drug combinations, including ACTH and ketogenic diet, most of the patients developed pharmacoresistant epilepsy. Of patients with KCNT1-mutations receiving quinidine as targeted therapy, one showed complete seizure control and significant developmental progress, while the other has a rather unfavorable course. KCNQ2 patients treated with carbamazepine/ oxcarbamazepine show partial seizure control.

**Conclusions:** Patients sharing the same mutation present with heterogeneity in phenotype, EEG features and disease progress. Although genetic identification in EIEE contributes to a better understanding of neuronal function and provides clues for discovering targeted therapies, beneficial effect of the latter in seizure control and development, has yet to be optimized.

**Disclosure:** No potential conflict stated.
POSTER PRESENTATIONS > POSTER SESSION 2
Epilepsy: diagnosis and investigations

P02-46

Genetic Epileptic Encephalopathies: review and analysis of diagnostic paradigm from a tertiary centre

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Introduction: With next generation sequencing (NGS) and whole exome sequencing (WES) several new genes implicated in pediatric epileptic encephalopathies (EE) have been identified. We aim to analyze a cohort of patients with EE regarding its main features and the diagnostic rentability of the genetic techniques used.

Methods: Retrospective descriptive study, of all patients under 6 years with the diagnosis of EE who had genetic study available (2008-2018). Type of study used was individualized. Three groups were analyzed (method used): multigene panel NGS (PNGS) or WES (Group 1), karyotype or array-CGH (Group 2) and specific gene study (Group 3).

Results: Total of 54 patients, 70% with definitive diagnosis. Group 1 (n=17): mutations in genes SCN1A (n=3), PCHD19 (n=2), RARS-2 (n=2), KCNT1 (n=2), MECP2, CHD2, KCNQ2, GPHN and STXBP1 by PNGS; genes DYNC1H1 and WWOW by WES. The most frequent clinical syndromes were early infantile EE (n=7), Dravet (n=3), Ohtahara (n=3) and West (n=2). Only DYNC1H1 patient presented dysmorphisms. Group 2 (n=12): 21 trisomy, ring 20 chromosome and isodicentric 15 chromosome; CNV (n=2) involving genes ABCB1 e MBDS. Group 3 (n=7): mutations in genes SNC1A (n=6), ZEB2 e MECP2 (n=2), corresponding to Dravet, Mowat-Wilson and Rett syndromes. The undiagnosed group included patients with negative PNGS and/or WES (n=16), 9 with variants of undetermined pathogenicity. Lennox-Gastaut syndrome without any positive result. The diagnostic rentability of PNGS was 45% and the direct study of a gene led to definite diagnosis in all cases requested.

Conclusions: Our sample was phenotypically and genetically heterogeneous. The investigation of EE by karyotype, array-CGH and gene analysis is indicated in cases with particular phenotype and/or dysmorphisms. Otherwise, PNGS and WES should be prioritized due to its cost-efficacy.

Disclosure: No potential conflict stated.

P02-47

Soccer and seizures – Case report of teenagers with exercise-induced Epilepsy

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Introduction: ILAE Task Force on Sports and Epilepsy supports active participation in sport for all patients suffering on epilepsy. But what happens when favorite sport elicits seizures? The precipitation of seizures by exercise has been documented with only a handful of cases reported in the current literature. These include patients with idiopathic generalized epilepsy (IGE) as well as focal epilepsies of frontal and temporal lobe origin.

Methods: We report on two male patients from a tertiary epilepsy center with a history of reproducible seizures occurring in association with exercise.

Results: The patients were 12 and 18 years old. The precipitating type of exercise were intensive soccer playing in both, running and inline skating. Not only the level of physical exertion correlated with the seizure occurrence but also the duration of physical activity. The seizure semiology comprised focal motor seizures with impairment of consciousness, automatisms, tonic and hyperkinetic elements. The seizures could be reproduced in both through typical sport activity (soccer). EEG recordings showed interictally left and right temporal discharges, respectively. Ictal recordings documented irregular bilateral synchronous spike and wave discharges. MRI were normal in both. In one patient an CPA6 mutation could be found. Both patients became seizure free on levetiracetam and perampanel, respectively.

Conclusion: Physical exertion can be precipitant for epileptic seizures. We believe, that there are several causes for the seizures in those patients: changes in the pH of serum, temperature and hyperventilation due to low oxygen levels. If a specific physical activity is identified as a trigger, a lower intensity of exercise or an alternative form should be advised. In combination with successive medical treatment complete avoidance can be prevented and fun on playing sports preserved.

Disclosure: No potential conflict stated.
A severe phenotype of early Infantile Epileptic Encephalopathy associated with mutation in CPLX1

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Introduction: CPLX1 gene encodes for a cytosolic protein called complexin 1, involved in modulating presynaptic neurotransmitter release through the SNARE complex. It is postulated that it presents a dual mechanism: on one hand it inhibits the spontaneous vesicular fusion and on the other hand it enhances stimulated neurotransmitter release. CPLX1 mutations have only recently been described in five patients with early infantile epileptic encephalopathy featuring prominent myoclonic seizures (EIEE 63, OMIM 617976).

Methods: We present two monochorionic twins of healthy consanguineous parents from Maghreb, referred for the study of early infantile epileptic encephalopathy. The first clinical signs of the disease appeared when they were 8 weeks old. They experienced clonic amb myoclonic seizures that were pharmacoresistant to multiple treatments and after three years of follow-up they had no acquisition whatsoever of developmental milestones (no eye-contact nor head support or purposeful movements). The EEG shows a severely abnormal background with marked generalized epileptiform activity and brain MRI noted signs of mild cerebral atrophy.

Results: Whole Exome Sequencing analysis identified a homozygous deletion of exon 3 and 4 of the CPLX1 gene. This results in a non-functional protein due to the absence of interaction domains with the SNARE complex.

Conclusion: CPLX1 mutations are consistently associated with a very severe phenotype including refractory myoclonic epilepsy and and no acquisition of developmental milestones.

Disclosure: No potential conflict stated.
P02-50

Neonatal onset Epileptic Encephalopathy, a new CACNA1C-related phenotype

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Introduction: Heterozygous CACNA1C mutations are known to cause Timothy and Brugada syndromes, but have only been associated with early-onset epileptic encephalopathy in a single patient. We report a further patient with a severe neonatal-onset epileptic encephalopathy caused by a CACNA1C mutation.

Methods/case: Newborn male who presented during the neonatal period with a very severe phenotype including refractory epilepsy. He subsequently did not attain any developmental milestones. He is currently 4 years old and requires feeding through a gastrostomy tube due to a severe dysphagia. Brain MRI shows mild global cerebral atrophy but no other remarkable findings. Serial EEG’s have shown a severely abnormal background activity and multifocal spike and wave activity.

Results: Trio-based exome sequencing analysis disclosed a de novo variant in CACNA1C (NM_000719: c.1973T>C; p.Leu658Pro) that is not found in any of the general population databases. This missense variant affects a highly conserved nucleotide on the evolutionary scale. This, together with the result of the pathogenicity predictors (Sift, Polyphen-2 and MutationTaster) that classify it as pathogenic, strongly suggesting that it is indeed disease-causing.

Conclusion: Our findings confirm the association of mutations in CACNA1C with a severe early-onset epileptic encephalopathy and thus expand the spectrum of genetic channelopathies causing of EIEE. Therefore it should be incorporated to EIEE differential diagnosis. Functional studies that provide insight into the underlying epileptogenic mechanisms are warranted.

Disclosure: No potential conflict stated.

P02-51

Diagnostic yield of WES following aCGH in the genetic aetiology of early onset Epileptic Encephalopathies

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Introduction: Early Infantile epileptic encephalopathies (EIEE) are characterized by intractable seizures in infancy, prominent epileptiform discharges and moderate to severe developmental delay. Structural, metabolic or genetic causes (mainly variants of single genes) are underlying etiologic factors of epilepsy and developmental delay. Genetic causes can be identified by chromosome analysis, microarray, targeted gene panels, whole exome sequencing (WES) or whole genome sequencing. Diagnostic yield of array comparative genomic hybridization (aCGH) ranges between 10% to 15% in children with severe epilepsy and of WES is about 35% in EIEE.

We aimed to study diagnostic value of WES following aCGH to detect genetic etiology in patients with EIEE.

Method: The study group consisted of 64 (51% male) patients from 62 families with an inconclusive etiology selected after a detailed work-up including metabolic tests with CSF analysis, high resolution cranial MRI, chromosome analysis and a clinical genetic evaluation to exclude well-known dysmorphic syndromes diagnosed by specific genetic tests. aCGH has been studied in the majority of patients (74.2%) before they were referred for WES.

Results: De novo heterozygous copy number variations (CNVs) related with EIEE were detected in 18.2% (10/55) patients. In 28 (80%) of 35 patients WES demonstrated single gene mutations associated with EIEE. All 7 patients with inconclusive WES results did not show any aCGH abnormalities.

Comments: The diagnostic yield of WES following aCGH in the present study is found to be remarkably high compared to previously reported WES data. Selection of patients with pathological copy number variants as a first step genetic study is recommended.

Disclosure: The first author executed this project granted by the Scientific and Technological Research Council of Turkey (Project No. 214S624) and the Marmara University Scientific Research Committee (No. SAG-B-120516-0209).
**P02-52**

**SLC13A5-related Encephalopathy with Epilepsy in the neonatal period: remarkable improvement on Carbamazepine and Pyridoxal-Phosphate. What worked out so well?**

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**Introduction:** Recessive mutations in the SLC13A5 gene represent a rare cause of early-onset epilepsy and developmental delay. Currently, little is known about electro-clinical presentation and the best management has not established yet. Our aim is to report the description of a severe neonatal case with favourable evolution and to bring more information about treatment response.

**Methods:** A female infant, issued from consanguineous parents, presented, soon after birth, with lethargy, recurrent polymorphic seizures and tonic spasms associated with suppression-bursts (SB) on EEG. Myoclonias were not observed. Preliminary exams including brain MRI were normal. Pheno-barbital showed poor efficacy as well as a trial with Pyridoxine 100 mg IV. Then, Carbamazepine was introduced and we continued Pyridoxine in addition to Folic Acid and Pyridoxal-Phosphate, orally.

**Results:** Seizures rapidly stopped and neurologic examination significantly improved. EEG showed resolution of SB-pattern. Laboratory findings were not suggestive of a specific inherited metabolic disease. Hence, we decided to stop Pyridoxine and Folic Acid and we empirically continued Pyridoxal-Phosphate in association with Carbamazepine (24 mg/kg/day), because of persistent positive EEG and clinical response. Months later, genetic analysis found a homozygous pathogenic variant c.1496C>T-p.507He in the SLC13A5 gene. Actually, at the age of 10 months, the child presents with moderate developmental delay and she only experienced sporadic febrile seizures.

**Discussion:** This case show that subjects harbouring SLC13A5 mutations can present with electro-clinical features of Ohtahara syndrome in the neonatal period. Nevertheless, evolution in our child largely differed from other known causes of Ohtahara syndrome, suggesting that this subgroup of patients could have a better prognosis. Regarding epilepsy treatment, Na+ channel blockers and drugs that enhance the GABA-ergic pathway (e.g. vitamin B6 compounds) seem to be the most efficacious options.

**Disclosure:** No potential conflict stated.

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**P03-01**

**Anti-MOG antibody associated Central Nervous System Demyelination following Bartonella Meningo-Encephalitis: a case report**

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**Introduction:** An unusual case of primary Bartonella meningoencephalitis with subsequent development of anti-MOG antibody central nervous system demyelination in a previously well 4 year old female.

**Methods:** Case notes reviewed.

**Results:** The patient presented with suspected meningitis, seizures and encephalopathic EEG. Antibiotic therapy was commenced followed by IVIG and later by methylprednisolone with some improvement. MRI demonstrated striatal changes suspicious for encephalitis. The patient was asymptomatic after 2 weeks of antibiotic therapy. 2 weeks later, the patient developed bilateral papilloedema with deterioration of vision. MRI demonstrated optic neuritis and new signal abnormality in the right cerebral peduncle. Methylprednisolone resolved her symptoms but the initial CSF showed Bartonella Henselae and appropriate antibiotic treatment was commenced with good response. She was then found to be anti-MOG positive. Follow-up MRI at 3 and 7 months demonstrated evolving relapsing remitting white matter changes with involvement of the right pulvinar nucleus and persistence of the optic nerves changes but the child remained asymptomatic.

**Conclusion:** It is uncommon for Bartonella to cause neurological symptoms (1-3) and associated radiological abnormalities are not well described. The infection either produces neurological compromise due to direct damage or secondary autoimmune/immune-mediated response. Most patients exhibit complete neurological improvement with antibiotics. However there are cases of secondary cerebral vasculitis, infarction and multiple sclerosis-like conditions (4-6). To the best of our knowledge, there are no reported cases of secondary development of anti-MOG antibodies in the literature. The evolving white matter abnormalities described may be due to anti-MOG demyelination or small vessel vasculitis. We also raise the question of whether pre-emptive treatment should be given in the context of progressive imaging abnormalities with a lack of clinical symptoms.

**Disclosure:** No potential conflict stated.
The diverse spectrum of Encephalopathy in Acute Paediatric Neurology Services: a multi-centre evaluation

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Introduction: Encephalopathy is a common acute presenting feature in paediatric neurology, with multiple aetiologies that may respond to different early intervention to avoid significant long-term morbidity. We aimed to estimate the frequency and aetiologies of encephalopathy within an inpatient paediatric neurology service.

Methods: Consecutive inpatient case notes were retrospectively reviewed at two paediatric neurology centres over a three month period. Those with features of encephalopathy (Lancet Infect Dis. 2010 10(12): 833-44) were included and then grouped into ‘encephalitis’, ‘epilepsy’, ‘stroke’, and ‘other’ based on the final clinical diagnosis.

Results: Encephalopathy featured in 43% (n=133/307, male 55%, median age 6.25 years, range 0.02 - 16.42) of all neurology inpatients. Epileptic encephalopathy was the most common aetiology, occurring in 47% (n=64), including 14% (n=18) with infantile spasms. Encephalitis occurred in 27% (n=36), with an infectious aetiology identified in 8% (n=11), and a likely autoimmune aetiology in 19% (n=25); this comprised acute disseminated encephalomyelitis in 3% (n=4), NMDAR-ab in 3% (n=4), immune-associated epilepsy in 2% (n=3), Rasmussen’s in 1% (n=1), and presumed antibody-negative in 11% (n=15). Stroke occurred in 11% (n=15), including four patients with an ischaemic middle cerebral artery infarction. The remaining 15% (n=18) comprised a variety of aetiologies including metabolic, toxic, and hypertensive.

Conclusion: Encephalopathy was a frequent presentation, occurring in almost half of paediatric neurology inpatients. The causes are diverse and investigative algorithms complex, often causing delays in initiating treatment. Newer approaches are required to identify potential systems-based biomarkers, in addition to disease specific biomarkers, that could guide early diagnosis and treatment across a range of aetiologies.

Disclosure: No potential conflict stated.

Hashimoto Encephalitis: a rare cause of Encephalitis associated with classical clinical profile

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Introduction: Antibody-mediated encephalitis constitutes a group of inflammatory brain diseases which can be associated with status Epilepticus (SE).

Methods: A 10-year-old girl was admitted for a persistent SE. Invasive ventilation was necessary as well as deep sedation and anti-epileptic treatment. Biological assessment, brain scan and bacteriological and viral cerebral spinal fluid (CSF) analysis were normal. MRI brain showed a vasogenic oedema. The initial search for autoimmune antibodies (NMDAR, GABA-B-R, GlutamateR, GlycineR antibody, etc.) on CSF was negative. Moderate hypothyroidism with high anti-TPO antibodies was noticed. Thyroid ultrasound confirmed the appearance of thyroiditis. Because of a likely autoimmune etiology, a high-dose corticosteroid therapy was introduced in combination with plasmapheresis, leading to clinical improvement.

Discussion: Hashimoto encephalitis is also known as Steroid Responsive Encephalopathy associated with Autoimmune Thyroiditis (SREAT). Epileptic seizures are observed in 70% of cases and require intensive treatment in order to limit brain damage. Thyroiditis is noticed with increased anti-thyroglobulin and TPO or anti-thyroperoxidase antibodies. It has not been shown that thyroid antibodies can directly affect the brain, and the abnormalities in thyroid hormone levels are generally too mild to explain the brain disease. Some of these encephalitis cases are due to other autoantibodies, such as to the NMD-A, GABA-B-R. The standard treatment consists in a systemic corticosteroid therapy, while other lines of immunotherapy are sometimes needed.

Conclusion: Most autoimmune encephalitis are infectious or paraneoplastic. When those causes are excluded, antibody-mediated encephalitis should be considered.

Disclosure: No potential conflict stated.
MOG-Ab-associated Disease presenting with relapsing Meningoencephalitis with high intracranial pressure in a four-year-old girl

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Objective: Antibody against myelin oligocendrocyte glycoprotein (MOG-Ab) is identified in a range of inflammatory disorders of central nervous system with a large spectrum of presentation. In children it is more associated with acute disseminated encephalomyelitis (ADEM) and multiphasic ADEM.

Methods: Case report of a four-year-old girl presenting with a second episode of meningoencephalitis and positive serum MOG-Ab.

Results: A previously health girl presented at 3-year-old with fever, vomiting, headache. She was admitted and investigation revealed: cerebrospinal fluid (CSF) 54 cells; magnetic resonance imaging (MRI): leptomeningeal enhancement and cortical-subcortical lesions in T2. She was started on antibiotics. After 48 hours she had seizure and after 1 week: aphasia, disarray, abnormal posture with mouth wide open. MRI got worse and then she was started at intravenous immunoglobulin (IVIG). Fever and neurologic symptoms stopped after IVIG. No infectious agent or autoimmune encephalitis antibodies were found (MOG-Ab not tested). She was discharged normal and MRI after 2 months was normal. After one and half year were found (MOG-Ab not tested). She was discharged normal and one child. Extensive viral PCR identified 3 viruses in a single patient only: enterovirus-D68, coxsackievirus A6 and sapovirus. Enhancing leptomeningeal gadolinium enhancement and T2-hyperintense lesions in brainstem, thalamus, cortical regions. Headache became worse, there was papilledema and slighted decreased level of consciousness. She was started at antibiotics and IVIG with excellent response after IVIG. Twenty days after IVIG she had headache again. MRI showed resolution of most lesions. CSF-12 cells, high opening pressure (38cmH2O). She was started at oral steroids and acetazolamide. Serum MOG-Ab came positive in high titer.

Conclusion: Recurrent meningoencephalitis with elevated intracranial pressure associated with MOG-Ab is not yet reported in pediatric population. This is an atypical presentation of MOG-Ab-associated disorder.

Disclosure: No potential conflict stated.
Paediatric Catatonia in a young child with anti NMDAR Autoimmune Encephalitis; a case report and brief literature review

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Introduction: Autoimmune encephalitis is a rare yet rising cause of immune mediated encephalopathy in children. Pediatric Anti-N-Methyl-d-Aspartate Receptor (NMDAR) Encephalitis is among the commonest variants of autoimmune encephalitis. Catatonia has been reported in pediatric Anti NMDAR encephalitis in adults but not a very typical symptoms in pediatric age group.

Clinical case: An 8 years old previously healthy girl presented initially with seizures and increased sleepiness following a 2 weeks of flu like illness. She then started to adopt a catatonic posturing for long time. She underwent extensive work up including infection screening, biomarkers of end organ damage, metabolic testing, autoimmune serology, serial CT/MRI scans and tumor surveillance work up. The diagnosis of anti NMDAR encephalitis was confirmed about 2 weeks after initial presentation.

Discussion: Anti NMDAR encephalitis continues to represent a challenging clinical syndrome with regard to clinical suspicion, laboratory testing and limited management options. Clinical symptoms are rather nonspecific adding to the diagnostic difficulty and treatment dilemma and include a wide range of neuropsychiatric symptoms. Catatonia is disturbance of motor behavior as a rigid, immobile position that is held for a long time. Catatonia was reported in the context of anti NMDAR encephalitis in adults whereas reporting in children is rather rare. We are reporting what we believe the youngest child presenting with catatonia in the context of anti NMDAR encephalitis in current literature up to our knowledge.

Conclusion: Catatonia is uncommon yet serious neuropsychiatric clinical feature which should raise suspicion of underlying autoimmune encephalitis as potential diagnosis. Although rare in children, catatonia cab be the major clinical presentation in children with anti NMDAR encephalitis. Urgent evaluation and utilization of available immunotherapies are crucial for improving future neurodevelopmental outcome.

Disclosure: No potential conflict stated.

An atypical presentation of Miller-Fisher Syndrome in an adolescent

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Introduction: Parinaud syndrome, also known as dorsal midbrain syndrome, is characterised by a combination of signs, including upgaze palsy, convergence-retraction nystagmus, eyelid retraction and pupillary light-near dissociation. It is caused by pretectal or tegmental lesions of upper brainstem. Miller Fisher syndrome, characterised by the triad of ataxia, areflexia, ophtalmoplegia, has rarely been reported to present as Parinaud syndrome in adults. To our knowledge, this clinical manifestation has not been previously described in children.

Methods: This is a case presentation of an adolescent girl with Miller Fisher syndrome presenting with Parinaud syndrome as a prominent clinical semiology.

Results: A previously healthy 13 year-old girl presented with blurred vision and diplopia, ten days after a viral infection. Initial examination revealed Parinaud’s syndrome. Rest of neurological examination on admission was normal. Brain imaging (MRI, MRA) did not reveal any abnormal findings and CSF findings were also normal. During the first days after admission she gradually deteriorated, showing complete external ophthalmoplegia, unsteady gait, absent deep tendon reflexes of lower limbs with normal muscle power. With the clinical suspicion of Miller Fisher syndrome IVIG was administered, leading to subsequent resolution of her symptoms. AntiGQ1b and antiGD1b antibodies came back positive. On one-month follow up, her neurological examination revealed diplopia in left gaze, and a second dose of IVIG was administered, with good response. She remains asymptomatic two months from disease onset.

Conclusion: Rarely Miller Fisher syndrome can present as Parinaud’s Syndrome. As the typical semiology of ataxia and areflexia may not be present initially, high index of suspicion is required in order to recognise and treat those patients promptly.

Disclosure: No potential conflict stated.
**Introduction:** Combined Central and Peripheral Demyelination (CCPD) is defined as concurrent demyelination of central and peripheral nervous system. It is a heterogenous group, that can run either a monophasic or a progressive course, fulfilling MS or NMOSD criteria. A minority of these patients shows positive Myelin Oligodendrocyte Glycoprotein (MOG) antibodies, which seem to be a biomarker of a phenotypically distinct group of demyelinating diseases, with unknown prognosis.

**Methods:** A previously healthy 9-year-old boy presented with gradually worsening bilateral leg weakness over the last month, as well as back pain and urine incontinence during the last 24 hours. At presentation, he had decreased muscle power of lower limbs, and absent deep tendon reflexes. Brain imaging revealed multiple non-contrast enhancing supra and infratentorial parenchymal lesions, while spine MRI showed an extensive lesion, as well as ippsauric thickening. Lumbar puncture revealed mild pleocytosis and elevated total protein, while extensive lesion, as well as ippouridic thickening. Lumbar puncture revealed mild pleocytosis and elevated total protein, while extensive lesion, as well as ippouridic thickening. Lumbar puncture revealed mild pleocytosis and elevated total protein, while extensive lesion, as well as ippouridic thickening. Lumbar puncture revealed mild pleocytosis and elevated total protein, while extensive lesion, as well as ippouridic thickening. Lumbar puncture revealed mild pleocytosis and elevated total protein, while extensive lesion, as well as ippouridic thickening. Lumbar puncture revealed mild pleocytosis and elevated total protein, while extensive lesion, as well as ippouridic thickening. Lumbar puncture revealed mild pleocytosis and elevated total protein, while extensive lesion, as well as ippouridic thickening. Lumbar puncture revealed mild pleocytosis and elevated total protein, while extensive lesion, as well as ippouridic thickening.

**Results:** Patient showed substantial improvement, and after a few days muscle power returned to normal. Repeat MRI initially was undifferentiated, but at 9 months brain lesions showed improvement, while a new lesion, as well as expansion of previous lesions were detected on spinal MRI, fulfilling NMOSD criteria (longitudinally extensive transverse myelitis). Three months later regular follow up revealed optic neuritis.

**Conclusion:** NMOSD can rarely present as CCPD with MOG antibodies. Close follow up is necessary in order to detect promptly disease progress and administer appropriate treatment.

**Disclosure:** No potential conflict stated.
An interesting case of Tuberculosis Pachymeningitis

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Introduction: Pachymeningitis is a fibrosing and inflammatory illness characterized by a thickening of dura mater, that can be caused by a number of autoimmune, malignant and infectious diseases. It is more frequently described in adults and rarely in children.

Methods: Case Report by medical records review.

Results: A previously healthy eight-years-old child presented with right hemibody paresthesias, followed by right hemiclonic movements which lasted approximately thirty minutes. She was taken to a local hospital, where the clonic movement ceased and she manifested right hemiparesis, slurred speech, and central facial palsy. Conscience was preserved at all times. Brain Magnetic Resonance Imaging (MRI) showed hemorrhagic venous infarction secondary to sigmoid and transverse sinus thrombosis. Thrombophilia causes were excluded after extensive investigation. She was started on enoxaparin and discharged a week later, with complete resolution of hemiparesis. She presented with two similar events in the following months, in one of which she also manifested bilateral amaurosis. Oxcarbazepine was introduced and the patient was referred to our service where pachymeningitis was identified as the cause of venous thrombosis. Brain MRI was repeated demonstrating diffuse leptomeningeal enhancement. Cerebral Spinal Fluid analysis showed 170 cells (30% lymphocytes, 26% monocytes, 40% plasmocytes), 0 blood cells, 40mg/dl protein, 42 mg/dl glucose, 16.2 lactate. She had a history of close contact with a school teacher who was withdrawn from activities due to the disease. Brain MRI revealed occipitoparietotemporal paroxysms. She was started on antituberculosis treatment and did not present any similar episodes.

Conclusion: Therefore, we conclude that tuberculosis must be considered as a likely cause of pachymeningitis in children, specially in endemic countries.

Disclosure: No potential conflict stated.

Clinical, therapeutic and evolutive features in Guillain-Barré Syndrome

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Introduction: Guillain-Barré syndrome is an acute immune-mediated polyneuropathy, with neurological symptoms two to four weeks after an infection. The classic presentation of Guillain-Barré syndrome begins with paresthesia in the toes and fingertips and asymmetric weakness that may involve the limbs and, in severe cases, the respiratory muscles.

Material and methods: This is a retrospective study which includes 46 patients admitted in the Pediatric Neurology Clinic at ‘Alexandru Obregia’ Clinical Hospital, between 01.01.2009 – 26.02.2019. They were diagnosed with Guillain-Barre syndrome based on clinical signs completed by lumbar punctions and electrophysiological examinations. The patients were admitted in the extension periods, at the onset of the disease in a few cases. We followed: the severity of the motor weakness, association of the impairment of the muscular cranial nerve or respiratory function, association of the vegetative symptoms, electrophysiologic features, therapeutic interventions, response to the treatment, duration of the remission, presence or absence of motor deficit after remission.

Results: In our study most of the patients did not associate respiratory or vegetative symptoms. The limb motor deficit was of varying degrees, ranging from motor deficit of the lower limbs with possible walking to lost ambulation and complete tetraplegia. The electrophysiological examination data correlated with the degree of motor deficit. Most patients received the first-line treatment with immunoglobulin 2g/kg/day within 5 days with complete remission of symptomatology and without any adverse events. In cases with severe motor weakness, we performed plasmapheresis after the immunoglobulin treatment, with slow remission.

Conclusions: Guillain Barre Syndrome is an autoimmune disorder that may be an urgent medical condition. Early diagnosis and initiation of appropriate treatment can have favorable outcome and complete remission without residual deficit.

Disclosure: No potential conflict stated.
A 10-year single centre review of Transverse Myelitis-Plus

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Introduction: The incidence of Acute Flaccid Myelitis (AFM) associated with enterovirus infection occurring in biennial clusters since 2012 has been reported in the US (BMJ 2018, 18; 363:k5246) and recently in Europe. Previously, cases with transverse myelitis (TM) with anterior-horn cell or peripheral nerve involvement have been collectively termed TM-plus (Neurology 2016; 87:S46-S52). We aimed to identify cases of TM-plus from a retrospective cohort of children to identify potential cases of “undiagnosed” AFM, and to evaluate the clinical and radiological features alongside long-term outcome.

Method: Consecutive cases of children (<16 years of age) who presented to a large paediatric neurosciences centre from 2009 to 2016 fulfilling the Transverse Myelitis Consortium Working Group criteria modified for the paediatric population (Neurology 2015; 84:341-349) were retrospectively evaluated for additional features of anterior horn-cell involvement (fulfilling criteria for AFM (current treat options neurol (2017) 19: 48)) or peripheral nervous involvement; and were collectively evaluated with the contemporary TM-plus cohort (2016-2018).

Results: 25 cases of TM were identified, 7 of which were excluded from further analysis; MS (n=6), ADEM (n=1). 8 cases of TM-plus were identified, 4 before 2016 and 4 after, all associated with a viral prodrome. Flaccidity (n=8) and asymmetry (n=6) was noted at presentation, with corresponding nerve conduction studies revealing a motor axonopathy with sensory sparing (n=6) and anterior horn cell involvement confirmed in 3 cases. All cases with anterior horn cell involvement had poor outcomes while both cases with good outcomes had peripheral involvement and normal MRI brains.

Conclusion: TM-plus was detected in our cohort from 2009 to 2016 with biennial clusters noted in 2016 and 2018. The clinical presentation, investigations and long term outcomes appear consistent in both groups.
**P03-14**

**Paediatric anti-MOG antibody-positive cortical Encephalitis – A rare presentation**

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**Introduction:** Myelin oligodendrocyte glycoprotein (MOG) is a protein present in the outer coating of the myelin sheath in the CNS (1). Anti-MOG antibodies have been implicated in several inflammatory neurological disorders. While anti-NMDAR encephalitis has been described post-varicella, we believe this is the first description of a child with a unique presentation of anti-MOG cortical encephalitis following chicken pox (2).

**Methods:** Case report

**Results:** A four-year-old boy presented with a 10-day history of fever, headache, irritability, abnormal gait and incontinence. The day following admission he was found to have a dense right hemiparesis and facial palsy. MRI revealed extensive cortical signal abnormality and restricted diffusion confined to the left hemisphere but not confined to a vascular territory. He then developed focal seizures with eye deviation and ipsilateral arm jerking. Repeat MRI four days later demonstrated progressive cortical signal changes involving the right cerebral hemisphere. A diagnosis of encephalitis was made. An extensive viral and autoimmune work up revealed positive anti-MOG-antibodies in serum. Other CNS autoantibodies and infection screen in blood and CSF were negative. He completed 14 days of acyclovir and antibiotics was also treated with high dose steroids, plasma exchange therapy followed by IV immunoglobulin and made a good recovery before being referred for neuro-rehabilitation.

**Conclusion:** To the best of the authors’ knowledge, we present the first known case of anti-MOG associated cortical encephalitis in a paediatric patient.

**Disclosure:** No potential conflict stated.

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**P03-15**

**A paediatric patient with Anti-N-Methyl-D-Aspartate Receptor Encephalitis: excellent outcome**

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**Introduction:** Anti-N-methyl-D-aspartate receptor (anti-NMDAR) encephalitis is a condition characterized by multi-stage progression with psychiatric and behavioural symptoms, movement disorder, seizures, speech disturbances, changes of consciousness and dysautonomias. The pediatric population with anti-NMDAR encephalitis may be different from that of the adults (more neurologic in children, more psychiatric in adults).

**Methods and Results:** A 8-month-old girl presented with fever and seizure and was subsequently treated for proven herpes simplex virus type 1 encephalitis. Shortly thereafter, she developed irritability, seizure, orolingual-facial dyskinesias, choreo-dystonic movements, hemiparesis, dysphagia and strabismus. Serum analysis confirmed anti-NMDAR antibodies. The second course of aciclovir was started. Electroencephalography showed poor organization of background activity with ‘extreme delta brush’ pattern. Brain magnetic resonance imaging showed abnormal signal in the right occipitotemporal parietal lobes with involvement of the cortex and the adjacent white matter. Firstly, the patient received intravenous immunoglobulin and then high-dose intravenous methylprednisolone followed by oral prednisolone. At 15 days’ follow up, irritability, orolingual-facial dyskinesias and dysphagia had disappeared. At 3 months’ follow-up, her abnormal movements, hemiparesis and strabismus had completely resolved.

**Conclusion:** As a result, early immunotherapy offers the potential for excellent neurological recovery.

**Disclosure:** No potential conflict stated.
P03-16

Key clues for diagnosis of Giant Axonal Neuropathy: a case report

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Introduction: Giant Axonal Neuropathy is a rare hereditary autosomal recessive neurodegenerative disease and characterized by neurons with abnormally large axons due to intracellular filament accumulation. The swollen axons affect both the peripheral and central nervous system.

Methods and Results: We report a 10-year-old male patient having walking problems with axonal sensory-motor neuropathy. The patient had also kinky hair. Brain magnetic resonance imaging showed periventricular and deep white matter, cerebellar white matter, brainstem involvement and increased T2 weighted signal intensities in the medial thalami. Sequence analysis of GAN gene demonstrated a previously unreported homozygous mutation c.1345A>C (p.Thr449Pro)(p.T449P).

Conclusion: We highlight clinical manifestations and findings of peripheral and central nervous system in diagnosing of Giant Axonal Neuropathy.

Disclosure: No potential conflict stated.

P03-17

Assessment of the clinical features of Migraine in children with signs of Immune Deficiency

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Objective: To evaluate the clinical features of migraine in children with signs of immune deficiency.

Materials and methods: We examined 45 children with migraine in the interictal period, aged 6 to 18 years, including 32 girls and 13 boys. In all patients, the nature of headaches corresponded to the diagnostic criteria of migraine, the secondary genesis of the disease was excluded with the help of a comprehensive examination. The ID-migrine test was used to confirm the diagnosis. Much attention was paid to immunological studies of cellular immunity factors.

Results: According to personal data, 38% of children had an allergic background, 25% of patients had a hereditary disease, 37% of patients had an unclear etiology of the onset of migraine attacks. Of the VAS scale, it was found in 87% of children during an attack that the headache intensity reached 9-10 points, in 13% of children this indicator varied between 7-9 balls. According to the ID-migrine test, 100% of the data gave a screening confirmation of the diagnosis. An assessment of VNS indicators from the Guillaume-Wayne table showed that in 59% of children with a diagnosis of childhood migraine, the parasympotic orientation of the tone prevailed, in 41% of children, signs of sympathetic orientation were observed. According to immunological analyzes, the absence of significant deviations of cellular immunity indices was revealed, with the exception of a significant increase in B-lymphocytes, which indicates a postponed inflammatory process.

Conclusion: A shift in indicators and signs of autonomic dysfunction (89%) were observed in the examined group. It was found a slight deviation of cellular immunity in the interictal period, compared with the period of a migraine attack.

Disclosure: No potential conflict stated.
First-line treatment with Natalizumab in paediatric Multiple Sclerosis

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Introduction: Natalizumab has been shown to be an effective treatment in Relapsing Remitting Multiple Sclerosis (RRMS). There are few reports of its use as first-line disease-modifying treatment (FL-DMT) in childhood RRMS. The risk of Natalizumab-associated progressive multifocal leucoencephalopathy (PML) is the major concern, and can be stratified by JC virus (JCV) antibody status.

Objective: To report 3 year follow-up of a child with RRMS treated with Natalizumab as FL-DMT; review the literature concerning paediatric use of Natalizumab and clinical outcomes.

Methods: A 10-year-old boy presented with an encephalopathic episode consistent with acute demyelinating encephalomyelitis (ADEM) followed by separate episodes of optic neuritis and status epilepticus over 12 months. Neuroimaging demonstrated demyelinating CNS lesions disseminated in space and time responsive to steroid treatment. A diagnosis of RRMS was confirmed. Due to the aggressive clinical course, he was commenced on Natalizumab as first-line therapy rather than beta interferon or glatirameric acetate.

Results: Treatment with Natalizumab resulted in cessation of MRI and clinical disease activity over a 3-year follow-up period. JCV status remaining negative. Annualized relapse rate reduced from 2.0 to zero. EDSS improved from 3.0 to 1.5. Investigation of hyperbilirubinemia during treatment uncovered an additional diagnosis of Gilbert syndrome in this patient.

Conclusion: Whilst the use of Natalizumab as FL-DMT could be considered in children with RRMS, the optimal duration of this treatment in children is unclear. The risk of PML appears lower in children. No cases of Natalizumab-associated PML have been reported in children < 18 years. Although the use of Natalizumab should be approached with caution, our case and reported literature suggest good outcomes in children who have negative JCV status. Seroconversion to JCV positivity should trigger consideration of alternate DMT.

Disclosure: No potential conflict stated.

Evolution of the neuroimaging findings in a patient with Enteroviral Infection: limbic involvement

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Objective: Enteroviruses are usually responsible for benign and reversible clinical syndromes. Postinfectious immune-mediated syndromes are increasingly being recognized. Here we present a patient who developed limbic encephalitis after enteroviral infection.

Case: A healthy immune-competent 13-year-old girl presented with vertigo and dystonia after a respiratory infection. One month later she developed stereotypic movements, unbalanced gait, speech difficulty. On admission she had normal conscious level, pyramidal signs, truncal ataxia, and dystonic episodes mainly involving the trunk. Physical examination, metabolic, paraneoplastic, rheumatologic and toxic screening were normal. CSF was clear, acellular, with normal protein and glucose levels. Cranial MRI showed symmetrical restricted diffusion of bilateral putamina and caudate. She received IVIg with limited response. Upon confirmation of enteroviral infection in the CSF, acyclovir, ribavirin and interferon were administered. Her clinical status, consciousness and tone worsened. She was intubated on day 13; developed severe oral dyskinesia treated with benzodiazepines and gabapentin. Follow-up MRI (20th day) showed disappearance of previous findings and new lesions in bilateral cingulate cortex and left hippocampus. A second lumbar puncture was positive for enterovirus RT-PCR and negative for NMDAR and VGKC antibodies. She received IVIg and steroids. When discharged after 3 months, she could sit with support and breathe spontaneously. Four years after presentation, she is able to attend school, and has a steppage, wide-based gait.

Conclusion: Enteroviruses can cause acute and delayed diseases in the nervous system. To our knowledge this is the first report of limbic encephalitis after enteroviral encephalitis. The absence of detectable antibodies against neuronal antigens suggest the role of cellular immunity or unknown antigens.

Disclosure: No potential conflict stated.
Acute Postinfectious Cerebellar Ataxia due to Adenovirus

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Introduction: The most common cause of Acute Cerebellar Ataxia (ACA) in children is a preceding infection. This is a report about a previously healthy three and a half year old girl presented to our emergency department with acute onset headache, gait difficulties and focal tremor. Four days prior to admission she developed a febrile upper respiratory infection.

Methods: The patient was conscious, with normal vital signs. Clinical and neurological examination revealed broad based ataxic gait and tremor in her left hand. Cranial nerve examination produced normal results. Muscle tone and strength were bilaterally normal. Deep tendon and plantar reflexes were normal. There were no signs of meningeal irritation. Lab tests (including creatine kinase) and Computed Tomography (CT) scan of the brain were performed at admission as well as lumbar puncture and brain Magnetic Resonance Imaging (MRI).

Results: Paraclinical and imaging investigations did not yield any pathological results except for the positivity for adenovirus DNA revealed by Polymerase Chain Reaction (PCR) in CSF. Intravenous pulse of methylprednisolone was given daily for three days along with simetidine. After completing the therapy, the child was able to walk without support but cerebellar ataxic gait was evident as well as fine tremor. Full recovery occurred after 5 days. On the base of performed investigations and clinical evolution the patient was diagnosed with Acute Postinfectious Cerebellar Ataxia (APCA) associated with adenovirus.

Conclusion: Our case study illustrates a rare cause of ACA but common cause of upper respiratory infection and the favorable outcome after short-term immunosuppressive treatment.

Disclosure: No potential conflict stated.

Paediatric-Onset Multiple Sclerosis: 8 years of experience in a tertiary centre

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Background: Multiple sclerosis (MS) is a chronic condition that may have pediatric onset. Our objective was to provide a detailed biodemographical and clinical characterization of the pediatric-onset MS population that has been accompanied at our centre, since 2010.

Materials and Methods: We performed a retrospective, observational and unicentric study. We included data of patients’ records with MS diagnosis confirmed before 18 years of age, according to current diagnostic criteria, since 1st January 2010.

Results: In a group of 32 patients, 30 (73.3% female gender) fulfilled the inclusion criteria, with mean age at diagnosis of 15.5±2.2 years and median value of Expanded Disability Status Scale (EDSS) score at diagnosis of 1.5±0.9. All cases had a diagnosis of Relapsing-Remitting MS and in 43.3% optic nerve involvement was the first clinical manifestation. A concomitant immune-mediated disease was found in 10 patients (26.7%) and a positive familial history of MS in 20% of them. At the time of diagnosis, 50% presented gadolinium enhancement lesions in magnetic resonance imaging (MRI) and the study of cerebrospinal fluid revealed the presence of oligoclonal bands in 85.7%. Interferon beta-1a was the first treatment option in the majority of the patients (30%) but, in 20%, the first therapeutic option was natalizumab. Considering a mean follow-up of 4.1±2.5 years, treatment was changed in 67.9% of cases. EDSS of last visit had a mean of 1.4±0.6.

Conclusion: This study provides new data coming from our pediatric-onset MS population and our results are in line with the most recent publications in the field. Besides allowing an important descriptive analysis of this population characteristics, so far, this study also provides a window of opportunity for further prospective analyses.

Disclosure: No potential conflict stated.
**P03-22**

**Demyelinating Diseases associated with anti-MOG Antibodies – 3 different cases of an expanding spectrum**

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**Background:** Anti-myelin oligodendrocyte glycoprotein (anti-MOG) antibodies are associated with a broad spectrum of central nervous system (CNS) demyelinating diseases. Our objective is to present 3 different phenotypes of the anti-MOG spectrum conditions.

**Clinical cases:**

Case 1: 13-year-old girl, evaluated for loss of right visual acuity and retroocular pain. Faced with the clinical diagnosis of optic neuritis (ON), an MRI confirmed diffuse edema of the optic nerve, with a remaining negative etiological study. Two years later, a new ON was diagnosed, with anti-MOG detected in circulation. The recovery was complete, under steroid therapy.

Case 2: 11-year-old boy, admitted for drowsiness, behavioral changes and gait instability. An MRI revealed multifocal lesions of the white matter, corroborating the diagnosis of acute disseminated encephalomyelitis (ADEM). After 17 months, he developed a right ON, which, 11 months later, relapsed, but on the left. Having identified anti-MOG antibodies in circulation, he started azathioprine after steroids, without new episodes.

Case 3: 2-year-old girl hospitalized for ADEM, with good response to intravenous corticosteroid therapy. Six months later, new exuberant white matter lesions were observed, with topography suggestive of the diagnosis of a neuromyelitis optica spectrum disease (NMOSD). Anti-MOG antibodies were identified in serum, at this moment. After a cycle of intravenous corticosteroid therapy, she initiated monthly intravenous immunoglobulin with favorable clinical and imaging evolution.

**Conclusion:** Anti-MOG mediated diseases constitute a very diverse and still expanding spectrum of neurological conditions. In these 3 cases, it was possible to illustrate 3 different clinical phenotypes, with different therapeutic approaches.

**Disclosure:** No potential conflict stated.

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**P03-23**

**Panuveitis, CNS involvement and skin manifestations in a 12.5 years old boy with Adamantiades- Behçet’s Disease**

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**Aim:** To present a boy with panuveitis, CNS involvement and skin manifestations due to Behçet’s disease.

**Case Report:** A boy, 12.5 years old, presented with red eyes and visual acuity reduction. He suffered from mild headache but neurological examination was normal. Folliculitis rush on arms and legs presented periodically. The fundoscopy revealed panuveitis, papilleoedema and macula of retina swelling. Laboratory testing was negative: TBC, biochemistry, antinuclear antibodies (abs), immunophenotyping blood analysis, HLA B27, B5, B51, Wright Coombs test, abs for treponema, toxoplasma, bartonella, and viruses, Coombs, serum angiotensin-converting enzyme and Mantoux. Erythrocyte sedimentation rate was 58 mm/h. Protein electrophoresis showed IgG polyclonal increase. A chest high resolution CT did not documented sarcoidosis. Brain MRI showed high resolution T2 signal frontal, parietal, occipital and cerebellar, suggestive of Behçet’s disease without thrombosis. CSF findings were: white blood cells 8/mm3, pressure 35cmH20. Culture, cytology, oligoclonal bands and IgG index were normal whereas increased Q index suggested BBB disruption. E.E.G did not reveal any epileptic activity. Cardiac ultrasound revealed mitral valve prolapse and insufficiency. Treatment included dexamethasone eye drops, parenteral methylprednisolone, 1 gr, 3 days, followed by 1 mg/kg, tapering up to prednisone 5 mg/day until now. He commenced simultaneously on infliximab, switched to adalimumab due to anaphylactic reaction. Azathioprine was added 5 months later. Improved brain M.R.I. findings reported after one month treatment whereas uveitis and vision after three weeks. During two uveitis relapses, 8 and 11 months later, improvement achieved with dexamethasone eye drops and without ulceration at the moment.

**Conclusion:** Behçet’s disease is a multisystematic vasculitis with severe complications, particularly impaired vision and CNS involvement. Our patient presented no CNS complications. We are monitoring closely the uveitis status.

**Disclosure:** No potential conflict stated.
**P03-24**

**Anorexia as presenting symptom of NMDA Receptor Encephalitis**

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**Introduction:** N-methyl-D-aspartate receptor (NMDAR) encephalitis is the most common form of antibody-mediated encephalitis, and surpasses the frequency of any single viral cause of encephalitis in young people. Adults typically present with psychiatric symptoms. Children usually present with seizures or movement disorders.

**Case report:** We report on a 10-year-old girl with NMDAR encephalitis presenting with anorexia and vomiting resulting in significant weight loss. Initially she was wrongly diagnosed as having an atypical form of anorexia nervosa. Extensive diagnostic investigations including inflammatory parameters in blood and cerebrospinal fluid and cerebral MRI were normal. The onset of symptoms two weeks after an infectious episode, however, was a clinical hint suggestive for an auto antibody-mediated encephalitis. The presence of anti-NMDAR antibodies in blood confirmed the diagnosis.

**Discussion:** NMDAR encephalitis may present with psychiatric symptoms, such as depression, anxiety, obsessions, hallucinations or delusions. Consequently, patients may initially be diagnosed with psychiatric diseases, hindering early correct diagnosis and treatment. Presentation with anorexia, as in the proposita is rare. To the best of our knowledge only two similar cases were reported in literature. However, studies with animal models showed that NMDAR might be involved in control of food intake.

**Conclusion:** Antibody-mediated encephalitis can present with psychiatric symptoms. Pediatric neurologists should be aware of the fact that anorexia may be the presenting symptom of NMDAR encephalitis. This is important given the fact that NMDAR encephalitis is a treatable disease. Only timely diagnosis can ensure correct treatment and will improve outcome.

**Disclosure:** No potential conflict stated.

**P03-25**

**Anti-N-methyl-D-Aspartate Receptor Encephalitis treated with Cyclophosphamide using the same protocol in children**

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**Background:** Although administration of cyclophosphamide or rituximab has been established as second line treatment for anti-N-methyl-D-aspartate receptor (anti-NMDA-R) encephalitis, detailed reports such as dosage for children are few. We report 3 patients who received cyclophosphamide including the dosage of drug.

**Methods:** We administered cyclophosphamide 500 mg/m² per months to three children with anti-NMDA-R encephalitis.

**Case:** Patient 1 was a 14-year-old girl who was diagnosed due to characteristic symptoms such as incomprehensible behavior, auditory hallucinations, and visual hallucinations, and anti-NMDA-R antibody. The patient received steroids, immunoglobulin, and plasma exchange therapy; however, this first-line treatment was ineffective. Three months after onset, the patient was administered cyclophosphamide 500 mg/m² per month for 3 months, which resulted in a decrease in abnormal movements, and she gradually began to recover. Seven months after onset, she was discharged without any apparent sequelae. Patient 2 was an 11-year old girl who was diagnosed due to disturbed consciousness, involuntary movements and anti-NMDA-R antibody. The patient responded to cyclophosphamide 500 mg/m², which was administered on day 18. After 2 courses of treatment, she was discharged without any apparent sequelae on day 72. Patient 3 was 15-yeae old boy who was diagnosed due to disturbed consciousness, involuntary movements and anti-NMDA-R antibody. The patient responded to cyclophosphamide 500 mg/m², which was administered on day 46. In three patients, there was no side effect except that transient hair loss and granulocytopenia were observed in patient 2.

**Conclusions:** We believe that cyclophosphamide 500mg/m² per month can be safely used in children without eliciting any serious side effects and that early treatment should be initiated.

**Disclosure:** No potential conflict stated.
Safety and efficacy of a Neurokinin–1 receptor antagonist in Subacute Sclerosing Panencephalitis: a Phase 2 randomized clinical trial

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Introduction: Subacute sclerosing panencephalitis (SSPE) is a chronic infection where measles virus (MV) spreads in the brain by fusion using, among others, neurokinin–1 receptors (NK–1R). Genetic and pharmacological inhibition of NK–1R reduces CNS infection and spreading of MV in mice. Aprepitant is a NK–1R antagonist used in treating chemotherapy-induced vomiting. We evaluated whether aprepitant has clinical effects on SSPE patients. Ethical approval was obtained (B104ISM4066849).

Methods: SSPE patients (n=62, age 10–25 years) in stage II (ambulatory) or III (nonambulatory) received 250 mg aprepitant or placebo for two weeks, and the same course was repeated after two months. Neurological state was assessed by SSPE Scoring Scale (SSS) before treatment and at 6 and 12 months. Patients who had less than two assessments within 6 months were excluded. EEGs were evaluated blindly according to a standard scoring system where higher scores signify improvement. Mental level was assessed by developmental tests or mini-mental scale and a standard parental questionnaire.

Results: Before- and after-assessments were completed in 47 patients (aprepitant group n=20, placebo group n=27). No serious adverse event occurred related to aprepitant at this dose and duration. Changes in total SSS over time were similar in aprepitant and placebo groups. EEG scores of the aprepitant group were higher at 12 months (p=0.029) but unchanged in the placebo group. Patients showing an increase in mental scores in aprepitant and placebo groups were 41% and 35% respectively (p=.88). Further analyses of SSS subscores reflecting pyramidal–extrapyramidal systems, myoclonia–seizures, motor and daily functions, and EEG sub-scores are underway.

Conclusion: Preliminary analyses showed no significant effect of NK–1R inhibitor in SSPE. Most patients were at late stages of the disease; NK–1 antagonists might be tried in early cases where the virus is spreading and the disease is progressing more actively.

Disclosure: No potential conflict stated.
**P03-28**

**Functional limitations in paediatric-onset Multiple Sclerosis**

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**Objective:** To evaluate the functional limitations and to determine the difficulties during the daily life activities in patients with pediatric multiple sclerosis (pMS).

**Patients and Method:** The study group consisted of 10 patients (6 F, 4 M) with pMS whose neurological examination was determined as normal by pediatric neurologists and 10 control subjects (5 F, 5 M). Mean age of the patient and control groups were 18.2±1.39 and 22.1±0.87 respectively. Static Posturography Functional Limitations subtests: sit to stand, walk across, tandem walk, step/quick turn, step up/over, forward lunge) were performed in both groups.

**Results:** Significant differences were observed between the groups in four parameters: walk across speed, tandem walk step width, forward lunge distance and forward lunge force impulse (p<0.05). On the other hand, sit to stand, step/quick turn, step up/over subtest results showed no difference between groups (p>0.05).

**Conclusions:** The speed of walk across was lower in pMS than the control group. Moreover, p MS patients’ tandem walk was impaired and they had a wide-based gait to provide their balance during the tandem walk. Also, they slogged on forward lunge task and used asymmetrical force between their legs. However, they have not any difficulty sit to stand, step/quick turn and step up/over. This preliminary study, if confirmed in larger groups, can provide important information to clinicians about practical but sensitive parameters to be used in the follow-up of pMS.

**Disclosure:** No potential conflict stated.

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**P03-29**

**Acute Disseminated Encephalomyelitis with longitudinally extensive transverse Myelitis: severe presentation of Yellow Fever vaccine-associated Neurtrophic Disease**

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**Introduction:** The temporal association between acute disseminated encephalomyelitis (ADEM) and vaccination is well recognized. Although yellow fever (YF) vaccine has been seldom associated with severe complications. We cared for a teenager with ADEM/longitudinally extensive transverse myelitis (LETM) temporally associated with the administration of YF vaccine.

**Methods:** Case report by medical records review.

**Results:** A 17-year-old male teenager received vaccine against YF (17DD strain). Seven weeks later he developed severe headaches followed by four limbs weakness, urinary retention, and reduction of consciousness level. On examination he had bilateral symmetric tetraparesis with pyramidal liberation without defined sensory level. Magnetic resonance imaging (MRI) showed T2 hyperintense signal in the right middle cerebellar peduncle and subcortical areas; LETM (from C4 to the conus medullaris) affecting primarily grey matter. Cerebrospinal fluid (CSF) cell count was 550 white blood cells (lymphocytes 78%, monocytes 10%), glucose 45 mg/100 mL, and protein 168 mg/dL. Serum and CSF evaluations for infection agents were negative. CSF oligoclonal bands, anti-myelin oligodendrocyte glycoprotein (MOG) and anti-aquaporin-4 antibodies were negative. Patient was started on intravenous methylprednisolone for two days, suspended due to pulmonary infectious, immediately followed by endovenous immunoglobulin, and then plasma exchange with clinical improvement, persisting with urinary retention and bilateral Babinski sign at the follow-up, without recurrences. MRI performed after 3 months, showed almost complete resolution of previous lesions.

**Discussion:** Diagnosis of YF vaccine-associated neuropathic disease was done based on close temporal proximity with the vaccination, and monophasic course of the disease of our patient. The presentation was characterized by severe LETM affecting the conus medullaris and gray matter predominance in the context of ADEM, mimicking anti-MOG disease, persisting with permanent sphincter impairment.

**Disclosure:** No potential conflict stated.
P03-30

Neurological Involvement of Behçet Disease on Brazilian children

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Introduction: Behçet’s disease (BD) is a rare multisystemic vasculitis with an etiology that is still unknown. Neurological involvement occurs in approximately 9% of cases, and both parenchymal inflammatory and/or vascular complications has been described. The most frequent vascular involvement is the thrombosis of venous sinuses and parenchymal inflammation mostly involves a subacute meningoencephalitis of the brainstem and diencephalon. Most cases worldwide have been reported from the Mediterranean region to Japan, so it is considered a rare disease in south american countries. The objective of this paper is described clinical and diagnostic methods in a group of paediatric brazilian neuro-BD.

Methods: Case report by medical records review

Results: Four patients were included, according to the International Consensus recommendations on neuro-BD only one was classified as definitive diagnosis, and the others as possible neuro-BD. All patients were boys with age of onset from 7 to 13 years. All patients presented recurrent oral ulcers as systemic manifestation, two had ocular manifestations (posterior uveitis and retinal vasculitis), and only one cutaneous lesions. None presented genital ulcers. They were classified as parenchymal presentation (one patient), non-parenchymal (one patient with cerebrovenous thrombosis) and two with mixed parenchymal/non-parenchymal form (one parenchymal asymptomatic and other with brainstem lesions, both of them with recurrent acute meningal syndrome). Regarding the cerebrospinal fluid (CSF) analysis, there were diversity, with pleocytosis ranging from 24 to 1040 cells, either with lymphocytic or neutrophilic predominance.

Discussion: Diagnosis of neuro-BD is based on clinical findings of the sistemic disease associated with image and CSF suggestive features. As previously described, neurological manifestations preceded the patognomonic signs of BD on our patients. Recurrent oral ulcers was common on all cases, and the neurological presentations were diverse.

Disclosure: No potential conflict stated.

P03-31

A case of Anti-NMDAR Encephalitis mimicking Leukodystrophy with poor response to immunosuppressive therapy

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Introduction: Anti-N-methyl D-aspartate receptor (NMDAR) is the antibody is the most common on autoimmune encephalitis in children, most frequently presenting with subacute encephalopathy, seizures, and involuntary movements. Brain magnetic resonance imaging (MRI) is quite often normal. Prognosis with immunosuppressive treatment is good in most cases.

Methods: Case report through medical report review.

Results: A previously health 1-year-old boy started with afebrile upper respiratory symptoms and one day after was admitted in intensive care unit with seizures. He was treated with antibiotics. First head computerized tomography scan and cerebrospinal fluid (CSF) were normal. After 5 days abnormal movements were noted as well as regression in development marks (truncal hypotonia, no social contact). He was transferred to our referred unit one month after beginning of symptoms. Brain MRI revealed extensive hyperintense lesion in T2-sequence and FLAIR in periventricular region and lentiform nucleus bilaterally. CSF was slightly inflammatory with 9 cells (lymphomono predominance). Autoimmune encephalitis antibody panel revealed positive anti-NMDAR in CSF. There is no evidence of neoplasm. Patient was treated with intravenous steroids for 5 days, intravenous immunoglobulin (2g/kg) and Rituximab (375mg/m2). He is also receiving bacoifox, clonazepam and clonidine. There was response regarding abnormal movements and seizures but no improvement in development (hypotonia and cognitive).

Discussion: We describe an atypical anti-NMDAR encephalitis presenting in a young child with acute onset, extensive white matter lesions and poor recovery after aggressive immunosuppression. Leukodystrophic-like patterns in brain MRI might represent an aggressive presentation of antibody-associated encephalitis.

Disclosure: No potential conflict stated.
Enterovirus D68 associated Transverse Myelitis: the new Polio of the 21st century?

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Objective: Acute flaccid paralysis (AFP) due to enterovirus D68 is an emergent disease entity sharing features of poliomyelitis which has been largely eradicated by polio prevention programmes. We describe the case of a 15-month old girl presenting with transverse myelitis and acute motor axonal neuropathy who was confirmed to have enterovirus D68 (EV-D68). Here we present the salient features of our case and neuroradiological phenotype.

Case: A 15-month old girl presented floppy and not mobilizing following a 2-day history of coryzal symptoms. She was previously fit and well, with an unremarkable perinatal and past medical history except recent hospitalization in South-East Asia with parainfluenza. Within a few hours of presentation she had rapidly progressive limb weakness; she was profoundly hypotonic with poor head control, no spontaneous movement of all 4 limbs and areflexic. She developed respiratory failure requiring ventilation on PICU.

MRI demonstrated long segment spinal cord T2 hyperintensity and an isolated area of high T2 signal in the right thalamus. CSF showed lymphocytosis with normal protein; bacterial and viral screening was negative. Based on this a presumptive diagnosis of transverse myelitis was made and she commenced intravenous steroids.

Nerve conduction studies revealed an acute motor axonal neuropathy. Autoimmune neuronal antibodies were negative. Cultures from throat swab and stools reported enterovirus. Further typing of this revealed it was EV-D68.

Conclusion: Our case illustrates the association of transverse myelitis and axonal neuropathy with EV-D68. Characteristically there is grey matter involvement of the spinal cord seen on MRI, which wasn’t seen in our case perhaps reflecting imaging done very early in the disease course. The prognosis remains poor with significant neurological sequelae with very few making complete recovery in the reported literature.

Disclosure: No potential conflict stated.

ADEM – A paediatric case series in a tertiary care hospital

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Introduction: Acute disseminated encephalomyelitis is an uncommon demyelinating disease of the CNS usually following a viral infection or vaccination. The clinical and imaging findings of 4 children with ADEM is presented in this paper. The aim is to look for the clinical presentation, imaging findings and outcome of children diagnosed with ADEM.

Methods: Reviewed were children who were diagnosed as ADEM from February 2015 to July 2018 treated in University Clinic for pediatric disease in Skopje. The criteria used for including the patient in this paper were monophasic disease, demyelinating findings in imaging and negative CSF for infection.

Results: The paper presents cases of four children diagnosed as ADEM by imaging studies. Two patients presented with focal presentation in the form of hemiparesis and cerebellar signs. There was a generalized seizure in one. MRI in all of them showed demyelination seen in T2wi and FLAIR as multiple bilateral hyperintense focal lesions in subcortical white matter. Steroids were administrated in all of them. Two of them made dramatic improvement over the next few days. In one hemiparesis persisted whereas one made improvement after 3 weeks.

Conclusion: MRI brain scan is the investigation of choice for identification of ADEM. The predominant white matter involvement suggests demyelination that is the hallmark of the disease. Short duration of illness prior to admission, age of the onset, simultaneous widespread multifocal involvement on MRI brain scan and the dramatic response to steroids favor the diagnosis of ADEM. Clinically and pathologically ADEM resembles MS where periventricular white matter involvement is present, not seen in these patients.

Keywords: Acute disseminated encephalomyelitis, MRI brain scan, white matter.

Disclosure: No potential conflict stated.
Two cases of paediatric AQP4–antibody positive Neuromyelitis Optica Spectrum Disorder successfully treated with Tocilizumab

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Introduction: B-cell depletion with the anti-CD20-antibody rituximab is widely considered treatment of choice for long term immunotherapy in AQP4–antibody positive neuromyelitis optica spectrum disorder (NMOSD). However, up to 30% of patients suffer from relapses despite complete B-cell depletion. In these cases, the IL6-receptor blocking antibody tocilizumab has been suggested as alternative.

Methods: We report two female adolescents with AQP4–antibody positive NMOSD who relapsed under rituximab treatment and were switched to monthly IV administrations of tocilizumab.

Results: Under rituximab treatment both patients showed severe disease progression both clinically and radiologically. After switching to monthly administrations of tocilizumab both stabilized clinically without relapse over the follow-up period of up to 36 months. There were no significant adverse effects associated with the treatment.

Discussion: Our data suggest that early escalation of therapy with tocilizumab may lead to stabilization of disease activity in pediatric NMOSD patients who relapse under B-cell depletion. As pathophysiological mechanism a rituximab treatment-resistant plasmablast subpopulation that secretes AQP4-antibodies in a IL-6 dependent manner has been suggested.

Disclosure: No potential conflict stated.

Disclosure: No potential conflict stated.

Handwriting in Paediatric Onset Multiple Sclerosis – Tracing strategy and kinematic analysis

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Introduction: Pediatric onset multiple sclerosis (PedMS) is a chronic, autoimmune, inflammatory, demyelinating disease of the central nervous system. In adult MS handwriting is affected due to the sensory-motor and cognitive impairment. Compared to healthy controls (HC) they write with higher movement duration, fragmented velocity profile and higher jerk. Handwriting can be assessed using graphic strategies in combination with kinematic analysis (using kinematic parameters). There are no studies using this approach in PedMS handwriting analysis. The aim of this study was to test handwriting kinematic and graphic strategies of PedMS in comparison to HC.

Methods: 10 PedMS (18.1±1.6 years; mean disability score 1.5 (Expanded Disability Status Scale - EDSS)) and 10 matched HC were enrolled. Subjects did a drawing task (three figures, F1-3) on a digitizing board using ink stylus. The kinematic parameters we analyzed were: pressure – P, velocity - V, acceleration – A, jerk – J, number of changes in velocity (NCV) and acceleration (NCA), stroke time and duration.

Results: PedMS compared to HC showed lower acceleration (p=0.04), lower jerk (p=0.005) and lower velocities (p=0.038) while tracing. NCA was significantly greater in PedMS for all figures (p F1=0.018, p F2=0.029, p F3=0.039). PedMS used more often tracing strategies without pauses (although without statistical significance, p=0.13).

Conclusion: PedMS subjects traced figures with lower V, A and J and made less stances. Their strokes were slower and less saccadic and strategies for tracking figures were more fluent compared to HC. However, movements were less automatic compared to HC (greater NCA values). Tracing strategies and kinematics are affected in PedMS compared to HC. It is a potential new neuropsychological assessment during follow-up of subjects with PedMS.

Disclosure: No potential conflict stated. 
**P03-36**

**Evaluation of mental state and cognitive functions of children with Radiologic Isolated Syndrome**

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**Introduction:** Incidental MR imaging findings resembling multiple sclerosis (MS) in asymptomatic individuals are termed "radiologically isolated syndrome (RIS)." Approximately one third of patients with radiologically isolated syndrome convert to MS. We aimed to study the predictive factors for converting to MS and evaluate mental state and cognitive functions in RIS patients.

**Methods:** There were 12 children and adolescent with the diagnosis of RIS in the study group, and the control group was consisted of 12 healthy children and adolescent paired for gender and age. Mental state and cognitive function of the patients in two groups were compared. Mental state was evaluated by semi-structured intervention, behaviour evaluation scale, depression scale and anxiety scale. Cognitive functions were evaluated by neuropsychological test battery and an intelligence test. Additionally, correlation of the findings in RIS group and demyelinating lesions were analyzed.

**Results:** There was no significant difference according to mental state between two groups, but maintenance of attention, visual screening, visual-motor coordination, obtaining and using visual spatial information, short-term memory and executive function control were worse in RIS group than the control group. There were no correlation between the findings in RIS group and demyelinating lesions.

**Conclusion:** There were significant impairment of cognitive functions in RIS patients, and the predictive value of these findings for converting to MS should be evaluated in large-scale studies.

**Disclosure:** No potential conflict stated.

**P03-37**

**Novel neuroimaging findings associated with Autoinflammatory Interferonopathies**

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**Introduction:** The neuroimaging findings most commonly reported in autoinflammatory interferonopathies are basal ganglia calcification. Non-specific high intensity white matter changes, and non-obstructive hydrocephalus have also been reported. Here we describe a case of a 9 year old girl with an autoinflammatory interferonopathy, clinically consistent with CANDLE syndrome, with previously undescribed brain imaging findings.

**Methods and Results:** In the first year of life she had presented with a head circumference above the 99th percentile, skin rash, and swollen knees and ankles. A skin biopsy revealed panniculitis, magnetic resonance imaging of her brain demonstrated increased extra-axial cerebrospinal fluid (CSF). At one year of age she had her first tonic-clonic seizure and was commenced on levetiracetam. By 16 months of age she had a persistent fever for four months, and an arthropathy with effusion of her right knee and elbow. Investigations revealed an ESR of 61mm/Hr, CRP of 129mg/L. Her CSF had an opening pressure of 33cmH2O and diagnosed aseptic meningitis. She continues to have severe recurrent fevers, arthralgia, and seizures.

On neuroimaging her Computerised Tomography (CT) scan revealed extensive calcification of her cavernous carotid artery (which was progressive), the peripheral branches of her intracranial circulation, and to a lesser extent of her basal ganglia. Her On Magnetic Resonance Imaging (MRI) she had blooming artefact corresponding to her peripheral calcification, her time of flight magnetic resonance angiogram (MRA) was normal.

**Conclusion:** These progressive intracranial calcifications are not typically described in interferonopathies and expand the phenotype of these autoinflammatory conditions.

**Disclosure:** No potential conflict stated.
**P03-38**

**Guillain–Barré Syndrome in children at quaternary level hospital: prevalence, clinical profile and outcomes, a retrospective chart review**

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**Background:** Guillain Barre Syndrome (GBS) is a common cause of acute flaccid paralysis with an incidence of up to 2/100,000. It has a highly variable clinical course and outcomes can result in protracted period of motor dysfunction. We aimed to describe the clinical profile, and factors associated with poor outcomes of GBS in a low resource setting.

**Methods:** A retrospective chart review of clinical records of patients with GBS admitted to a quaternary level hospital in the KwaZulu-Natal Province of South Africa from 01 January 2015 to 31 December 2018 was undertaken.

**Results:** A total number of 36 cases was included in the study. The mean age was 5 years (range 3 months – 11,5 years), males 53% (n = 19), females 47% (n=17). Of the 34 cases whose preceding illness was documented, 47% (n=16) had respiratory illness and 17,6% (n=6) had gastrointestinal symptoms, while other conditions were 14,7% (n=5). There was no preceding illness in 23,5 % (n=8) of these cases. 28% required assisted ventilation and bulbar dysfunction was significantly associated with assisted mechanical ventilation (p = 0,003). 6% (n=2) had normal motor function at discharge and of the 61% (n=22) who had a record at approximately 12 months follow up, 33% (n=12) had residual motor weakness and some with limb deformities.

**Conclusion:** The clinical presentation of patients with GBS is variable, can be life threatening and the clinical course is determined by the early diagnosis and appropriate management. The outcomes include complete recovery for a proportion of patients, residual weakness for some and while persistent pain can interfere with daily activities in others.

**Disclosure:** No potential conflict stated.

**Objective:** Acute flaccid myelitis (AFM) is a polio-like neuroinflammatory disease of the spinal cord defined by acute onset of asymmetric flaccid weakness of the extremities associated with magnetic resonance imaging (MRI) lesions in the spinal cord gray matter and CSF pleocytosis. The disease is seen in outbreaks spiking every two years since 2012 associated with entroviral infections.

**Methods:** We enrolled a retrospective cohort of 32 children diagnosed with confirmed and probable AFM according to Center for disease Control (CDC) criteria between 2016-2018 from 10 centers in Turkey.

**Results:** Seventeen patients were males. Twenty-four patients were admitted in 2018. All patients had asymmetric flaccid paralysis. Median age at onset was 51 months (15-192 months, 25 of the cases were younger than 7 years). Magnetic resonance imaging of the spinal cord demonstrated longitudinally extended T2 hyperintensity mainly involving cervical regions with or without contrast in 30 children. An infectious agent is detected in 10 patients either by nasopharyngeal swabs or serum serology. (entero/rhinovirus in 3, EBV infection in 4 patients). Eleven patients presented with monoparesis involving mainly upper extremities, 11 with quadripareisis. Electromyography (when available) demonstrated neuropathy with or without polyradiculoneuropathy in all except 1 patient. All patients ex-
Acute flaccid myelitis is a cause of persistent weakness and disability affecting young children. In summer, fall and early winter of 2018 the outbreak of AFM affected more children than 2016. Immunotherapy seems to be ineffective. The new outbreak is anticipated in 2020. Physicians should be familiar with signs and symptoms of AFM for prompt intervention and early start of physical therapy.

Disclosure: No potential conflict stated.

Objective: Neuromyelitis Optica Spectrum Disorders (NMOSD) and Multiple Sclerosis (MS) are well described central nervous system demyelinating disorders mostly affecting adults. Pediatric manifestation have been described in different populations but there is no comparison between these two disorders in children ≤ 11 years of age.

Methods: Retrospective review of medical report including clinical and demographic data of MS and NMOSD pediatric patients actively attending Neuroimmunology out-patient clinic of a Brazilian tertiary center. Inclusion of patients whose symptoms began ≤ 11 years fulfilling IPND-2015 NMOSD criteria and IPMSSG-2012 criteria for MS.

Results: We identified 19 MS and 19 NMOSD patients. Median age at onset 8.39 (±2.3) years, most were female (63.2%) and had recurrent course (89.5%) with ARR of 0.54. White ethnicity was more common except in NMOSD patients. NMOSD patients were AQP4-Ab+ (73.6%), MOG-Ab+ (15.7%), double-seronegative (10.5%). No MS patient tested positive for AQP4-Ab or MOG-Ab. NMOSD patients mostly manifested the disease with optic neuritis while MS patients presented more commonly with brainstem syndrome. Pleocytosis was found in most NMOSD patients. Neutrophils was seen more frequently in NMOSD. Last EDSS was higher in NMOSD patients.

Conclusion: Demographic and clinical presentation in patients ≤ 11 years of age might help differentiate NMOSD and MS in this age group.

Retrospective analysis of 13 paediatric patients with clinically Mild Encephalitis/encephalopathy with a Reversible Splenial Lesion (MERS)

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Objective: To describe the clinical and laboratory features of clinically mild encephalitis/encephalopathy with a reversible splenial lesion (MERS) in children.

Methods: We retrospectively analyzed 13 pediatric cases (10 boys and three girls; median age 13.2 years; range 2.4–15.8 years) diagnosed with MERS between June 2011 and September 2018. We reviewed the patients’ data including associated pathogens, neurologic symptoms, MR images and electroencephalography (EEG) findings, laboratory data, treatment, and prognosis.

Results: The associated pathogens were influenza virus (n=4), rotavirus (n=1), HHV-7 (n=1), Salmonella enteridis (n=1), E. coli O117 (n=1), and unknown (n=5). Initial neurologic symptoms were delirious behavior (n=7), seizures (n=4), disturbance of consciousness (n=1), ataxia (n=1), and headache (n=1). Ten patients had type I lesions on MRI, exhibiting characteristic reduced diffusion at the splenium of the corpus callosum, and three patients had type II lesions with additional posterior white matter lesions. Four patients underwent initial EEG examinations within 2 days after the onset of neurological manifestations; one of the four patients showed abnormality with posterior high voltage slow waves in the background activity. Hyponatremia (serum Na <135 mEq/l) was observed in eight patients and lasted 1–12 days (median 2.5 days). Pleocytosis of cerebrospinal fluid was observed in three of the nine patients so examined. The treatments were methylprednisolone pulse therapy (n=11), intravenous immunoglobulin (n=8), and antiepileptic drugs (n=6). In all patients, neurologic symptoms completely normalized within 9 days with no sequelae. Nine patients recovered within 2 days.

Conclusion: MERS has characteristic imaging features and a favorable outcome. Supportive treatment withholding methylprednisolone pulse therapy and immunoglobulin might be appropriate for the majority of patients.

Disclosure: No potential conflict stated.

Paediatric presentation of CASPR2 Encephalitis

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Objective: To show the pediatric presentation of CASPR2 encephalitis. CASPR2 encephalitis is a rare autoimmune encephalitis, typically presenting in middle aged male patients with clinical features of limbic encephalitis and/or peripheral nerve hyperexcitability. Few pediatric cases are known, with slightly different presentation.

Methods: Authors describe the clinical and laboratory course of a patient. Results: A four year old girl presented at our hospital because of a prolonged seizure. One month prior to it she had an upper respiratory illness, followed by insomnia, fatigue, increased water intake and itching over three weeks. She had 3 main groups of symptoms. Dysautonomic features: consistent hyponatremia, high blood pressure, apneas. Central nervous symptoms: fluctuating encephalopathy, mutism, insomnia. Peripheral signs: constant scratching of the distal parts of hands and feet. Autoimmune encephalitis was assumed, but high-dose methylprednisolone failed to improve her symptoms. Laboratory findings were normal, except for consistently elevated CSF protein. Brain and spinal MRIs were normal. CSF culture, HSV PCR and serology were negative. EEG showed slow background activity. A mild slowing of motor nerve conduction velocities were detected. Autoantibody panel for systemic autoimmune diseases and paraneoplastic antibodies were normal. Serum CASPR 2 antibody proved positive. On combined immunotherapy with high dose methylprednisolone and iv. immunoglobulin she improved slowly, and CASPR2 titer decreased. She fully recovered in two months.

Conclusions: The presentation of peripheral symptoms in CASPR2 encephalitis can be itching and scratching of the distal parts of the extremities. Hyponatremia was also a main feature hardly responding to correction. The presentation of central nervous, dysautonomic and peripheral involvement are typical of CASPR2 encephalitis. Combined, slowly tapered immunotherapy is effective, the outcome is favorable in most cases.

Disclosure: No potential conflict stated.
P03-43

Radiologically Isolated Syndrome in children
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Objective: The term “radiologically isolated syndrome” (RIS) defines the presence of lesions meeting the criteria of multiple sclerosis (MS) on MRI without any clinical event compatible with MS in the patient. RIS has been described in adults and recently, in the pediatric age group.

Cases: Seven patients, 4 girls and 3 boys aged 12-16 years, presented with various neurological symptoms: headache, vision problems, drowsiness, dizziness. MRI met the 2010 criteria for MS with periventricular, juxtacortical lesions, some enhancing. One/4 patients with spinal MRI had multiple demyelinating lesions in the spinal cord. Three patients had vitamin D deficiency. Vasculitic serology was negative in all. Two had lumbar puncture: IgG index and oligoclonal bands were positive in one but the other developed radiologic progression on follow-up and interferon treatment was started.

Conclusion: The outcome and rate of conversion to MS are unclear in pediatric RIS. In adult patients radiologic progression occurs in 59% and a first clinical event, in 34% in 5 years. These rates were 61% and 42% in the largest pediatric series (n=38) published by Makhani et al. Pediatric RIS may change to MS sooner than adult patients. In our follow-up of 3 months-4 years one case converted to MS. Risk factors for conversion and methods of prevention will constitute an important area of research in the near future.

Disclosure: No potential conflict stated.

P03-44

12-year-old girl with possible Vogt-Kayanagi-Harada Disease requiring treatment with systemic corticosteroids and Cyclosporine
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Introduction: Vogt-Kayanagi-Harada (VKH) disease is an autoimmune multisystemic disorder, characterized by serous retinal detachment, iridocyclitis and choroidal swelling. Neurological, auditory and cutaneous signs are also seen. Revised diagnostic criteria for VKH disease categorized disease as complete VKH, incomplete VKH and probable VKH. The onset age of VKH disease tends to be approximately from 20 to 50 years. Therefore, pediatric VKH disease is extremely rare.

Methods: Here, we report a twelve-year-old girl with possible VKH disease.

Results: A twelve-year-old girl is presented with severe headache, blurred vision, left ocular hyperemia and pain. In ocular examination, the ophthalmologist documented bilateral serous retinal detachment and disc edema. Her vital signs, medical history, neurological examination, brain and orbital magnetic resonance imaging were all normal. Extensive laboratory, serologic Cerebrospinal fluid (CSF) testing were either negative or within normal range. Judging from ocular symptoms and neurological findings in the form of severe headache, the patient was diagnosed as incomplete VKH disease. She was admitted for pulse intravenous methylprednisolone 20mg/kg/day for three days and showed significant improvement. The patient was discharged on oral prednisone (2 mg/kg/day) with slow tapering. Since disease was reappeared during the tapering of prednisone to 0.5mg/kg/day treatment with oral cyclosporine added to oral prednisone after the new pulse intravenous methylprednisolone treatment. A follow-up appointment during 1 year revealed that her vision and headaches improved with cyclosporine and only 1mg/day prednisone treatment.

Conclusion: VKH disease is uncommon in pediatric population and can have aggressive course with serious visual loss. Occasionally, treatment with systemic corticosteroids cannot control ocular inflammation. In these conditions, the loss of vision can be prevented by aggressive treatment with other immune suppressants together with very low dose of oral corticosteroid.

Disclosure: No potential conflict stated.

P03-45

This poster was withdrawn by the author.
**P03-46**

**Efficacy of a drug cocktail containing vitamins to prevent Acute Encephalopathy with Biphasic Seizures and Late Reduced Diffusion (AESD)**

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**Introduction:** Acute encephalopathy with biphasic seizures and late reduced diffusion (AESD) is mainly reported in East Asia. Initially, it is difficult to distinguish AESD from prolonged febrile seizures (PFS). Previously, we reported that early (<24 hours) drug cocktail (vitamin cocktail: vitamin B1, vitamin C, biotin, vitamin E, coenzyme Q10, and L-carnitine) administration could contribute to an improvement in the prognosis of acute encephalopathy. This study aimed to examine the efficacy of this drug cocktail to prevent AESD.

**Methods:** We studied 16 patients with a febrile seizure lasting over 30 minutes from February 2016 to October 2017 in whom the drug cocktail was administered.

**Results:** The final diagnosis revealed 2 acute brain swelling type cases), 1 AESD case, and 13 PFS cases. Patients were aged 10–74 months (average 33.8 months) with seizure duration of 30–195 minutes (average 71.8 minutes). The time from seizure onset to medication was 2–14 hours (average 4.84 hours) and the AESD predictive score, designed by Tada et al., was 0–9 (average 3.06). In 14 cases, except 2 of acute encephalopathy, the AESD predictive score had 100% sensitivity and 86.7% specificity.

**Discussion:** Here, the average time from seizure onset to medication was 4.84 hours suggesting that drugs could have been administered early. Although the AESD prediction score has high sensitivity and specificity it may cause delays in diagnosis because patients can only be evaluated 12–24 hours following consciousness. Here, false positives were observed but not false negatives. Hence, early administration of the drug cocktail containing vitamins may have been effective. Further prospective studies are required.

**Disclosure:** No potential conflict stated.

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**P03-47**

**A case of Autoimmune Encephalitis with cerebellar damage associated with anti-GAD65 antibodies in a child**

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**Introduction:** Autoimmune diseases of the nervous system in childhood have been diagnosed more frequently in recent years, new antibodies against neurons are being discovered. Parainfectious genesis of autoimmune changes in the nervous system is basically diagnosed in children. An immunosuppressed ataxia has been detected due to antibodies to glutamic acid decarboxylase, one of the enzymes involved in the synthesis of GABA [Mitoma H.et al, 2019].

**Aim:** To present the case of immune-mediated cerebellar ataxia associated with antibodies to glutamic acid decarboxylase in childhood.

**Methods:** A boy at the age of three years old got sick unexpectedly. During the next 5 days the child stopped walking. There was no fever. A week before the child had had symptoms of a cold. The baby was born healthy from healthy parents. The child development was normal. In region hospital herpetic encephalitis was excluded. Liquor was normal. MRI of the brain showed mild ventricular dilation, no changes in the cerebellum. After treatment pulse therapy with methylprednisolone intravenously, the condition of the child improved and he was discharged from the hospital. But in 1 month after the symptoms of cold and fever 39C, ataxia appeared.

**Results:** In hospital in neurological status were ataxia and mild eye opsoclonus and muscular hypotonia. While CT any tumors were not detected. AntiGAD-65 - 376 IE / ml (normal range up to 10) was detected. The child received a course of intravenous immunoglobulin in a standard dose after that he was healthy.

**Conclusions:** The child had a typical course of the infective immune-mediated disease of the nervous system with cerebellar damage, but we confirmed the pathogenesis of this condition for the first time, found antibodies to glutamic acid decarboxylase.

**Disclosure:** No potential conflict stated.
P03-48

Challenges in the treatment and prognosis of Chronic Opsoclonus-Myoclonus-Ataxia Syndrome-OMAS

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Objective: To evaluate the therapeutic response and clinical outcome of children with chronic relapsing OMAS, as its high morbidity leaves permanent neurological, behavioral, and cognitive sequelae.

Methods: Children at any stage of the disease were included. Clinical data: age, gender, age at disease onset, etiology (inflammatory, paraneoplastic), treatment options, and outcome were analyzed. The neurological examinations were videotaped after written parental consent. OMA severity was scored using OMA evaluation scale (Pranzatelli et al, 2001).

Results: 6 children (4M, 2F) with chronic relapsing OMAS were analyzed over a 5y period. The median age of the disease onset was 20m, range 13-60m. One child was diagnosed with neurolastoma; in the remaining no laboratory or radiological evidence of neoplasm was found. Laboratory findings in sera (including NSE) and CSF were unremarkable. Autoantibody screening study for anti-Hu, anti-Ri, anti-Yo and Purkinje cells showed negative results in all tested patients. 5 children received corticosteroid therapy (dexamathasone/ACTH/methylprednisolone/prednisolone) and repeated IVIg in the initial stage of the disease. 4 children with chronic relapsing and/or progressive clinical course who failure to respond (median 7.5y, range 3-14y), were treated with a combination of immunosuppressive agents (prednisolone 1.5mg/kg, azathioprine 1.5mg/kg) in a long-term period (mean 2y). Outcome was favorable in 3, without side effects; OMA ES dropped for mean 13.6 points.

Conclusion: Combined immunosuppressive therapy (oral prednisolone and azathioprine) was effective and safe for the long-term treatment of chronic relapsing/progressive OMAS. Although all treated children showed a good and substantial response, certain neurological and cognitive sequelae were observed.

Disclosure: No potential conflict stated.

P03-49

A 17-year-old girl with Anti-NMDA Receptor Encephalitis with Ovarian Teratoma and pure psychiatric symptoms

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Introduction: Anti-NMDA receptor encephalitis in children is one of the most common forms of antibody-mediated encephalitis in children. It often begins with psychiatric symptoms, and progresses to seizures, reduction of speech, dyskinesias, coma, and autonomic symptoms. Monosymptomatic (eg only with psychiatric symptoms) anti-NMDA receptor encephalitis is very rare.

Here we present a 17 year old female who developed after a mild head trauma a lack of sense of time, concentration difficulties, anxiety, insomnia and suicidal thoughts.

Neurologic examination, cerebral MRI and EEG were normal. CSF analysis showed a mild pleocytosis with 7 cells/ul. Pending serum and CSF NMDA antibody testing, steroids were administered in view of a possible autoimmune-mediated encephalitis. The psychotic symptoms worsened, and antipsychotic therapy was initiated. Then autoantibody testing revealed the presence of anti-NMDAR-antibodies. A second steroid pulse and intravenous immunoglobulin were given, followed by a therapy with Rituximab and monthly steroids pulses for further 4 months, which led to a significant improvement. Further work-up with an abdominal ultrasound was normal but the following abdominal MRI showed signs of a small tumor in the center of the right ovary. An abdominal laparoscopy was performed, but the histological examination showed no signs of teratoma. A repeat pelvic MRI scan afterwards showed a progression of the lesion. A third MRI scan confirmed these findings. A resection of the right ovary was performed. The new histological examination showed this a small teratoma.

Conclusion: Monosymptomatic anti-NMDA receptor encephalitis is rare and should be included in the differential diagnosis of new psychiatric symptoms. In young females, the presence of a teratom must be excluded.

Disclosure: No potential conflict stated.
High prevalence of minor neurological dysfunction after Acute Encephalitis in childhood

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Objective: Motor symptoms are common in children with acute encephalitis. Long-term sequelae presenting as motor deficits have varied in earlier studies. Our objective was to investigate the prevalence of minor neurological dysfunction (MND) after childhood acute encephalitis.

Methods: We retrospectively identified and contacted the patients treated for acute encephalitis (n=82) at age 0-16 years in Turku University Hospital, Department of Pediatrics and Adolescent Medicine, during years 1994-2016. Forty-two (51%) patients agreed to participate in the follow-up. The Touwen neurological examination was used for the assessment of MND. The outcome was categorized as normal, simple MND or complex MND. Patients were asked to fill the questionnaire about subjective residual symptoms. The questionnaire was returned by 41 (98%) patients who participated in the follow-up.

Results: The mean age at the time of encephalitis was 6 years (range 7 months-16 years), and at the time of the neurological examination 13 years (range 4-29 years). The mean follow-up time was 7 years (range 1-23 years). Twenty-two (52%) of participants were male. The Touwen examination was normal in 12 (29%) patients. Simple MND was noted in 16 (38%) and complex MND in 14 (33%) patients. Four (10%) patients reported problems in motor skills. All of them had MND in the Touwen examination. Problems in daily performance were reported by 13 (32%) patients, and 12 (92%) of them had MND in the Touwen examination.

Conclusion: The prevalence of MND was high after history of childhood acute encephalitis, compared to normal pediatric population with reported prevalences of simple MND of 15-20% and complex MND of 6-7%. Abnormal neurological performance associated with subjective problems with motor skills and daily performance that can affect physical activity and social life.

Disclosure: No potential conflict stated.

A rare case of paediatric Chronic Granulomatous Herpes Simplex Encephalitis

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Introduction: HSV encephalitis (HSVE) is most commonly an acute monophasic disease process. A minority of cases relapse, a small percentage of which progress to necrotizing granulomatous encephalitis. Typically, this delayed disease recurrence manifests with a combination of intractable seizures and progressive neurological deficits. This entity is rarely considered in the differential diagnosis of brain parenchymal granulomas.

Case: A 3.5 year old girl, born at 30 weeks gestation, with a history of focal seizures at 2 months of age and previously treated HSV1 haemorrhagic encephalitis at 2 years of age and presented with 3 days of early morning headaches and vomiting. CSF demonstrated significantly raised protein and a high opening pressures but extended viral serology was negative on serial sampling. MRI brain revealed interval development of multiple confluent areas vasogenic oedema with encephalomalacia. Biopsy of brain tissue demonstrated florid granulomatous and necrotizing inflammation. HSV1 PCR was positive on biopsy and she was treated with high dose intravenous acyclovir for 6 weeks, followed by prophylactic oral acyclovir and a course of IV methylprednisolone followed by oral steroid taper for a total of 4 weeks.

Conclusion: Our patient was diagnosed with this rarely reported disease process with a benign clinical picture in contrast to previous reports, no reported seizures or neurological deficits except longstanding right-sided lower limb weakness. Clinicians should be cognisant of the pathological spectrum of neurological signs in patients with previous HSVE. Granulomas within the brain parenchyma can easily be misinterpreted as more common entities, such as tuberculosis or malignancy; however, it is imperative to be certain of the underlying diagnosis of the granuloma prior to initiating definitive therapy.

Disclosure: No potential conflict stated.

Disclosure: No potential conflict stated.
10-year-old female with Seronegative Autoimmune Encephalitis due to HHV-7 infection

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Introduction: Early diagnosis and prompt immunomodulatory therapy in cases of seronegative autoimmune encephalitis (AE) is challenging.

Aim: Herein, we present the diagnostic approach and therapeutic outcome of a seronegative AE related to HHV-7 CNS infection, in a girl aged 10 years old.

Methods: 10-year-old female, presented with impaired level of consciousness and convulsions, in remission of febrile disease. Brain MRI scan and CSF tests were insignificant, while HHV-7 in CSF was detected through PCR. Acyclovir and IVIG, were immediately administered. During the third day of treatment, neuropsychiatric manifestations deteriorated, setting the suspicion of HHV-7 infection-triggered AE, thus, treatment was altered to Ganciclovir combined with methylprednisolone pulses. Brain MRI, the 11th day of treatment, showed: high intensity signal in T2W-FLAIR, in external capsule-claustrum. Clinical improvement was noted after the 3rd week of hospitalization. Re-evaluation of PCR/HHV-7 and CSF autoantibodies, were negative, while oligoclonal zones in CSF and IgG Index were compatible with CNS inflammation. The patient was discharged, free of neuropsychiatric manifestations, under antiepileptic treatment, and progressive steroid tapering. The next two months, she had brief recurrences of mild psychiatric manifestations and seizures, which resolved with alterations in antiepileptic medication and cycles of immunotherapy (IVIG, methylprednisolone pulses). Therapy was repeated through one day courses monthly for three more months (IVIG 1 gr/Kg, methylprednisolone 30 mg/Kg), without steroid tapering. In 4 months follow up, the patient remains asymptomatic, with gradual decrease in antiepileptic treatment (levetiracetam, valproic acid, oxcarbazepine).

Conclusion: Prompt diagnosis and administration of immunotherapy in children who meet the criteria of seronegative AE, regardless of the infectious factor, is associated with satisfactory outcome.

Disclosure: No potential conflict stated.

Acute Flaccid Paralysis in paediatric patients the last 11 years in the island of Crete

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Objective: Acute flaccid paralysis (AFP) is an entity with various underlying etiologies. Our goal was to study the incidence per year per 100,000 children (0-16 yr), the diagnostic procedures, the treatment and the evolution of all AFP reported pediatric cases, the last 11 years in the island of Crete along with the incidence per year per 100,000 children of the leading etiology of AFP, Guillain – Barre syndrome (GBS).

Methods: Clinical picture, cerebrospinal fluid analysis, nerve conduction velocity and neuroimaging documented the diagnosis of AFP cases. Immunology and autoimmunology investigations added to the etiologic approach of the patients. The dominating diagnosis was GBS. One year close clinical follow-up ensured the evolution of our patients.

Results: 18 new AFP cases were reported from January 2008 to December 2018 in the island of Crete. Sixteen cases (88.8 %) of GBS, one Transverse Myelitis (TM) (5.6%) and one Acute Flaccid Paralysis with myelopathy and peripheral nerve involvement (5.6%) were the yield of the study. All GBS patients were treated with IVIG while two (12.5%) relapsed and four developed complications demanding additional treatment. A triggering factor was found at 63% of patients. All GBS children fully recovered. The two non GBS patients had remaining deficits. No polio related AFP patients were found.

Conclusions: The incidence per year per 100.000 children of AFP in our population is 1.39/100.000 during the study period. Respectively for GBS the value is 1.24/100.000. It seems higher from the respective European value (around 0.6/100.000) although insufficient study period, incomplete spectrum age accordance between the two populations and finally some exceptional missing cases from the sample size can’t be excluded.

Disclosure: No potential conflict stated.
P03-54

Treatment-Refractory CNS Cryptococcosis – What failed?

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Introduction: Microbiologic diagnosis in CNS infections is often difficult, being even more important when the causal microorganism isn’t covered by most empiric antimicrobial regimens.

Methods: Case report.

Results: 16 year-old male who, at the age of 4, had 2 episodes (5-month interval) of acute fever, vomiting and impaired consciousness, without focal neurological signs. In the first episode CSF revealed mild polymorphonuclear pleocytosis and hyperproteinorrachia, which were much more pronounced in the second episode, with associated hypoglycorrachia. MRI in the first episode showed leptomeningeal enhancement, with additional multiple small infra and supratentorial subpial cysts in the second. In both episodes he greatly improved after ceftriaxone, vancomycin and acyclovir, having been discharged without neurological deficits. No microbe was isolated in the first, but cryptococcal antigen was positive in CSF in the second episode. There was no clinical or laboratory evidence of immune deficiency. Antifungal treatment with intravenous amphotericin B and, later, oral fluconazole and voriconazole for 2 years, led to improvement of laboratory parameters and clinical and radiological stabilization.

At the age of 11, a subacute-onset scoliosis was noticed. MRI showed several cervical and dorsal cystic lesions and a de novo paravertebral cerebellar enhancing lesion. CSF exam showed a moderate hyperproteinorrachia without pleocytosis and fungal structures compatible with Cryptococcus in the cytology. Again treated with a prolonged antifungal drug regimen, he developed no new symptoms since, but no significant radiological improvement was observed, still having some enhancing lesions.

Conclusion: Considering brain imaging and the CSF positivity for the antigen, we assume the diagnosis of CNS cryptococcosis. However, considering this atypical evolution, we would like to discuss the future management of this patient, not only in terms of treatment but also diagnosis.

Disclosure: No potential conflict stated.

P03-55

Acute Longitudinal Extensive Transverse Myelitis – A rare clinical manifestation of Lyme Neuroborreliosis

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Introduction: Acute transverse myelitis (ATM) is a rare, immune-mediated disease that affects the sensory and motor pathways of the spinal cord. ATM is an extremely rare neurologic complication of Lyme disease (LD). We present the case of a 3-year-old male who developed acute longitudinal extensive transverse myelitis (ALTM) secondary to LD.

Case Report: A 3-year-old male patient was admitted to the pediatric neurology department because of progressive generalized weakness which had started 5 day before. On physical examination his vital signs were within normal limits. He was not able to move any limbs, muscle tone was increased and deep tendon reflexes were absent in his extremities. Babinski sign was absent. On the T2 weighted images, a diffuse, symmetrical increased signal within the cervical, distal thoracic spinal cord and conus was observed. (Fig.1). On laboratory examinations for serum were within normal ranges. Cerebrospinal fluid did not show any features except lymphocytic pleocytosis. Serum Borrelia burgdorferi IgM was negative and IgG was positive. Anti-Borreia antibodies were positive by Western blot test. The patient was diagnosed with ALTM and ceftriaxone treatment was started.

Conclusion: Children with neuroborreliosis commonly present with facial nerve neuropathy, aseptic meningitis, but the involvement of the spinal cord is very rare. In conclusion, we report the case of a patient with ALTM caused by LD with surprisingly few clinical signs—in contrasts to the severe MRI findings. If there is strong clinical suspicion of Lyme neuroborreliosis irrespective of a history of a recent tick bite or erythema migrans—appropriate treatment should be started.

Disclosure: No potential conflict stated.
Progressive Encephalomyelitis with Rigidity and Myoclonus (PERM) associated with Glycine receptor antibodies

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Introduction: Glycine receptor antibodies (GlyR-abs) have recently been associated with Stiff Person Syndrome, including Progressive Encephalomyelitis with Rigidity and Myoclonus (PERM). PERM is a severe autoimmune disorder, particularly rare in childhood, characterized by variable brainstem signs, myoclonus, stiffness, rigidity, muscle spasms, autonomic dys-function and hyperekplexia. PERM usually responds well to immunotherapy, including corticosteroids and/or immuno-suppressive agents characterized by variable expression of brainstem signs, myoclonus, stiffness, rigidity, muscle spasms, autonomic dysfunction, and hyperekplexia.

Description: We present a 17-year-old girl with progressive neurological condition since the age of 10, characterized by recurrent episodes of bilateral ptosis, myoclonic tremor, pyramidal signs, dysarthria and gait disturbances (no ataxia). Thorough and repetitive diagnostic workup (infections, systemic autoimmune and metabolic diseases, neoplasms-para-neoplastic syndromes, myasthenia and autoimmune encephalitis) was negative. Neuroimaging (brain-spinal MRI, PET-CT) and telemetry were normal. The only indicative findings of a CNS immune-mediated process were ESR elevation during exacerbations, (+) OCBs and increased IgG index on CSF. She responded well to corticosteroids, but relapsed at any discontinuation attempt. Trial of Mycophenolate Mofetyl was unsuccessful. Corticosteroids reintroduction in combination with a sixth-month IVIG course contributed to impressive, however, temporary improvement. The last diagnostic workup including old samples GlyR-abs titters came out positive. Currently, being on low corticosteroids dose (10mg/day) and Azathioprine (2mg/kg), remains symptom-free.

Conclusion: Discovery of new autoantibodies associated with immune-mediated CNS diseases contributes to better understanding of pathogenesis and causative therapeutic approach, reducing clinician’s uncertainty as to the choice of appropriate treatment. Presence of OCBs and increased IgG-index are early, often unique, immunological markers, underlining their clinical value in CNS autoimmune processes.

Disclosure: No potential conflict stated.

Fulminant Susac’s Syndrome: case report – A rare immunological disease in comparison to other autoimmune Encephalopathies

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Objective: Susac’s Syndrome (SS) is an orphan autoimmune endotheliopathy affecting the precapillary arterioles of the brain, retina and inner ear. Documented cases show a female predominance (approximately 1:3.5). Due to the general unawareness of SS, overlapping symptoms with other immunological diseases, diagnosis can be difficult in early stages of disease. Our aim was to present a rare entity and discuss clinical and imagiological differential diagnosis.

Methods: We present a pediatric case of fulminant SS, with a step-by-step clinical process and decision making, imaging characteristic of early and chronic stages of disease as well as histopathological features.

Results: A 17-year-old girl was referred to the General Hospital of Vienna presenting with progressive left-sided hemiparesis and symptoms of acute encephalopathy. MRI showed pathognomonic signs for SS: icicles, spokes, and snowball-lesions in the Corpus Callosum (T2), punctuate lesions in the internal capsule (DWI), which were guiding features in differentiating SS from Multiple Sclerosis, Acute Disseminated Encephalomyelitis, Cerebral Lupus Erythematosus and ANCA-negative CNS-Vasculitis. Due to unawareness of the syndrome and severe disease course diagnosis was delayed, even though imaging showed characteristic findings. In a next step, brain biopsy of the patient indicated acute ischemic cortical micro-infarction with perivascular lymphocytic inflammation, mainly composed of CD3+ and CD8+ T cells. Despite aggressive immunotherapy the patient did not fully recover.

Conclusion: Demands in diagnostic process especially in pediatric populations are high and awareness to characteristic imaging and histopathological features in SS needs to be raised to avoid misdiagnosis and prolongation of the diagnostic process, especially at early and acute stages of the disease where aggressive immunotherapy is needed.

Disclosure: No potential conflict stated.
Acute Encephalopathy in an adolescent associated with Bartonella Henselae Infection

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Introduction/Aim: Cat scratch disease (CSD) is an infectious disease caused by a scratch or bite of a cat, infected with Bartonella henselae. The disease can cause rare complications including encephalopathy, seizures and aphasias.

Methods: We present a case of a 17-year-old girl with acute encephalopathy, who was admitted after a generalized epileptic seizure. She was somnolent on admission, afebrile, cardiocirculatory stable without signs of meningeal irritation. At manipulation she was agitated, aphasic, except for groaning, without eye contact. Pupillary response and reflexes were normal, she had no motor deficits. In a few hours after admittance her conscious level deteriorated to stupor.

Results: Blood tests revealed only leucocytosis with negative C-reactive protein. Urine and blood toxico logical screening was negative. MRI of the head showed a small hyperintensive lesion periaqueductually on T2 and subtle hyperintensive signal of left parieto-occipito-temporal cortex on FLAIR. Cerebral spinal fluid (CSF) findings showed elevated proteins and positive oligoclonal bands. CSF was negative for neurotropic viruses, Borrelia burgdorferi, Mycoplasma pneumoniae and Gram stain. Due to exposure and history of a cat bite and swollen lymph nodes a few weeks before admission, serologic testing for Bartonella henselae IgM titer of 1:80 and IgG > 1:512. PCR of lymph node, blood and CSF were negative for Bartonella sp. No immune defects were detected.

EEG on admission was severely abnormal with generalized continuous slow activity (delta activity 3 Hz). She was first treated with cefotaxime and later with rifampicin and doxycycline. She rapidly recovered and EEG normalized within 7 days.

Conclusion: Infection with Bartonella henselae is a self-limiting disease that can present with serious neurological manifestations as acute and severe encephalopathy in an immunocompetent patient.

Disclosure: No potential conflict stated.

Autoimmune Encephalitis. When the medical history and the clinical picture are suspicious, the investigation procedure must go further. A case report

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Objective/Methods: To report a pediatric case of anti-NMDAR positive encephalitis with negative autoantibodies in the first place and a particular personal history. Both parents during conception and pregnancy were narcotic users.

Results: A 7-year-old boy with known mild learning difficulties and behavior problems was admitted at a local hospital with vomiting and multiple brief focal seizures. Ten days before admission he had a virus febrile infection. CSF lymphocytic pleocytosis leaded to an empirical antibiotic/antiviral treatment coupled with antiepileptic medication. Because of further deterioration, he was transferred to our Hospital. CSF PCR and cultures were negative for infectious causes. Oligoclonal bands and autoantibodies were both negative. Cerebral MRI revealed multiple cortical and basal ganglia lesions. EEG showed generalized slowing. Treatment with IVIG was started. Shortly thereafter he developed focal seizures followed a week later by extreme psychiatric symptoms and debilitating chorioaethetosis. Two serial 5 days courses of IV methylprednisolone pulses with slow tapering were added on. A new CSF analysis this time turned of positive for both oligoclonal bands and anti-NMDAR autoantibodies. Plasma- exchange courses gave no clinical effect and a second-line immunomodifying therapy with IV rituximab was offered. Chorioaethetosis showed a slight improvement, but behavior disorder with obsession compulsive symptoms coupled with repetitive oral insults persisted. Surprisingly he preserved his judgment and memory but executive function was affected.

Conclusions: Anti-NMDAR encephalitis is always a possible diagnosis when an encephalitis has a particular clinical course with seizures, dyskinesias and psychiatric symptoms even if at the beginning all characteristic biomarkers are absent. In our case the pregnancy history might turned this brain sensitive to an autoimmune dysregulation after a common virus infection.

Disclosure: No potential conflict stated.
P03-60

Immunosuppressive therapy in a five-year-old girl with Parry-Romberg Syndrome

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Introduction: Localized scleroderma is very rare disease and the most common subtype in children is linear scleroderma. Linear scleroderma in the face or scalp may be classified as en coup de sabre. This form is considered to be the mild form of a spectrum of craniofacial disease, the more severe form is called as Parry-Romberg syndrome (PRS) which is characterized by slow progressive atrophy of facial skin, soft tissues, bone, cartilage and muscles. Both diseases named as localized craniofacial scleroderma (LCS). Associated findings are seizures, headaches, cranial nerve involvement, hemiparesis, corneal and retinal changes. While the precise etiology is unknown, the recent studies suggest there is an underlying autoimmune process.

Methods: Herein we report a five-year-old girl with PRS who was treated with methotrexate.

Results: A five-year-old girl presented to our hospital’s dermatology clinic with atrophy and discoloration on the left side of her face during the past 3 months. She was referred to child neurology department as Parry Romberg syndrome. On physical examination, she had facial asymmetry with atrophic plaques and hyperpigmentation on her left face. On brain MRI, posterior periventricular nonspecific foci of white matter hyperintensity was demonstrated on left hemisphere. She was diagnosed as PRS and treatment with oral methotrexate was initiated. The lesion was stable for the past 6 months and there were no extra-cutaneous manifestations.

Conclusion: Although standard treatment regimen did not exist for LCS. Treatments with corticosteroid and immunosuppressant were reported. Since the recent studies have shown that neurological abnormalities may develop at any time during the course of the disease. Early diagnosis and treatment may prevent the development or worsening of neurological findings.

Disclosure: No potential conflict stated.

P03-61

Clinical and laboratory differential diagnostic aspects of Multiple Sclerosis, Disseminated Encephalitis and Encephalitis in children

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The aim: To identify clinical and laboratory features of differential diagnosis of encephalitis, disseminated encephalomyelitis (DEM) and multiple sclerosis (MS) in children.

Materials and methods: Children aged 1 month -17 years with encephalitis (n=52), DEM (n=46) and MS (n=40) were observed. All patients experienced brain and spinal cord MRI, PCR, ELISA, immunocytochemistry on herpes viruses of types 1,2,3,4,5,6, enteroviruses (EV), tick-borne encephalitis virus (CE) and Borrelia burgdorferi. The level of myelin basic protein (OBM) was determined in CSF. Serum IgG was determined by isoelectric focusing method.

Results and discussion: EF characterized by inconsciousness (86.5%), epileptic seizures (76.9%). Optic neuritis was observed in EF in 88.4%, in DEM - in 84.7%, and in MS – in 45% of cases. In 63% EF cases varicella-zoster virus, EV and CE were detected. Epstein-Barr virus and Borrelia burgdorferi dominated in DEM. In MS patients Epstein-Barr virus in 2/3 cases was combined with herpes virus 6 type. DEM and especially MS were associated with reactivation of a persistent or chronic infection. EF was characterized by pleocytosis in CSF and high level of D-dimer in serum and OBM in 87% cases and polyclonal IgG in blood and CSF in more than I cases in comparison with DEM. MS patients had oligoclonal IgG bands in CSF in 80% cases, and highest levels of IgG autoantibodies to OBM in serum. In I DEM cases oligoclonal IgG bands were detected more in serum than in CSF, and OBM autoantibodies were significantly lower than in MS.

Conclusion: Thus, clinical features in combination with results of laboratory studies can provide important additional information for the differential diagnosis of MS, DEM and EF in children.

Disclosure: No potential conflict stated.
The relationship between Herpes Viruses and Endothelium Dysfunction in paediatric CNS Demyelinating Diseases

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The aim: To determine the role of herpesviruses in endothelial dysfunction development in demyelinating diseases of central nervous system (CNS) in children.

Materials and methods: 65 children from 5 to 17 years old were observed: disseminated encephalomyelitis (DEM, n=37), clinically isolated syndrome (CIS, n=8), multiple sclerosis (MS, n=20) who had acute monophase (n=28), prolonged (n=13) and chronic course (n=24). Etiological diagnostics for herpes viruses of 1-6 types in blood and CSF were detected by PCR, ELISA, immunocytochemistry. MRI in T1-VI, T2-VI, DWI-IP and contrast MRI was provided to all patients. Desquamated endothelial cells (DEC) and D-dimer were detected in serum on 1, 30 days, 3 and 6 months.

Results: Acute course was characterised by d-dimer and DEC increase (1358.3±356.5 µg/ml and 12.2±2.5 KL / µl). In 82% cases parameters were still high by 30 days and decreased to normal after 3 months. Prolonged course characterised high parameters up to 6 months. Exacerbations of chronic cases were characterised by lower parameters of D-dimer and DEC (on average 825±188 µg/ml and 6.4±0.5 KL/µl). Herpes viruses were detected in 82% cases in serum and/or CSF. Reactivation was observed in 2/3 cases and primary infection – in 1/3 cases. Acute period was dominated in case of varicella-zoster virus (76%), while prolonged period – in case of Epstein-Barr (EBV) and cytomegalovirus, and chronic - mixed infection (EBV and herpes type 6) in 83%.

Conclusion: Herpesvirus infection is important in the formation of endothelial dysfunction in pediatric CNS demyelinating diseases.

Disclosure: No potential conflict stated.

A rare case of Acute Demyelinating Encephalomyelitis associated with Kawasaki Disease

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Introduction: Kawasaki Disease is an acute systemic small and medium-sized arteritis of pediatric population. %1-30 of patients with Kawasaki Disease can be complicated with central nervous system involvement. To our knowledge, only one case has been reported in the literature regarding its association with acute demyelinating encephalomyelitis (ADEM).

Case: A 4 year-old female patient admitted to pediatric neurology clinic with the complaints of tetraplegia, ataxia and globus vesicalis. She had been diagnosed Kawasaki disease 9 days ago and 2 gr/kg total dose of IVIG was given. Kranial and spinal magnetic resonance imaging revealed acute demyelinating lesions. She was treated with pulse steroid for 7 days with the diagnosis of ADEM and discharged from hospital on 15th day of admission with complete recovery.

Conclusion: Coexistence of ADEM and Kawasaki disease can be seen rarely. In this case, prognosis is good without any persistent neurological injury.

Disclosure: No potential conflict stated.
**P04-01**

**KCNT1 related severe Early Onset Epilepsy – A promising example of Precision Medicine**

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**Objective:** KCNT1 gene codes a voltage-dependent sodium-activated potassium channel. Gain-of-function mutations have been associated with a wide spectrum of epileptic disorders: Severe early onset epileptic encephalopathies, West syndromes, Epilepsy of infancy with migrating focal seizures (EIMFS), and more. Quinidine ameliorates resultant abnormally increased potassium currents in-vitro. Its clinical use has recently been reported. Response was observed in some. We describe a recent treatment in two additional patients in our hospital.

**Methods:** We identified KCNT1 mutation in two patients with intractable epilepsy. The first was a 3 months old infant who presented to our hospital with EIMFS and severe developmental delay. He was resistant to various anti-epileptic drugs, steroids, ketogenic diet and cannabis. We promptly found a de novo missense mutation in the KCNT1 gene by epileptic panel: Gly288Ser. Quinidine was then started at increasing doses. The second was a 3 years old child who presented to our hospital with West syndrome at the age of 5 months old. He was resistant to various anti-epileptic drugs, steroids, ketogenic diet. At the age of 3 years we identified a KCNT1 heterozygous mutation: Gly288Ser by Whole Exome Sequencing. The mother was also heterozygous. There were previous reports of somatic mosaicism or partial penetrance. He still suffered from intractable epilepsy and severe developmental delay. Quinidine was then started.

**Results:** Quinidine significantly reduced seizure burden by about 90% to the younger child and by almost 100% to the older child. Both were treated with increasing doses for up to 40mg/kg. No improvement was noted in developmental status.

**Conclusions:** We found a promising response to quinidine treatment in KCNT1 related severe early onset epilepsy. Due to new evolving precision medicine early genetic testing is recommended.

**Disclosure:** No potential conflict stated.

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**P04-02**

**T2w Hypointense MRI Lesions may represent an early marker of the Epileptogenic Zone in infants with Tuberous Sclerosis Complex. A case series**

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**Objective:** Drug-resistant epilepsy occurs in about 60% of patients with tuberous sclerosis complex (TSC). Seizures originate from tubers that display MRI features consistent with those of focal cortical dysplasia. Previous studies have shown that type II FCD lesions can be hypointense in T2w MRI sequences of unmyelinated brain. We aimed to study whether presumed epileptogenic dysplastic TSC lesions have a similar evolution of MRI abnormalities. We hypothesized that T2w hypointense areas can serve as an early marker of the epileptogenic zone.

**Methods:** We retrospectively evaluated MRI scans performed before the age of 12 months in nine TSC patients who underwent resective epilepsy surgery in Prague and Utrecht. On these MRI scans of unmyelinated brains, the neuroradiologists selected the largest hypointense areas on T2w sequences, expected to relate to the epileptogenic zone. We correlated their findings with latest presurgical MRI scans at older age, seizure outcome, and post-surgical MRI scans.

**Results:** In all but one case, the selected hypointense areas were included in the eventual resection since considered concordant with other results of presurgical diagnostic work-up. 5/9 patients were seizure-free at the last follow-up visit (mean duration 64 months), one with a history of seizure relapse. In 4/9 patients who had preoperative follow-up MRI at age > 12 months, repeated MRI scans of the selected (not-yet resected) lesions revealed evolution of MRI features consistent with FCD (e.g. transmantle sign, blurring of gray and white matter, increased cortical thickness).

**Conclusion:** T2w hypointense areas on MRI sequences of unmyelinated brain may represent an early marker of FCD-like tubers that represent the epileptogenic zone in TSC patients. This explorative pilot case series need further validation, planned in a larger cohort in the near future.

**Disclosure:** No potential conflict stated.
Fenfluramine HCl oral solution provides long-term, clinically meaningful (≥50%) reduction in seizure frequency in Dravet Syndrome: interim analysis of a long-term open-label extension study

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Objective: To characterize long-term safety and durability of effect for adjunctive fenfluramine (FFA) in treating Dravet syndrome (DS).

Methods: Patients (2-18 y/o) with DS entered a long-term open-label extension (OLE) (1503) after completing one of two Phase 3 studies: Study 1 (14 weeks; placebo or FFA 0.2 or 0.8 mg/kg/d; max, 30 mg/d) or Study 1504 (15 weeks; placebo or FFA 0.5 mg/kg/d; max, 20 mg/d); stiripentol was excluded in Study 1 but mandatory in Study 1504. In 1503, patients received FFA 0.2 mg/kg/d for Month 1; dosing was titrated to effect thereafter. Effectiveness and tolerability were assessed at Months 1, 2, and 3, then at 3-month intervals.

Results: At interim analysis (13-Mar-2018), 158/187 patients continued into OLE: 89% completed 12 months of FFA (mean dose, 15.2 mg/d; median duration, 400 d [range, 71-703]). During the entire OLE, median percent change in monthly convulsive seizure frequency (MCSF) for FFA vs pretreatment Phase 3 study baseline was -63.6% (P < 0.001); clinically meaningful (≥50%) and profound (≥75%) MCSF reduction from baseline were 63% and 41%. At Month 12, median and mean longest interval between convulsive seizures were 26 and 60 days (range: 2-589); 71% of caregivers and 83% of investigators rated patients’ “Much Improved/Very Much Improved.” Most common adverse events included appetite decrease, pyrexia, nasopharyngitis, and diarrhea. No valvular heart disease or pulmonary hypertension were observed in any patient.

Conclusions: Treatment with FFA resulted in robust, sustained reductions in MCSF and was generally well tolerated. No valvular heart disease or pulmonary arterial hypertension were observed in any patient at any time. FFA may be an important, novel antiepileptic drug for long-term DS treatment.

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**Suspected Autoimmune Epilepsy in children**

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**Introduction:** Lately, rising interest exists in possible autoimmune mechanisms in the pathogenesis of epilepsy. For an official diagnosis, evidence of autoimmune-mediated CNS inflammation is required. At times, though, despite the presence of clinical features suggestive of autoimmune epilepsy, such as acute or subacute onset or deterioration of seizures, multiple seizure types, antiepileptic drug resistance, varied neuropsychiatric symptoms, acute EEG deterioration and no other known cause identified, the evidence of neureinflammation might be scant. We present 4 cases of children with intractable seizures and various combinations of the above stated features that responded well to immunotherapy.

**Methods:** Presenting the cases of 4 girls, aged 8-13 years old, admitted to our department during the years 2016-2019. All had basic labs, ESR, metabolic and autoimmunity testing. They underwent lumbar puncture with full CSF analysis, IgG index, virologic and neuronal antibody screening. EEG and brain MRI scans were performed. All children showed antiepileptic drug resistance. They all received intravenous methylprednisolone and immunoglobulin after the sample collection, while 2 of the children also received intravenous acyclovir.

**Results:** 1 child had CSF evidence of neuroinflammation. All children had normal MRI scans. They all presented acute EEG deterioration, 2 of them developing non-convulsive status and the other 2 generalized slow activity. 1 child had other autoimmunity findings (antithyroid antibodies). The neuronal antibodies' screening was negative and no other underlying cause was discovered. All patients responded well to immunotherapy with clinoico-EEG improvement.

**Conclusion:** In cases of clinical presentation suggestive of autoimmune epilepsy and no other causative factor found, the consideration of an immunotherapy trial with careful monitoring of the patient’s response is justified and might have catalytic effect.

**Disclosure:** No potential conflict stated.

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**KCNQ2-Related Disorders: clinical spectrum and response to sodium channel blockers**

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**Introduction:** KCNQ2-related disorders are among the most frequent causes of neonatal seizures. We aim to characterize the clinical and molecular findings in a series of patients, with particular interest in the response to sodium channel blockers.

**Methods:** Retrospective descriptive study. This study included patients with neonatal seizures and de novo mutations in the KCNQ2 gene, attended at a tertiary pediatric hospital in the last 5 years.

**Results:** Ten patients were included, among which 5 out of 10 were male. The median age at seizures onset was 1 day of life (p25-p75:0.5-1.4 days). At disease onset, 9/10 patients presented with tonic seizures, often followed by focal clonic jerking and accompanied by apnea with desaturation (sequential seizures). The video-EEG showed epileptiform abnormalities in 9/10. All of them exhibited normal brain MRI. All patients who received oxcarbazepine, carbamazepine or lacosamide were seizure-free or achieved seizure control (7/10) and 3/10 patients achieved seizure control after receiving sodium valproate. During the first years of life, 2/10 patients had a positive outcome (seizure-free and normal psychomotor development); 6/10 presented with psychomotor delay/intellectual disability; 1/10 presented with language impairment and 1/10 with autism spectrum disorder. Three categories of KCNQ2 variants were found: missense (7/10), frameshift (2/1) and duplication (1/10). Four out of ten variants had not been reported in the literature, but were classified as likely pathogenic using in silico prediction tools.

**Conclusions:** KCNQ2-related disorders are an emergent cause of neonatal seizures. Early treatment with sodium channel blockers should be considered in neonatal seizures treatment protocols specifically when seizure type is sequential, and seizures are refractory to first line antiepileptic drugs. Prospective studies based on the outcome of early treated patients should be performed.

**Disclosure:** No potential conflict stated.
Adjuvant Perampanel and Health-Related Quality of Life (HRQoL) in paediatric patients (aged 4 to <12 years) with Partial-Onset Seizures (POS) or Primary Generalised Tonic-Clonic Seizures (PGTCS) in Study 311

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Objective: Study 311 (NCT02846626) was an open-label, single-arm study of adjuvant perampanel oral suspension in patients aged 4 to <12 years with inadequately controlled POS (with/without secondarily generalised seizures [SGS]) or PGTCS. Here, we assess the impact of adjuvant perampanel on HRQoL using the EuroQol 5 Dimensions-Youth (EQ-5D-Y) scale during the 311 Core Study.

Methods: The Core Study consisted of 4-week Pre-treatment, 23-week Treatment and 4-week Follow-up Periods. The EQ-5D-Y was assessed in the Full Analysis Set (FAS), administered during Baseline and at Week 23, and included 5 domains with 3 levels: no problems, some problems and a lot of problems. Change from Baseline in the EQ-5D-Y visual analogue scale (VAS) at Week 23 (last observation carried forward) was an exploratory endpoint.

Results: The FAS included 180 patients. In general, the proportions of patients reporting no problems or some/a lot of problems were similar during Baseline vs Week 23: mobility, 64/112 (57.1%) and 48/112 (42.9%) vs 59/108 (54.6%) and 49/108 (45.4%), respectively; self-care, 42/112 (37.5%) and 70/112 (62.5%) vs 39/109 (35.8%) and 70/109 (64.2%), respectively; doing usual activities, 53/112 (47.3%) and 59/112 (52.7%) vs 45/109 (41.3%) and 64/109 (58.7%), respectively; having pain/discomfort, 78/115 (67.8%) and 37/115 (32.2%) vs 71/110 (64.5%) and 39/110 (35.5%), respectively; feeling worried/sad/happy, 80/113 (70.8%) and 33/113 (29.2%) vs 77/109 (70.6%) and 32/109 (29.4%), respectively. The mean (standard deviation [SD]) EQ-5D-Y VAS during Baseline (n=115) was 73.8 (23.0); at Week 23 (n=109), mean (SD) change from Baseline in EQ-5D-Y VAS was 2.3 (21.1).

Conclusion: These data do not indicate any significant changes in HRQoL in patients aged 4 to <12 years with POS (with/without SGS) or PGTCS during adjuvant perampanel treatment.

Disclosure: Elena Arce Portillo has no conflicts of interest to disclose. Anna Patten is an employee of Eisai Ltd. Manoj Malhotra and Leock Y Ngo are employees of Eisai Inc.
P04-08

Preliminary results of the project: “Supporting a Pilot Program for the Creation of Medical Centre Specialized in Diagnosis and Therapy for Children with Fetal Alcohol Spectrum Disorder (FASD)”

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Introduction: Fetal Alcohol Spectrum Disorder is defined by evidence of growth deficiency, characteristic features of dysmorphia and evidence of central nervous system dysfunction occurring in patients exposed to alcohol during gestation. In Poland FASD occurs among about 2% population. The aim of the project was to create a model of diagnostic centre for patients with FASD.

Methods: Over 50 patients aged between 1 month and 14 years, with a history of alcohol exposure during pregnancy examined by the multidisciplinary team: child neurologist, paediatrician, child psychiatrist, speech therapist, physical therapist, specialist in genetics, neuropsychologist. Patients also underwent additional laboratory tests such as blood tests, brain imaging (MRI), genetic examinations (including NGS if necessary). At the end of the diagnostic part each patient received from all specialists a holistic medical and psychological diagnosis and recommendations for parents, school teachers, therapists, etc. After that the group has been followed up for 2 years. This is the period of assessment of the implementation of those recommendations.

Preliminary Results: Patients presented various neuropsychological deficits (in: memory, abstract reasoning, language, nonverbal reasoning, sensory integration, executive function) and intellectual disability. Due to low specificity of these deficits, the characteristic neurobehavioral profile of the FASD patient could not be created. Neuropsychological deficits did not correlate with dysmorphic features nor microcephaly. Despite exposure to alcohol in the fetal period, not all patients received the diagnosis of FASD – these patients are “at the risk group” and should be regularly examined.

Conclusion: The FASD diagnostic process should be complex, best accomplished by a multidisciplinary clinical team. Because it is a diagnosis of exclusion and each patient requires specialist consultations and additional examinations should be made in highly specialized centres.

Disclosure: No potential conflict stated.

P04-09

Clinical characteristics of Tic Disorders in children

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Objective: Tic disorder is a neurodevelopmental disorder that begins in early childhood and continues into adolescence and adults. Tic disorder affects 1–2% of the population, with highly varying severity. In this study, we aimed to investigate the clinical characteristics and neuropsychiatric comorbidities of patients with tic disorder.

Methods: We retrospectively reviewed the medical records of pediatric patients with tic disorder who were examined and diagnosed from January 2012 to April 2018 at Uijeongbu St. Mary’s Hospital, The Catholic University of Korea.

Results: A total of 86 pediatric patients (62 males, 24 females) were identified. The mean age at diagnosis was 7.8 years (range, 1 – 17). The mean time period between symptom onset and diagnosis was 10.4 months (range, 0.25 – 96). The most common symptoms that patients reported on their first visit were eye blinking (55.8%), head turning or nodding (16.4%), and eyebrow rolling (8.2%). Thirty-three of 86 patients (38.3%) had neuropsychiatric comorbidities; attention deficit hyperactivity disorder (12.8%), epilepsy (9.3%), developmental delay (3.5%), enuresis (3.5%), anxiety disorder (3.5%), and depressive mood disorder (1.2%). A significant relation was found between the presence of tic disorder and impaired school performance.

Conclusion: Tic disorder is a fairly uncommon but disabling clinical disorder among children. Clinical assessment of children with tic disorder warrants examination of other neuropsychiatric problems.

Disclosure: No potential conflict stated.
Long-term efficacy and safety of Eslicarbazepine Acetate in children: an open-label extension following the double-blind, randomized, placebo-controlled study

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Introduction: Eslicarbazepine acetate (ESL) is an anticonvulsant approved by EMA for treatment of focal onset seizures (-FOS) in children aged above 6 years. A phase III study assessed efficacy and safety of ESL as adjunctive therapy in children and adolescents with refractory partial epilepsy. Patients completing double-blind (DB) and 1-year open label extension (OLE), Part II, were followed-up in additional OLEs: Part III-IV (1 year each) and Part V (2 years). In this work, the therapeutic effect and safety profile of ESL during long-term treatment (Part III-V) in children is presented.

Methods: ESL 20 mg/kg/day, up to a maximum of 1200 mg/day, was provided as oral suspension (2–6 years) or tablets (≥7 years). Responder rate (RR) (relative seizure reduction ≥50% compared to Baseline Part III–V), standardized seizure frequency (SSF) as well as safety parameters were assessed. Results: 152 patients from Part II continued into Part III, 94 into Part IV and 67 into Part V (289.9 patient-years exposure to ESL). At start of Part III, 87 patients (57.2%) were male, 137 (90.1%) Caucasian, and mean age was 10.2 years. Overall RR during Part III–V was 25.7%, total median SSF was 3.0 at baseline (end of Part II) decreasing to 2.4 (overall) during Part III–V, resulting in median relative change of -22.9%. Safety results were as follows: 97 patients (63.8%) experienced at least 1 treatment emergent adverse event (TEAE). The majority of TEAEs (87.6%) were mild or moderate in intensity and resolved without sequelae. Most frequently reported TEAEs were convulsion (13.2%), nasopharyngitis and pyrexia (10.5% each), bronchitis and upper respiratory tract infection (8.6% each). 19 patients had at least 1 serious TEAE; none considered related to ESL. No patient experienced TEAE that led to treatment discontinuation.

Conclusion: Overall efficacy data of ESL as long-term treatment of FOS in children was observed and no new specific safety issue is identified after over 5 years of exposure.


Neurological and neuropsychological assessment in young children with Isolated Basal Ganglia Stroke

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Objective: Arterial ischemic stroke of the basal ganglia (AIS-BG) has a relatively long-term benign evolution in children. However, little is known about neurological and neuropsychological features in the pre-scholar age group. Since this information may be important to guide rehabilitation interventions, we aim to describe neurological and cognitive features in the acute and early chronic phases in a small series of children with AIS-BG.

Methods: We selected children with isolated AIS-BG diagnosed at our Institution from 2016–2019 who underwent a detailed neurological and neurodevelopmental assessment with Griffiths and PSOM scales at onset and after 6–18 months. Data on brain MRI and EEG were also evaluated.

Results: Five patients were recruited (4 males, age 8months – 3.4years), with post-ictive (2/5 cases) or post traumatic AIS-BG (3/5 subjects). Symptoms at onset (age 6 months – 3 years) included motor deficits (5/5), involuntary movements (1/5), language disorders (2/5), and seizures (1/5). EEG showed in 3/5 cases non-specific abnormalities. At 6–18 months, Griffiths scales revealed normal-borderline development in all cases, with better rates on personal ability and performance, but mild impairment in motor abilities, coordination and language. PSOM revealed a good evolution (0–1.5 points), especially in one patient with post-traumatic AIS-BG (PSOM 0). Persistence of mild motor impairment was observed in 4/5 patients and language disorders in 3/5 subjects.

Conclusion: Despite the relative good evolution of AIS-BG in infants and young children, residual impairment in motor, executive functions and language skills may be observed 6–18 months after the acute event, indicating the importance of prolonged and targeted rehabilitation strategies in this group age to improve the long-term neurological outcome.

Disclosure: No potential conflict stated.
P04-12

Ketogenic diet experience of our clinic in Epileptic Encephalopathy patients

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Introduction: Ketogenic diet (KD) is accepted as a treatment modality for refractory childhood epilepsy. Response to treatment depends on the appropriate patient selection as well as compliance to treatment. We aim to present the treatment response of KD in patients with epileptic encephalopathy followed by our clinic.

Method: 14 patients (57% male) with epileptic encephalopathy who underwent KD were enrolled in the study. The patients records were retrospectively reviewed and information about etiology of encephalopathy, response rate to treatment, side effects and discontinuation reasons were noted.

Results: Mean first seizure age was 4.3±6.2 (0-22) months. 85.7% of the patients had daily numerous seizures before treatment. Mean treatment duration was 11.35±7.7 (2-29) months. 4 patients (28.6%) were seizure free at 3 months visit (1 patient with WWOX mutation, 1 patient with SCN2A mutation, 1 patient pyruvate dehydrogenase deficiency and 1 cortical dysplasia with epileptic encephalopathy). 4 patients were non responsive (2 patients with tubers sclerosis, 1 KCNQ2 mutation,1 Dravet syndrome) and 4 patients had partial response (>50% decrease in seizure frequency and severity)(1 patient with KCNQ2 mutation, 1 mitochondrial diesese with unknown genetic etiology, 2 patients with hypoxia secquela). Most common side effect was constipation but none of the side effects caused discontinuation of the treatment. Two patients ceased the diet early because of compliance problems.

Conclusion: KD is a safe and effective treatment modality for patients with epileptic encephalopathy and should be considered as an early intervention if no contraindications exist.

Disclosure: No potential conflict stated.

P04-13

Specific personality and amygdala volume in Gorlin Syndrome

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Objective: Gorlin syndrome (GS), characterized by developmental abnormality and tumorigenesis, involves enhanced sonic hedgehog (Shh) signaling from the prenatal period. Shh signaling has an important role in the development of neurotransmitter production cells. We studied the personality and the amygdala volume of patients with GS.

Methods: We enrolled 13 patients with GS (7 males and 6 females, mean age 24.0) and 16 control subjects (6 males and 10 females, mean age 28.8). The Japanese version of Temperament and Character Inventory (TCI), a self-fill questionnaire consists of 125 questions, was used. TCI is based on the seven-dimensional model of temperament and character by Cloninger, and is controlled by the neurotransmitter. Next the amygdala was measured by determining its volume on magnetic resonance imaging with image processing software. This study was approved by the Ethics Committee of Chiba University.

Result: The control as a 1.00, patients with GS were 0.98 in novelty seeking, 0.89 (p=0.006) in harm avoidance which is related to serotonin, 0.97 in reward dependence, 1.10 in persistence, 1.03 in self-directedness, 1.06 in cooperativeness and 0.99 in self-transcendence. In addition, in the GS patients with developmental abnormality, harm avoidance was significantly decrease as 0.83 (p=0.002). Mean amygdala volumes for patients with GS were 1.52 cm³ (right), 1.26 cm³ (left); mean amygdala volumes for control subjects were 1.53 cm³ (right) and 1.53 cm³ (left). The left amygdala was significantly reduced in patients with GS (P = 0.002).

Conclusion: Patients with GS showed low score in serotonin-related harm avoidance, especially with developmental abnormalities were significantly lower. And the left amygdala volume was significantly reduced from control levels in patients with GS. Shh signaling may be involved in human personality formation.

Disclosure: No potential conflict stated.
Our experience of Perampanel, a newer Antiepileptic Drug (AED), in the treatment of children with difficult to manage Epilepsy – A 4-year retrospective, single quaternary centre study

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Objective: To determine the efficacy, side effects and retention rates of Perampanel in children with refractory epilepsy at our hospital.

Methods: Retrospective data was collected from clinical letters and pharmacy records for N=79 children treated with Perampanel in the past 4 years. Data included demographics, seizure types, additional impairments, previous AEDs, other treatments, Perampanel starting dosage, side effects, treatment effects and duration of use. N=15 were omitted due to insufficient data.

Results:
Demographics:
N=64
Age range: 0-16 years, mean 4.7 years, median 4 years
Primary seizure type: N=60 focal onset (N=31 generalised tonic-clonic, N=11 myoclonic, N=18 other), N=3 absence, N=1 myoclonic (JME)

Prior treatments:
Number of AEDs=4.4 (range 1-10), mean 4.4, median 4
N=14(22%) on epilepsy surgery pathway
N=8(13%) had a VNS
N=10(16%) tried ketogenic diet

Perampanel dosages:
Starting: N=5(8%) 1mg, N=53(83%) 2mg, N=1(2%) 6mg, N=5(8%) unclear
At 3 months:
N=12(19%) 2mg, N=1(2%) 3mg, N=26(41%) 4mg, N=14(22%) 6mg, N=2(3%) 8mg
N=9(14%) stopped due to side effects

Side effects: N=24(38%) patients displayed side effects (N=4 multiple):
N=8(13%) - aggression
N=2(3%) - reduced affect
N=4(7%) - poor tolerance
N=8(13%) - deteriorating epilepsy control
N=6(9%) - lethargy

Impact on seizures:
N=5(8%) increased seizures
N=19(30%) no effect
N=36(56%) seizure suppression [N=19(30%) <50%, N=15(23%) >50%, N=2(3%) 100%]
N=4(6%) unclear
Some improvement seen with all seizure types

Treatment duration:
N=9(14%) <3 months
N=19(30%) at least 3 months-1 year
N=16(25%) at least 1-2 years
N=11(17%) at least 2-3 years
N=6(9%) at least 3-4 years
N=1(2%) >4 years
N=2(3%) unclear

Outcomes/Conclusion:
Perampanel is an effective AED for many children with intractable epilepsy
Side effects include behavioural problems, lethargy and increased seizures
Most patients continued Perampanel beyond 3 months
Further studies are necessary to better determine which children may benefit and optimal dosing regimes

Disclosure: No potential conflict stated.
The association of EEG abnormalities and core symptoms in children with Attention-Deficit/Hyperactivity Disorder

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Objective: Electroencephalography (EEG) has played some role in the assessment of neural function in children with Attention-Deficit/Hyperactivity Disorder (ADHD). We've investigated the EEG characteristics in children with ADHD and its association with ADHD core symptoms.

Methods: We've enrolled children newly diagnosed as ADHD from the Pediatric Outpatient Clinics for EEG study and classified into subtypes based on DSM-5 criteria, including inattentive type, hyperactive-impulsive type, and combined type. EEGs were regarded as abnormal based on the presence of focal or generalized epileptiform discharges and/or background slowing.

Results: From Jan, 2007 to Dec, 2018, 148 ADHD children (M/F=120/28, aged 3~15 years) receiving complete EEG study were recruited. Children with abnormal EEG (n=59) were slightly older than those with normal EEG (n=89) (7.9±3.1 v.s. 7.8±2.4 yr, p=0.03). Of 53 patients (35.8%) with inattentive type, 14 (26.4%) revealed EEG abnormalities, including 1 with focal background slowing and 13 with focal or generalized epileptiform discharges. However, of 95 patients (64.2%) with hyperactive-impulsive type or combined type, 45 (47.4%) showed EEG abnormalities, including 7 with focal background slowing and 42 with focal or generalized epileptiform discharges. Abnormal EEG was found significantly more in children with hyperactive-impulsive or combined type (47.4% v.s. 26.4%, p=0.01). Total 50 children (84.7%) had focal epileptiform discharges and most commonly seen foci were bilateral central regions (n=22, 44.0%). Four children (6.8%) with abnormal EEG developed epilepsy later, however, no children with normal EEG evolved into epilepsy.

Conclusion: The hyperactive-impulsive symptoms in children with ADHD seemed significantly correlated with EEG abnormalities, especially focal epileptiform discharges over bilateral central areas. These findings indicated that dysfunction of supplementary motor cortex or primary motor cortex may be associated with hyperactive-impulsive symptoms.

Disclosure: No potential conflict stated.

Childhood Absence Epilepsy. Does it really have a good prognosis?

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Introduction: Childhood absence epilepsy (CAE) has been considered as “benign” epilepsy for a long time because the majority of patients treated with antiepileptic drugs (AED) become seizure-free, but there are data about relapses and other associated, non-absence seizures. Our aim was to study the outcome and the possible prognostic factors of CAE.

Methods: Data collected about 57 patients with CAE were the following: the age at the onset of absence seizures, duration of time between the onset of seizures and the initiation of AED treatment, occurrence and characteristics of the typical 3c/s EEG patterns, efficacy of the administered AED and frequency of relapses.

Results: Average age at the onset of CAE was 7.7 (1-16) years. The period between the onset of seizures and the initiation of AED treatment lasted 4.9 (0-26) months. 30/57 of the patients became seizure-free after administration of the first-choice AED (valproic acid, lamotrigine or ethosuximide). In 27/57 children, therapy had to be changed: in 16 cases a new monotherapy, while in 11 cases add-on therapy was initiated. In 33.3% of the patients, a third-choice antiepileptic drug was necessary. The rate of periods containing the characteristic 3c/s spike and wave complexes on EEG was 1.5 times higher in the cured group than in the non-cured group.

Conclusion: CAE cannot be considered a clearly “benign” type of epilepsy, as 1/ the first-choice AED was effective in 52.6% of patients; 2/ only 45% of those children who had been diagnosed for at least 3 years were cured. Second-choice monotherapy seemed to be more effective than the add-on therapy. A higher rate of periods containing 3c/s spike and wave complexes on the EEG can be a good prognostic factor.

Disclosure: No potential conflict stated.
Amantadine – An optional treatment for Sever Secondary Myoclonic Epilepsy and Hyperkinetic Dyskinesia

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Introduction: Herpes encephalitis is a devastating disease with poor prognosis and neuro-developmental complications. We present a patient who was diagnosed with herpes encephalitis at the age of 6 months and treated with IV Acyclovir, steroids and anti-epileptic therapy. After a few weeks with partial gradual improvement a second clinical regression occurred including: clinical and electrographic myoclonic seizures, hyperkinetic dyskinesia mainly choreathotic movements and functional regression.

A secondary anti-NMDA autoimmune encephalitis was suspected and anti-neuronal antibodies were demonstrated in his CSF samples.

Methods and Results: The patient was treated with several anti-inflammatory therapies including rituximab, several anti-epileptic drugs, ketogenic diet and medical cannabis with no significant clinical improvement. His repeated EEG tests demonstrated bilateral spike-wave and polyspikes discharges with decrement and multifocal spikes. At the age of 20 months Amantadine treatment was started and few weeks later a remarkable clinical and electrographic response was shown.

Conclusion: We will discuss the mechanism, pharmacology and new interesting clinical implications of Amantadine therapy.

Disclosure: No potential conflict stated.
Co-infection Neuroborreliosis and Ehrlichiosis mimicking Paraneoplastic Syndrome – Progressive Encephalomyelitis with Rigidity and Myoclonus (PERM) in teenage girl

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**Case description:** A 16 years old girl presented with 2 weeks of severe headache, nausea, vomiting, fever, later gradually developed leg stiffness and difficulty in ambulation. She also admitted having itchy skin prior to the original complaints. Examination of the cerebrospinal fluid showed pleocytosis. Due to suspicion of neuroborreliosis and ehrlichiosis (epidemiological anamnesis) she received antibacterial therapy. The headache and fever abated and the patient was discharged. Shoulder stiffness, spastic paraparesis in lower extremities, pain in joints, emotional lability, panic attacks and anxiety persisted so the patient received rehabilitation and psychotherapy. Five months after the initial presentation she developed sudden episodes of axial hyperextension (opisthotonus), rigidity, generalized myoclonus (sensitive to auditory stimuli). She was able to walk only with assistance. Symptomatic treatment of neurologic symptoms offered no relief. Chronic neuroinfections were excluded, paraneoplastic antibody and autoimmune encephalitis panels were negative. Magnetic resonance imaging revealed inflammatory changes in medulla oblongata, leptomeningitis, polyradiculoneuritis, and multiple thoracic compression fractures. Due to suspicion of malignant process positron emission tomography (PET) was performed and revealed changes in clavicular lymph nodes leading to biopsy and diagnosis of Hodgkin's lymphoma. Neurologic symptoms resolved completely when specific therapy for the lymphoma was initiated.

**Conclusion:** Paraneoplastic syndromes are very rare in pediatric population, when there is an initial failure in therapy, other diagnoses should be considered.

**Disclosure:** No potential conflict stated.

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Anti-epileptic drugs do not resolve impaired memory consolidation in Idiopathic Epilepsy Syndromes of childhood

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**Objective:** Preliminary studies suggest that sleep-related memory consolidation is altered in idiopathic epilepsy syndromes of childhood, possibly in relationship with activation of interictal epileptiform discharges (IED) during sleep. Here we tested the hypothesis that an anti-epileptic drug (AED) aimed to decrease IED during sleep could improve memory consolidation.

**Methods:** Verbal (word-pair association) and nonverbal (2D object location) declarative memory tasks were administrated to patients at baseline, in sleep condition (learning and immediate retrieval in the evening), and delayed retrieval on the next morning after a night of sleep) and in awake condition (learning and immediate retrieval in the morning, and delayed retrieval in the evening without sleep during the day). The procedure was replicated one month after the introduction of an AED. Electroencephalogram was recorded during the 24-hours procedures.

**Results:** Ten patients (4 males) aged 6-10 years were enrolled (idiopathic focal epilepsy complicated by continuous spikes-waves during slow sleep, CSWS: 2; childhood epilepsy with centro-temporal spikes, CECTS: 4; childhood absence epilepsy, CAE: 4). At baseline, the expected profile of improved overnight but not overnight memory consolidation was observed in only 3 patients, with CAE. After one-month treatment (CSWS: clobazam in 1, hydrocortisone in 1; CECTS: levetiracetam in 3, valproate in 1; CAE: ethosuximide in 3, lamotrigine in 1), overnight consolidation was improved in 3 patients and overnight consolidation in 4 patients, but changes were not significant at the group level. There was no correlation between the improvement of memory consolidation and the AED-induced decrease of IED.

**Conclusion:** These results confirm that memory consolidation processes are impaired in childhood idiopathic epilepsy syndromes but do not support the hypothesis of a pathophysiological role of IED during sleep.

**Disclosure:** No potential conflict stated.
**P04-21**

**Potassium Bromide in Dravet Syndrome and Lennox-Gastaut Syndrome: an underutilized option?**

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**Purpose:** Potassium bromide (KBr) is the oldest known anti-epileptic drug (AED) and has recently regained attention thanks to the efficacy reported in Dravet Syndrome (DS). Only anecdotal reports are available for structural focal epilepsies and Lennox-Gastaut Syndrome (LGS). Despite those encouraging reports this inexpensive medication is still underutilized in many countries. The aim of our study was to evaluate efficacy and safety of KBr in patients with DS and LGS.

**Method:** We retrospectively analyzed all the 20 consecutive patients (median age 11.5, range 2-38) with DS (6) and LGS (14) that, from March-2009 to December-2018, have been prescribed with KBr at our Institution. Etiology of LGS was malformation of cortical development (3), Aicardi Syndrome (1), COL4A1-encephalopathy (1), LAMA2-related encephalopathy (1) and postpnemococcal-encephalopathy (1). KBr was titrated up to a median dose of 38mg/Kg (range 15-85mg/Kg). We used seizure diaries to evaluate efficacy at 3-, 6-, 12- and 24-months, according to treatment duration (2months-3.9years, median 1.9years). Adverse effects and chloremia where monitored in all patients.

**Results:** At 3 months 15 of the 18 patients analyzed (2 were excluded for shorter follow-up) had a significant seizure reduction (>50%). Significant seizure reduction was persistent in 11/16 at 6months, 7/13 at 12months, 4/8 at 24months. Of the 10 patients that had status epilepticus (SE) in the 3 months before KBr treatment only one presented non convulsive SE during KBr treatment. Five of 22 patients presented adverse effects (acneiform rash in 2 and somnolence in 3), that led to drug withdrawal in 2 patients. All of our patient presented during the treatment spurious hypochloremia that well correlated with KBr dose.

**Conclusion:** At relatively low doses, Potassium Bromide is a safe and effective option not only in Dravet Syndrome, as reported in literature, but also for Lennox-Gastaut Syndrome.

**Disclosure:** No potential conflict stated.

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**P04-22**

**«Masks» of Ischemic Stroke in children with malignancies**

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**Introduction:** The main reasons for neurological consultation of patients with malignances are seizures, acute focal neurological symptoms, alteration of consciousness. Differential diagnosis of ischemic stroke is particular difficulty due to the risk factors of cerebrovascular disorders in children with cancer.

**Materials and methods:** A series of clinical cases of 13 children (5 boys and 8 girls aged 4 to 17 years) with different malignances treated at the Pediatric Oncology and Hematology Center Morozov City Children Hospital from 2017 to 2019 with acute focal neurological symptoms. Methods: clinical, laboratory, neuroimage (computed and magnetic resonance imaging - CT, MRI), functional (electroencephalography - EEG).

**Results:** 13 patients with pineoblastoma, medulloblastoma, acute lymphoblastic leukemia (ALL) Burkitt’s lymphoma. Polychemotherapy included methotrexate in all cases. Neurological symptoms, alteration of consciousness-7/13, seizures and alteration of consciousness-7/13, headache-1/13, CT, MRI, EEG were carried out in all cases. Hyponatremia and hypocalemia were not revealed in all 7 cases of seizures. Three patients were diagnosed with ischemic stroke, but in the reassessment of MR studies in 2 of them the diagnosis of stroke was changed: in 1 case «Stroke-like leukoencephalopathy», in the other case - a combined recurrence of ALL. «Posterior reversible leukoencephalopathy» was diagnosed in four cases. Toxic leukoencephalopathy after the therapy was seen in five patients. «Stroke-like migraine attacks after radiation therapy syndrome» was noticed once.

**Conclusion:** The underlying disease and therapy, symptoms of debut neurological complications make it necessary to exclude a stroke at the first diagnostic step. The "masks" of ischemic stroke are varied in pediatric practice. The “gold standard” of diagnostics is MRI of the brain. Diagnosis of stroke and adequate patient management play an important role in reducing forced breaks in programmed cancer therapy in children.

**Disclosure:** No potential conflict stated.
Use of a medium chain Triglyceride-based food for special medical purposes in children with Epilepsy: compliance, tolerability and acceptability

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Introduction: Ketogenic diets (KDs) are an effective option for drug-resistant epilepsy, although they are often associated with poor compliance and dissatisfaction. Medium chain triglycerides (MCT) can improve the palatability of KDs, but their use is limited due to poor acceptability, taste and lack of convenience. Betashot, a ready-to-use, palatable MCT emulsion, aims to address these issues. This study evaluates the compliance, tolerability and acceptability of Betashot in individuals with epilepsy.

Methods: Children with epilepsy took Betashot daily for 12 weeks, whilst consuming their normal diets but limiting intake of high refined-sugar foods. Betashot recommended intake was calculated as a percentage of total energy intake, up to a maximum of 35%, and was adjusted according to tolerability. Study visits were conducted at baseline, 5 and 12 weeks; visits included dietetic and medical assessment, quality of life questionnaires and biochemical investigations.

Results: 35 children (51% male, mean age 10.8 years) commenced Betashot. 8(23%) had Dravet syndrome, 4(11%) had alternating hemiplegia of childhood, 3(9%) had Glut-1 transporter deficiency syndrome and the remaining 20(57%) had other genetic or presumed genetic diagnoses of epilepsy. 21(60%) children completed the 12-week study. The most common known reason for discontinuation was gastrointestinal side effects (abdominal pain/discomfort, diarrhoea and/or vomiting). 21(60%) children remained on Betashot after the study end point.

Conclusion: Betashot was well-tolerated. This is reflected by attrition rates and the proportion of participants remaining on Betashot past the study end point. Adverse side effects were predominantly mild and gastrointestinal. The effect of dietary modification with Betashot on seizure frequency is to be reported at a later date.

Disclosure: No potential conflict stated.

Comparison of neurocognitive outcomes between Levetiracetam and Phenobarbital monotherapy for the treatment of neonatal seizures

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Introduction: Neonatal seizures are the frequent manifestations of central nervous system dysfunction. In this study, we aimed to evaluate the neurodevelopmental outcomes between monotherapy levetiracetam and phenobarbital use in neonatal period.

Methods: This prospective observational study was performed on infants, having neonatal seizures and requiring anticonvulsant treatment in neonatal period. Children who exposed to levetiracetam or phenobarbital monotherapy in neonatal period and aged between 6 to 42 months old were enrolled to study. Neurodevelopmental outcomes were assessed as measured by motor, cognitive and language performance on the Bayley Scales of Infant Development, third edition (BSID-III).

Results: A total number of 62 patients were assessed with BSD-III of whom 40 received levetiracetam monotherapy, 22 received phenobarbital monotherapy. Twenty-five (40%) patients had structural etiologies, 5 (8%) patients had metabolic etiologies, one (2%) patient had infectious etiology and 31 (50%) patients had unknown etiologies. Cranial MRI was obtained in 61 patients and was normal in 27 (44%) patients. Electroencephalography was obtained in 62 patients and was normal in 40 (65%) patients. The mean duration of treatment was 8.6 months. There were no significant intergroup differences in sex, age, seizure etiology, cranial MRI findings, EEG findings and duration of treatment (p >.05). Children with BSD-III cognitive, receptive language, expressive language, fine motor, gross motor scale scores and cognitive, language, motor composite scores had no statistically significant differences between levetiracetam and phenobarbital monotherapy groups.

Discussion: Our findings suggest that both levetiracetam and phenobarbital therapy were considered equally safe as monotherapy for the treatment of neonatal seizures. Because of treatment duration short in our study, clinical studies with longer treatment duration could provide more definitive evidence.

Disclosure: No potential conflict stated.
POSTER PRESENTATIONS > POSTER SESSION 4
Epilepsy: medical and surgical treatment, Neuro-oncology, Neuro-psychiatry

P04-25

Long-term therapeutic effect of Eslicarbazepine Acetate in children: an open-label extension of cognition study in children 6-16 years

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Introduction: Eslicarbazepine acetate (ESL) is approved by EMA for treatment of focal onset seizures (FOS) in children aged 6 years above 6 years. A phase II study in patients 6-16 years with FOS assessed cognitive effects, efficacy and safety of ESL as adjunctive therapy (BIA-2093-208). Patients completing double-blind (DB) entered a 1-year open label extension (OLE) Part II, followed by an additional OLE Part III (2 years). We here-by present therapeutic effect and safety profile of ESL during this two-year Part III.

Methods: ESL (10-30 mg/kg/day, up to maximum 1200 mg/day) was provided as 200 mg tablets. Efficacy endpoints were the treatment retention time (as actual time treated) and Clinical Global Impression-Severity (CGI-S) scale change from baseline (end of Part II). Safety was assessed by incidence of treatment-emergent adverse events (TEAEs).

Results: 123/133 patients continued to OLE: 94 completed Part II and 42 entered Part III of which 31 (73.8%) completed this 2-year OLE. Group was equally balanced for gender, mean age 12.2 years (distributed across 2 age groups: 6-11y and 12-16y), mostly Caucasians. Median treatment retention time was 735 days (95% CI: 728.0, 741.0) similar in both age groups. Mean values and changes from baseline in CGI-S scale parameters at last assessment had a reduction from baseline in the severity of illness (-0.5); all other categories were unchanged from baseline. Results were similar for the two age groups. Overall, 7 patients (16.7%) experienced at least one TEAE during the two-year OLE, mostly mild or moderate in intensity. Only pyrexia and cough were reported more than once. Incidence of SAEs was low (4.8%), none considered related to study drug.

Conclusion: A majority of patients remained on treatment during this two-year OLE. There was no apparent worsening of disease severity. Adverse events were similar to those observed in adult studies and no new signal was identified.


P04-26

Study 311: evaluation of adjunctive Perampanel on mental health in children (aged 4 to <12 years) with Partial-Onset Seizures (POS) or Primary Generalised Tonic-Clonic Seizures (PGTCS)

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Objective: Study 311 (NCT02849626) was an open-label, single-arm study of adjunctive perampanel oral suspension in patients aged 4-<12 years with uncontrolled POS or PGTCS. Since suicidal thoughts and behaviour have been associated with anti-seizure drug usage, treatment-emergent suicidal ideation and behaviour were assessed during the 311 Core Study.

Methods: The Core Study consisted of 4-week Pre-treatment, 23-week Treatment and 4-week Follow-up Periods. Suicidal ideation and behaviour were monitored clinically for all patients throughout the study; any clinically significant observations were recorded as adverse events (AEs). Additionally, the Columbia-Suicide Severity Rating Scale (C-SSRS) was used to assess suicidality during Screening/Baseline and throughout the Treatment Period in patients aged 6-<12 years at consent/assent. Here, we report events of suicidal ideation that were deemed to be clinically significant and recorded as AEs.

Results: Of 180 patients, only 1 (0.6%) patient (PGTCS; aged 30 years), who had no lifetime history of suicidal ideation, reported two AEs of suicidal ideation while receiving perampanel 10 mg/day. These incidences were reported as ‘wish to be dead’ (Day 131) and ‘wish to be dead’, ‘active nonspecific’ and ‘active without intent’ (Day 165) on the C-SSRS; both incidences were mild and resolved. Three patients reported a lifetime history of suicidality but none of these experienced suicidality during perampanel treatment. No patients reported ‘active thoughts with plan and intent’ or completed suicide.

Conclusions: The rare incidence of suicidality in Study 311 suggests that adjunctive perampanel is safe and well tolerated in terms of mental health in children aged 4-12 years with POS or PGTCS; however, patients receiving perampanel should be monitored for signs of suicidal ideation or behaviour, as recommended in the prescribing information.

Disclosure: Rohit Shankar is a principal stakeholder of ‘SUDEP and Seizure Safety Checklist’, a developer of EpSMon and is on the advisory committee for the UK epilepsy death register.
He has also received institutional and research support and personal fees from Bial, Desitin, Eisai, LivaNova, UCB Pharma and Veriton Pharma outside of the submitted work, and is an advisor on the NHS England committee looking to improve epilepsy pathways. Jay Salpekar is a consultant for Eisai and Sunovion, and has received institutional research funding from Lundbeck. Anna Patten is an employee of Eisai Ltd. Manoj Malhotra and Leock Y. Ngo are employees of Eisai Inc.

P04-27

Natural History of “Congenital” Neurofibromatosis Type 2 (NF2)

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Aim of study and methods: We (a) prospectively (years 1997-2019) followed up eight unrelated neurofibromatosis type 2 (NF2) children [5 males, 3 females; currently aged 2 to 23 years], harbouring different types of mutations of the MERLIN gene whose onset of disease was before age 1 year, and (b) systematically reviewed published reports on NF2 in the youngest age group (i.e. onset < 1 year).

Results: The eight children had (1) small (< 1 cm), bilateral vestibular schwannomas (VSs) detected in 6/8 at MRI by the age of 4 to 5 months [these VSs were asymptomatic for > 10 years, with later sudden and rapid (<12 months) progression]; (2) multiple non-VIII-nerve cranial nerves schwannomas; (3) [usually unilateral] optic nerve and large intracranial meningiomas; (4) intraspinal ependymomas; (5) large numbers of skin NF2 plaques in atypical locations; (6) NF2 epiretinal membranes (n=7) detected as early as the first months of age; (7) diffuse high signal lesions at MRI in the periventricular regions; and (8) unaffected first-degree relatives without MERLIN gene
abnormalities. Two of these children had, in addition, cerebrovascular abnormalities. One of these children had mosaic NF2. Three of these patients underwent therapy with Avastin [5 mg/Kg/i.v. every 15 days] with good results.

**Conclusions:** This represents the youngest NF2 group with the longest [up to 20 years] prospective follow-up so far reported. NF2 may present as a “congenital” form with bilateral VSs, multiple non-VIII-nerve cranial nerves schwannomas, optic nerve and intracranial meningiomas, atypical NF2-plaques and/or epiretinal membranes presenting as early as the first months of life and with natural history different from classical NF2.

**Disclosure:** No potential conflict stated.

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**PO4-28**

**Seizures in children with Acute Lymphoblastic Leukaemia: incidence, risk factors, aetiology and prognosis**

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**Introduction:** Seizures are not uncommon in children with acute lymphoblastic leukemia (ALL). Seizures occur both as isolated central nervous system (CNS) toxicity and as symptom of other underlying neurotoxicities. Our aim is to explore the incidence, risk factors, etiology and prognosis of seizures in children with ALL.

**Methods:** Our study group included patients between 1 and 18 years of age at diagnosis of ALL, between 2008 and 2015, in the five Nordic and two Baltic countries. All patients were treated according to the NOPHO ALL-2008 protocol. Cox proportional hazards models were used in statistical analyses.

**Results:** Seizures were reported in 81/1464 (5.5%) of the patients. The cumulative incidence of seizures at one month was 1.7% (95% CI: 1.2-2.5) and 5.3% (95% CI: 4.2-6.5) at one year. The patients were divided in two age groups 1-9 and 10-17 years old. Older age (HR=2.2; 95% CI: 1.4 - 3.4; p=0.0010), T-cell immunophenotype (HR=2.4; 95% CI: 1.4 - 3.9; p=0.00089), CNS involvement (HR=1.8; 95% CI: 1.07 - 3.13; p=0.026) and high risk ALL (HR=2.1; 95% CI: 1.3 - 3.3; p=0.0026) showed higher risk for seizures at univariable analyses. Only older age remained as a risk factor in multivariable analyses. Of 81 patients with seizures, 43 had posterior reversible encephalopathy syndrome, 16 had isolated seizures, 9 had sinus venous thrombosis, 4 had methotrexate related stroke-like syndrome and 9 had various neurotoxicities. Epilepsy was reported in 11 and cognitive difficulties in 7 patients at last follow up.

**Conclusion:** Seizures are relatively common in ALL patients treated with the NOPHO ALL-2008 protocol. Older patients are at greater risk for seizures. Clinicians need to follow up the neurocognitive outcome to be able to support the patient.

**Disclosure:** No potential conflict stated.
P04-29

A retrospective study of effectiveness and compliance of Ketogenic diet in a single unit

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Introduction: Ketogenic Diet has been proven beneficial in refractory epilepsy and is a treatment of choice in certain neurometabolic disorders.

Methods: We report our experience with KD in our centre since 2008. We studied children with various conditions causing refractory epilepsy who were placed on KD. Patients were divided in groups according to their seizure frequency (SF) before KD (A:<10,B:10-20,C>20 episodes per day). Effectiveness, defined as seizure reduction >50% and compliance, defined as blood ketones>2mmol/l were assessed at 3,6,12 and 24 months. Patients were monitored closely for adverse events.

Results: Forty-three patients were included, 20 boys and 23 girls. Age at commencement was between 43 days-old and 16.5 years-old. AED treatment on KD commencement was 1-6 medications, while 77% were receiving between 2 and 4 AED. Group A, B and C consisted of 10,23 and 10 children respectively (23.3%)/(53.5%)/(23.3%). Effectiveness at 3 months was 70%/80%/100% in the above groups with an inversion at 6 months to 100%/80%/66.6%, showing a relapse of the group C.

Of the total number of patients’ effectiveness at 3,6,12 and 24 months after KD commencement and was 82%/82%/100% and 100% respectively. Seizure reduction >90% was achieved by 26%, 39%, 53% and 50% respectively. Compliance was noted at 84%/36) of the children. Mean duration of KD was 2 years. A number of 21 children quit the diet (mean duration:5.8 months), while 22 children are still on the diet (mean duration 3.3 years). Adverse events included constipation, hyperlipidaemia, fatty infiltration of the liver, hypercalciuria and nephrocalcinosis.

Conclusions: Our study showed seizure reduction >50% in 100% of the children that stayed on KD for 2 years, with half of them achieving >90% seizure reduction. Adverse events were controlled and did not attribute to KD cessation.

Disclosure: No potential conflict stated.

P04-30

Impact of Methylphenidate on cognitive profile in children with Attention Deficit Hyperactivity Disorder

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Background and Aims: Attention Deficit Hyperactivity Disorder (ADHD) is one of the commonest condition affected approximately 5% of children and adolescents. Main treatment is cognitive behavioral therapy but in some cases drug management with Methylphenidate also can be considered which is known to improve behavioral profile and decrease restlessness and impulsivity.

The aim of our study was to assess the impact of methylphenidate on cognitive profile of ADHD children by assessing the most valid objective method event related potentials (ERPs) parameters before and after treatment.

Methods: We have examined 44 children with ADHD (28 boys, 16 girls) aged 9-12 years. All of them were diagnosed as ADHD of combined forms presenting with both inattentiveness and restlessness. The diagnosis was done by DSM-V criteria. IQ was measured by Wechsler Scale. All children with IQ lower than 80 were excluded from the study. ERP was registered by using of oddball paradigm. The latency of ERP (P300) was assessed before and after Methylphenidate intake. Drug dosage was 1 mg/kg. Statistical analysis was performed by ANOVA.

Results: P300 latency before Methylphenidate treatment ranged from 350-400 msc (mean 370msc). Amplitude was between 50-90 mV (mean 70 mV). The latency decreased within 20 days from treatment ranging from 300-330 msc (mean 310msc) while amplitude stayed the same 50-90 mV (mean 70 mV) after treatment. Reduction of latency was statistically significant (p<.0001).

Conclusions: Methylphenidate can affect not only on behavioral disorders in ADHD children but it can significantly improve cognitive profile by decreasing the latency of P300 which correlates with attention parameters.

Disclosure: No potential conflict stated.
**P04-31**

**Description of the use of Levetiracetam in a cohort of Neonatal Onset Epileptic Encephalopathies**

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**Objective:** We aimed to review the efficacy and tolerability of levetiracetam (LEV), recently reported to have good utility in neonatal seizures, in a group of genetically confirmed and/or suspected neonatal onset epileptic encephalopathies.

**Methods:** 5 years (2013-2018) retrospective review of neonates with clinical and neurophysiological diagnosis of neonatal onset epileptic encephalopathy who received treatment with levetiracetam. We reviewed the effect of treatment on changes in frequency, intensity, nature of seizures and improvement in medical condition.

**Results:** 13 patients were treated with LEV at mean age 15 days ± 11 SD. 7/13 had a diagnosis of a genetic epilepsy, 2/13 had a metabolic condition, 1 had a cortical malformation and 3 remain undiagnosed. 12/13 had at least one other AED and/or trial of vitamins prior to LEV that had no effect on seizure control. All of them received the minimum dose of 20mg/kg/d but none achieved the target dose (60mg/kg/day). Only one patient suffered a secondary effect with worsening of hyperkinetic movements. In 3/13 seizures evolved. Patients with a confirmed genetic diagnosis do not appear to respond differently to LEV. Neurodevelopmental outcome was difficult to evaluate in this group with profound disability with 42% mortality at mean age of 4 months old.

**Conclusion:** Evaluating the effect of LEV in this heterogeneous group of patients is difficult with many confounders. Nevertheless, we observed a transient decrease in seizure burden in the majority of neonates as a possible additive effect of LEV with other AED.

**Disclosure:** No potential conflict stated.

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**P04-32**

**Treatment with Adrenocorticotropin hormone in Drug Resistant Epilepsy – Efficacy in very young infants and older children**

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**Objective:** ACTH increase neurosteroids synthesis and reduce CRH, neurotrophic factors synthesis as well as glutamate concentration. Therapy with ACTH is well known and very useful in infants with infantile spasms, but the knownlage about efficacy in other types of epileptic seizures, especially in very young infants and older children is insufficient. The purpose of the study was evaluation of treatment results with synthetic ACTH in different types of drug resistant epilepsy in very young infants and older children.

**Methods:** 260 children were treated with ACTH from January 2012 to December 2018. In 3 infants therapy started at the age of (4–6) weeks and in 29 after 6 to 10 years. Before ACTH therapy introduction children received without efficacy 2 and 3 or 4 antiepileptic drugs. Electrocencephalography, neuroimaging examinations, genetic tests were performed. Patients were followed up at least 2 years.

**Results:** Female, term born infant with KCNQ2/3 mutation and intractable clonic seizures from 1st week of life started ACTH regimen when she was 4 weeks old. The spectacular effect of ACTH was observed after 3rd dose of when epileptic seizures passed off without reversion. There were no side effects of so early ACTH therapy. Her psychomotor development is delayed at the age of 3 years. Ten years old male received ACTH course with 100% reduction of polymorphic seizures. In one 7 years old girl epileptic spasms and hypsarrythmia disappeared after ACTH, but during therapy she was very nervous and weak. Six years old girl with polymicrogyria required callasotomy, because efficacy of ACTH was temporary.

**Conclusion:** Even in very young and older children with different types of epilepsy ACTH may be effective and safe.

**Disclosure:** No potential conflict stated.
P04-33

Estimation of Malondialdehyde, total antioxidant capacity, and Selenium levels in serum of intractable epileptic children receiving treatment with Ketogenic diet

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Background: Epilepsy results from abnormal excessive or hyper synchronous neuronal activity in the brain that leads to high rate of oxidative metabolism. Ketogenic diet plays a major role in management of refractory epilepsy. However, it is low in certain trace elements as Selenium which is essential for protecting the body against free radicals and oxidative damage.

Objective: To evaluate serum Selenium (Se), Malondialdehyde (MDA) and total anti-oxidant capacity (TAC) levels in children receiving KD treatment for intractable seizures for 6 months.

Subjects & Methods: The study included 90 infants and children with age from 6 months to 6 years; they were sub-divided into 3 groups. Group I: 30 patients with refractory epilepsy under pharmacological treatments only, Group II: 30 patients with refractory epilepsy under treatment with KD for 6 months and pharmacological treatments. Group III: 30 age and sex matched healthy children as controls. The following was done: Full history taking with emphasis on: Severity and frequency of seizures and laboratory analysis for serum (TAC), (MDA) and (Se).

Results: The frequency and severity of seizures were significantly lower in group II than group I. Se level was lower in overall epileptic patients compared to controls but was markedly lower in group I. Serum MDA levels was found to be higher in overall epileptic patients compared to controls but was markedly higher in group I Serum TAC levels was found to be lower in overall epileptic patients compared to controls but was markedly lower in group I.

Conclusion: Ketogenic diet is an effective treatment for refractory epilepsy epileptic, yet the nutrient content of ketogenic diet may not meet the daily allowance (RDA) for Selenium and so we recommend supplementation with Selenium.

Disclosure: No potential conflict stated.

P04-34

Hemimegalencephaly and Epilepsy

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Introduction: Hemimegalencephaly (HME) is a rare congenital disorder of cortical formation with hamartomatous overgrowth of all or a part of a cerebral hemisphere. HME is divided into three forms: isolated, syndromic (associated with a variety of syndromes typically including hemihypertrophy of the ipsilateral part of the body) and total HME (hemihypertrophy also involves the brain stem and cerebellum). The consequences of asymmetric brain development are contralateral hemiparesis, developmental delay and intractable epilepsy. Recent studies have demonstrated the association of HME with the mutations of AKT3, PK3CA and mTOR genes. mTOR pathway activation causes excitability of neurons, which explains the occurrence of epilepsy in patients with HME.

Methods: This small case-series includes six children with different types of HME and epilepsy treated in the Children’s Hospital Zagreb.

Results: Out of the six children (3 male and 3 female), three had isolated HME, with the onset of convulsions in the first days of life. In 2/3 (with tonic seizures and a “burst-suppression” pattern in EEG) there was Ohtahara syndrome and the third child (with persistent myoclonic and tonic seizures) had extreme megalencephalia with hypertrophy of right hemisphere and accelerated head growth dynamics of 1 cm per week. Two children had syndromic HME (Klippel-Trénaunay-Weber and Epidermal nevus syndrome) and one child (with myoclonic seizures) had total HME, with hemihypertrophy of cerebellum and brain stem. All our patients had refractory epilepsy, psychomotor retardation, and contralateral hemiparesis.

Conclusion: In patients with HME treatment is targeted to the control of epilepsy, which can be difficult to manage medically. In refractory cases, hemispherectomy or new therapy with mTOR inhibitors should be considered.

Disclosure: No potential conflict stated.
**P04-35**
A case of rapidly progressing Pineal Cyst – Is it Pineoblastoma?

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**Introduction:** Pineal cysts are often considered as incidentalomas and are becoming a common finding with the availability and advances in brain neuroimaging. Based on their MRI characteristics they are divided into typical and atypical cysts, latter being more related to neoplasms of pineal region. Progressing pineal cysts are very rarely reported, associated particularly with pineoblastomas. The present case was observed on a 7-month-old male with a suspicion of trilateral retinoblastoma, in which atypical pineal cyst was discovered on a first brain MRI. Patient was treated with chemotherapy (cyclophosphamide, carboplatin, etoposide and vincristine) followed-up at Department of child, adolescent and development neurology at the University children's hospital in Ljubljana, Slovenia.

**Methods:** The data was obtained by interviewing the patient relatives and reviewing medical reports. The case discussion was based with literature review and complementary tests.

**Results:** The first brain MRI was performed at patients age of 7 months and it showed an atypical pineal cyst, measuring 8 mm in diameter, with non-homogenous interior structure and marginal contrast-enhancement, suspicious for pineoblastoma. After 6 weeks a second brain MRI was performed, showing considerably larger cyst (13 x 11 mm), compressing lamina quadrigemina. Next brain MRI was done after 6 months with pineal cyst measuring 16 x 14 mm. Neurosurgical resection was done 15 months after the diagnosis. Histopathological report of a resected pineal cyst was concluding on a benign glial pineal cyst with no signs of malignant neoplasm.

**Conclusion:** Pineal cysts are usually an incidental finding on brain neuroimaging. Most do not change their characteristics during radiological follow-up. Even when atypical features of pineal cysts are described, they are very rarely associated with a malignant neoplasm.

**Disclosure:** No potential conflict stated.

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**P05-01**
This poster was withdrawn by the Author.

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**P05-02**
Rare combination of Oculo Cutaneous Albinism and MEGDEL Syndrome in one patient

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**Introduction:** MEGDEL syndrome (OMIM 614739), is an autosomal recessive disorder which is clinically characterized by deafness, encephalopathy, progressive spasticity, dystonia, and Leigh like lesions on neuroimaging. Oculocutaneous albinism (OCA) describes a group of inherited disorders of melanin biosynthesis characterized by a generalized reduction in pigmentation of hair, skin and eyes and variable ocular findings.

**Methods, Case report:** The 33-month-old albino female patient was the fourth child of consanguineous parents. On neurological examination, microcephaly, axial hypotonia with generalized hypotonia, seating with support, growth retardation were identified. She had sensorineural hearing loss. Urine organic acid analysis showed 2-fold increase in 3-methyl glutaric acid, 2-fold increase in 4 OH fenil acetic acid, 1.5-fold increase in lactic acid. Brain magnetic resonance imaging at 2 years old of showed hyperintensity of bilateral caudate and lentiform nuclei, were seen on T2A weighted sequences, frontal horns of lateral ventricles were mild dilated due to volume loss of caudate nuclei. Wholeexome sequencing (WES) was performed to identify causative variants, and all the candidate pathogenic mutations were further analyzed by bioinformatic analyses and confirmed through Sanger sequencing. The candidate pathogenic mutations in their families were sequenced through Sanger sequencing too.

**Results:** Patient carried two homozygous mutations in SERAC1 (c. 1435_1437delCTT, p. 478delLeu and c. G8030A, p. R2677Q) and in TYR (c.1255G>A, p.Gly419Arg) which were co-segregated with disease in this family.

**Conclusion:** To our knowledge, this is the first report on a Turkish patient with the coexistence of MEGDEL Syndrome and OCA. In addition, this report showed that WES may be the first choice in patients with multiple undiagnosed clinical findings.

**Disclosure:** No potential conflict stated.
P05-03

Different clinical manifestations of TREX1 mutation: a case series

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Objective: Three prime repair exonuclease 1 (TREX1) degrades single and double stranded DNA with 3’-5’ exonuclease activity. TREX1 mutations are related to type 1 interferon mediated autoinflammation owing to accumulated intracellular nucleic acids. Several cases of systemic lupus erythematosus, Aicardi-Goutieres Syndrome, familial chilblain lupus, retinal vasculopathy-cerebral leucodystrophy caused by TREX1 mutations have been reported, so far. Methods: We described 3 different phenotypes in 5 patients with TREX1 mutations.

Results: These identified diseases are Aicardi-Goutieres Syndrome, Familial Chilblain Lupus, and Familial Chilblain Lupus with central nervous system vasculitis. Conclusion: We highlighted that patients with biallelic or monoallelic TREX1 mutations may be associated with various phenotypes including Aicardi-Goutieres Syndrome, Familial Chilblain Lupus, and Familial Chilblain Lupus with central nervous system vasculitis.

Disclosure: No potential conflict stated.

P05-04

Mitochondrial DNA Depletion Syndrome 7 (OMIM #271245) – A case report of a Rare Hepatocerebral Disease

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Objective: To expand the phenotypic spectrum of the mitochondrial DNA depletion syndrome 7.

Methods: A 6-week-old boy presented with muscular hypotonia, generalized seizures, and a strong evidence for hearing and vision deficit (abnormal brainstem auditory evoked potentials and visually evoked potentials). Laboratory work-up revealed fluctuating elevated lactate (max. 17 mmol/l) and signs of hepatopathy with elevated serum transaminases and pathologic coagulation. The patient showed feeding difficulties and a failure to thrive, being fed by a total parenteral nutrition. The familial history is relevant for distant consanguinity of the parents and four older siblings, all of them neurologically impaired and one boy deceased.

Results: Broad metabolic screening showed no relevant abnormalities. Brain MRI and MR spectroscopy were normal. Histological analysis of liver tissue revealed a fatty degeneration, immunohistological and biochemical investigations of muscle tissue were normal without signs of myopathy. An exome sequencing from blood remained initially inconclusive. RNA sequencing performed with fibroblasts finally revealed a mutation in the C10ORF2 gene (TWNK), indicating the diagnosis of mitochondrial DNA depletion syndrome 7 (MTDPS7). Re-analysis of exome data showed afterwards a homozygote variant c.1302C>G. Functionally, the mutation is associated with mitochondrial DNA depletion in brain and liver leading to severe neurodegenerative disorder with hepatopathy.

Conclusion: MTDPS7 should be considered in patients with hepatopathy, lactate acidosis and progressive neurological disease including refractory epilepsy and muscular hypotonia. The present case report underlines the importance of genetic testing in different tissues in the work-up of infants with suspected mitochondrial disease.

Disclosure: No potential conflict stated.
Rare monogenic causes of Microcephaly: clinical and genetic heterogeneity in a Hungarian cohort

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Objective: Mutations in various genes result in congenital and/or postnatal microcephaly. Our aim is to present the clinical and genetic heterogeneity of microcephaly in ten patients ascertained with monogenic aetiology in a Hungarian cohort.

Methods: Environmental causative factors were excluded by clinical evaluation. Brain MRI was carried out by conventional techniques. Array comparative genome hybridization, next generation and Sanger sequencing were performed.

Results: Homozygous mutations were identified in four patients. ASPM mutation was associated with bilateral diffuse polymicrogyria in a boy, while identical mutations in WDR62 were found in a boy and a girl, who were related and had bilateral pachygyria. Homozygous WDR81 mutation caused microcephalencephaly. Heterozygous de novo mutations were found in six patients. Visual impairment and chorioretinopathy were associated with postnatal microcephaly in a patient with KIF11 mutation. TUBA1A mutation caused agyria-pachygyria, partial corpus callosum agenesis and vermis hypoplasia. FOXG1 mutations led to movement disorder in addition to microcephaly in two girls. Pontocerebellar hypoplasia and intractable epilepsy were the main features of CASK mutations in two girls.

Conclusion: Our results confirm the molecular diversity of pathophysiological events leading to microcephaly. ASPM and WDR62 proteins interact in cell cycle dynamics as centriole-associated proteins. Mutations in WDR81, the recently described microcephaly gene impair mitotic progression of the neural progenitor cells. KIF11 encodes a molecular motor protein required for establishing bipolar spindle during mitosis. TUBA1A encodes alpha tubulin, which is a constituent of the microtubules. FOXG1 protein plays critical role in the induction of the telencephalon and forebrain patterning. The CASK gene on the X chromosome encodes a nuclear protein that contributes to neural development and synaptic functions.

Disclosure: No potential conflict stated.

TRAPPC12 related progressive Encephalopathy: 2 cases and expanding phenotype

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Introduction: Biallelic mutations in the TRAPPC12 gene are responsible for early-onset progressive encephalopathy with brain atrophy and spasticity (PEBAS). Next generation sequencing (NGS) allowed novel mutations of this gene and expanding phenotype. We report on two patients carrying homozygous TRAPPC12 mutations, one previously reported and one known mutation, with severe neurodevelopmental delay and brain atrophy.

Methods and Results: Clinical examinations and cranial imaging studies were performed for two unrelated patients. In addition, whole-exome sequencing was performed for patient’s DNA, followed by Sanger sequencing to verify the variants. The unreported mutation of the TRAPPC12 gene in a 9-year-old Turkish patient who presented with severe hypotonia and developmental delay, progressive cerebellar atrophy, mild cortical atrophy. To date, three allelic variants in the TRAPPC12 gene have been reported. The clinical findings observed in previously reported three patients described as progressive encephalopathy with microcephaly, although a larger number of observations is necessary to reveal the whole phenotypic spectrum.

Disclosure: No potential conflict stated.
Cerebellar Atrophy and Cerebellar Cortex Hyperintensity – Think about Christianson Syndrome

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Disclosure: No potential conflict stated.

Objective: To draw attention to the clinical presentation and the potentially diagnostic imaging pattern of Christianson syndrome (OMIM#300243).

Methods: Case report with clinical, neuroimaging, and genetic data.

Results: We present a 15-year-old boy with severe intellectual disability, absent speech, autistic behavior, ataxia, refractory epilepsy and joint contractures in elbows and valgus deformities in feet. The boy was born after uneventful term pregnancy in a non-consanguineous family. He had normal early development until 14 months. Disease had slowly progressive course: child lost ability of independent walking, eating, understanding, playing and speech. Chewing and swallowing became difficult with age. He developed marked truncal ataxia and drug-resistant epilepsy. He was microcephalic (HC 9 mm below 3rd P).

Repeated MRI showed moderate cerebral and marked cerebellar atrophy, inferior and posterior parts being more affected. There was cerebellar cortex hyperintensity (in FLAIR sequence) involving mainly the inferior part of cerebellum. Next Generation Sequencing identified one variant in exon 4 of SLC9A6 gene located on X chromosome. A hemizygous out-of-frame variant at genomic position chrX:135080, NM_001042537.1:c.608delA was classified as probably pathogenic according to ACMG criteria and was not found in databases. The pathogenicity of this variant was not possible to predict by in silico analysis with the aid of different bioinformatics tools (Polyphen2-HDIV, Polyphen2-HVAR, SIFT). Pathogenic hemizygous mutations in SLC9A6 gene have been proven to cause X-linked Christianson syndrome. Cerebellar atrophy and cerebellar cortex hyperintensity (although the latter is not consistent) are imaging hallmarks of Christianson syndrome.

Conclusion: We conclude that typical Angelman syndrome-like clinical presentation, slow progressive course and peculiar cerebellar involvement should raise suspicion of Christianson syndrome.

Disclosure: No potential conflict stated.

Poretti Boltshauser Syndrome: a novel variant in LAMA1 gene

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Introduction: Poretti–Boltshauser syndrome is an autosomal recessive, LAMA1-associated disorder characterized by non-progressive cerebellar ataxia, developmental delay and ocular involvement affecting eye movements and visual acuity which is accompanied by cerebellar dysplasia and cysts.

Methods: A three-year-old boy, presented with global developmental delay and gait disturbance and was the first living child of healthy parents who were first cousins. On neurological examination he had oculomotor apraxia and wide-based, ataxic gait with normal deep tendon reflexes, no muscular weakness and pyramidal signs. His laboratory tests, cranial computed tomography at two months of age were normal. His brain magnetic resonance imaging(MRI) showed cerebellar cortical dysplasia and cysts both in anterior and posterior regions, hypoplasia and dysplasia of cerebellar vermis, elongated fourth ventricle, decreased anteroposterior diameter of CC and T2-hyperintense signals in centrum semiovale areas of the cerebral white matter. Based on his findings we suspected a variant in LAMA1 gene, thus have asked for ophthalmological evaluation. He then was diagnosed with hypermetropia and prescribed glasses. After receiving a written informed consent from the parents for genetic testing, targeted direct sequencing identified homozygous nonsense p.Q1257* (c.3769C>T) variant in the LAMA1 gene. The parents were heterozygote for this variant which supported recessive inheritance and segregation within the family. We present the case after having obtained informed consent from the family.

Results: Genotype-phenotype correlation cannot be identified and our patient is an example of this with a typical but milder phenotype with a nonsense, pathological variant who has both supratentorial and infratentorial findings.

Conclusion: This recently defined disorder must be kept in mind in patients with ataxic gait disturbances, developmental delay, problems with visual acuity and eye movements, so that targeted analysis would be sufficient for diagnosis.

Disclosure: No potential conflict stated.
A novel CACNA1A variant in a child with Hemiplegia and Coma – A case report highlighting the importance of early history

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Introduction: The spectrum of disorders associated with CACNA1A gene variants is wide and includes familial hemiplegic migraine, episodic ataxia and epilepsy. We describe a child with familial hemiplegic migraine and novel CACNA1A variant.

Case Report: 13-year-old boy was transferred to our hospital with headache, acute right facial weakness, left arm and leg weakness, and reduced level of consciousness. Background of mild gross motor developmental delay and oculomotor apraxia. No cause identified but an MRI at age 7 years found reduced cerebellar volume. MRI at presentation found multiple foci of diffusion restriction in the right cerebral cortex and further cerebellar volume loss. He gradually recovered function over the next 3 weeks. He was investigated for mitochondrial disorders. Over the next 4 months he had 6 similar episodes with alternating weakness; none were as severe. He was empirically given L-arginine; this was ineffective.

He re-presented to hospital with a severe episode including focal seizures. His parents subsequently recalled episodes of minor head injuries between ages 4 – 6 years leading to brief periods of unconsciousness. CT brain scans were normal. Sequencing of CACNA1A found a previously undescribed missense variant - c.3883A>G; p.(Lys1295Glu). The variant is predicted to result in a conservative substitution of a highly conserved amino acid in a functional domain. The same variant c.3883A>G; p.(Lys1295Glu) has been identified in control databases. In silico prediction tools support the pathogenicity of the variant. Mutagenesis of the equivalent amino acid, has not been reported before and has not been identified in control databases. In silico prediction tools supports the pathogenicity of the variant. Mutagenesis of the equivalent amino acid in mice produces impaired motor control and denervation. Parental samples are awaited.

The patient was started on topiramate and is symptom free after dose escalation.

Conclusion: Familial hemiplegic migraine due to CACNA1A variants has considerable phenotypic variation masquerading as other conditions including epilepsy, mitochondrial disorders, and ischemia. Correct diagnosis can lead to effective treatment; our case adds to the knowledge of this condition.

Disclosure: No potential conflict stated.

Likely pathogenic GARS variant associated with infantile onset Spinobulbar Muscular Atrophy

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Introduction: We describe a novel case of infantile onset spinobulbar muscular atrophy (SBMA) associated with a likely pathogenic heterozygous missense variant c. 631T>C, p.(Cys211Arg) in the GARS gene.

Methods: Inherited Peripheral Neuropathy Gene Panel next generation sequencing

Results: Our proband presented at five weeks with marked striidor and bulbar weakness after a normal pregnancy. He subsequently developed respiratory failure requiring Nocturnal BiPap and was found to have a Type I Laryngeal Cleft. Initially he met developmental milestones but at 5months developed features of axial weakness with further regression at 9months with limb weakness and loss of deep tendon reflexes. EMG confirmed denervation in genioglossus, as well as proximal and distal limb muscles without evidence of neuropathy. Genetics for SMN1 gene and SMARD were negative. Inherited Peripheral Neuropathy 56 gene panel testing identified a heterozygous missense variant c. 631T>C, p.(Cys211Arg) in exon 5. The variant is predicted to alter a highly conserved amino acid, has not been reported before and has not been identified in control databases. In silico prediction tools supports the pathogenicity of the variant. Mutagenesis of the equivalent amino acid in mice produces impaired motor control and denervation. Parental samples are awaited.

Conclusion: The GARS gene encodes an ubiquitously expressed glycy1 tRNA synthetase which has an integral role in protein synthesis in all eukaryotic cells. Missense GARS mutations can lead to distal hereditary motor neuropathy as well as a sensorimotor neuropathy phenotype (CMT2D) typically with adolescent or early adulthood onset. There have been 2 cases in the literature to date describing infantile onset. We postulate that the previously undescribed heterozygous GARS variant c. [631T>C]; p. [Cys211Arg] is responsible for infantile SBMA in our proband.

Disclosure: No potential conflict stated.
Partial trisomy of chromosome 13 – A rare cause of developmental delay, Epilepsy and brain malformation

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Introduction: Complete trisomy of chromosome 13 is a severe chromosomal anomaly, lethal in most cases in the first year of life. Partial trisomy of chromosome 13 is a rare condition, associated with a severe phenotype, which includes severe developmental delay, dysmorphic features, brain and cardiac malformations. In this paper we report on a new case with partial chromosome 13 trisomy with a complex phenotype.

Methods and Results: The patient is a 8 year-old girl who was referred to our department for epileptic seizures (complex partial seizures, some of them with secondary generalization) refractory to antiepileptic drugs. The clinical evaluation revealed dysmorphic facial features, severe global developmental delay, and autistic behavior. Her brain MRI showed agenesis of corpus callosum and cortical atrophy. Genetic investigations by array CGH showed a partial trisomy of chromosome 13 - arr 13q12.11(210479924-21475992)x3, 13q14.33q34(467995619-115105806)x3dn. The karyotype and FISH testing confirmed the duplication, revealing an isochromosome 13q.

The 13q duplication has a size of approximately 68 Mb and contains numerous genes, including OMIM genes involved in neurodevelopmental disorders. Our results highlights the importance of accurate diagnosis through array CGH of patients with global developmental delay and brain malformations.

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Disclosure: No potential conflict stated.

Novel mutations in MCT8 associated with a less severe phenotype of MCT8 Deficiency

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Introduction: Mutations in the thyroid hormone transporter MCT8 cause MCT8 deficiency, clinically characterized by intellectual and motor disability and abnormal serum thyroid function tests. Although the majority of patients are unable to sit or walk independently and do not develop any speech, a few have a less severe clinical presentation. Here, we report on two novel mutations associated with such a less severe phenotype.

Methods: SLC16A2 was analyzed by Sanger sequencing. The impact of the identified mutations on MCT8 function was studied in vitro in transiently transfected COS-1 and JEG-3 cells, and ex vivo in patient-derived fibroblasts.

Results: Classical clinical hallmarks of MCT8 deficiency, including hypotonia and extrapyramidal symptoms, were relatively mild, and both patients achieved several motor milestones. In one patient, cerebral calcifications were observed in the basal ganglia at the age of 29 years. This uncommon clinical presentation lead to a gross delay in diagnosis. Nevertheless, serum T3 concentrations were elevated in both patients. Two novel hemizygous mutations in SLC16A2 were identified, leading to a p.Thr239Pro and a p.Leu543Pro substitution in the MCT8 protein. In vitro and ex vivo studies revealed substantial residual uptake capacity of both mutant proteins. Both mutations impaired MCT8 protein stability and interfered with proper subcellular trafficking.

Conclusions: Our studies extend the clinical phenotype of MCT8 deficiency. The substantial residual function of both mutants likely explains the less severe clinical presentation. Moreover, the detection of calcifications in the basal ganglia may fuel further research onto the pathophysiological consequences of MCT8 deficiency on the brain.

Disclosure: No potential conflict stated.
P05-13

Pyrurate Carboxylase Deficiency Type A and Type C: a genotype-phenotype correlation

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Introduction: Pyruvate carboxylase deficiency (PCD) is caused by bi-allelic mutations of the PC gene. The reported clinical spectrum includes a neonatal form with early death (type B), an infantile fatal form (type A), and an late onset form with isolated mild intellectual delay (type C). Apart from homozygous stop-codon mutations leading to type B PCD, a genotype-phenotype correlation has not otherwise been discernible. Indeed, patients harboring bi-allelic heterozygous variants leading to PC activity near zero can present either with a fatal infantile type A or with a benign late onset type C form.

Methods and Results: In this study, we analyzed six novel patients with type A (three) and type C (three) PCD, and compared them with previously reported cases. Firstly, we observed that type C PCD is not associated to homozygous variants in PC. In-silico modeling was used to map former and novel variants associated to type A and C PCD, and to predict their potential effects on the enzyme structure and function. We found that variants lead to type A or type C phenotype based on the destabilization between the two major enzyme conformers. In general, our study on novel and previously reported patients improves the overall understanding on type A and C PCD.

Disclosure: No potential conflict stated.

P05-14

Hypokalemic Periodic Paralysis due to a new mutation in CACNA1S gene

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Introduction: Hypokalemic periodic paralysis (HPP) is a rare neuromuscular disorder caused by mutations in skeletal muscle potassium channel genes. HPP is characterized by episodes of muscle weakness, which may be precipitated by heavy exercise, fasting or high-carbohydrate meals. We present a rare case of a girl with recurrent episodes of sudden paralysis of the extremities due to a new mutation in CACNA1S gene.

Clinical Report: A 15-year-old girl was admitted in the emergency department with a 12-hour history of extreme difficulty to move her limbs. She had one previous episode, which led to investigation to rule out a Guillain Barre syndrome: complete blood count, hepatic transaminases, renal function, LP, brain and neuroaxis-MRI were normal. Within three days she spontaneously recovered from all of her symptoms. On this second episode she was tachycardic and neurological examination revealed a symmetrical bilateral weakness on upper (4/5) and lower limbs (3/5); cranial nerve function, sensation and deep tendon reflexes were intact. Complete blood count, routine chemistry and renal function were normal except for a potassium level of 2.3 mmol/L. ECG revealed sinus tachycardia and flattening of the T wave. Three hours after intravenous potassium replacement, the neurologic symptoms had resolved and ECG returned to normal. Laboratory work-up excluded renal, thyroid or adrenal dysfunctions. Panel gene for HPP revealed new pathogenic heterizigous mutation in CACNA1S gene (c.3715C>G p.Arg1239Gly), not previously described. Currently, attacks are controlled with lifestyle changes and nutritional advice.

Conclusion: Although rare, HPP should be considerer as a differential diagnosis of recurrent flaccid paralysis. After replenishment of potassium, secondary causes of HPP should be excluded. The treatment of this disease should follow a progressive strategy to reduce the frequency and severity of the attacks.

Disclosure: No potential conflict stated.
The Italian cohort of STXBP1 mutated patients: phenotypic spectrum and novel mutations

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Introduction: STXBP1 encephalopathy is caused by de novo mutations in the STXBP1 gene, encoding a synaptic protein with a crucial role in vesicular docking and fusion. The core clinical features are intellectual disability (ID) and epileptic seizures (95%), with onset in the first months of life. EEG often presents multifocal epileptiform activity, hypsarrhythmia and burst-suppression. Additional neurologic features are autistic features (ASD), dyskinesia, dystonia, tremor, axial hypotonia, and ataxia, suggesting a broader neurologic system’s impairment.

Methods: Multicentric retrospective study on patients with STXBP1 mutations collected through the LICE (ILAE Italian chapter) collaborative group on STXBP1. The information collected include epileptic history and treatment, general and neurological examination, cognitive evaluation, family history, EEG and MRI studies, genetic analysis.

Results: We collected 28 patients (age 1-24 y) carrying 20 different de novo heterozygous mutations in STXBP1 (9 unreported). The mutations span the protein domains without clustering. The cohort presents with a broad epileptic phenotype, with seizure onset range 1 day - 17 months, and different seizure types at onset; furthermore, the majority of the patients show intellectual disability, movement disorders and ASD. 10 are seizure-free.

Conclusion: STXBP1 mutations are one of the major causes of early onset encephalopathy with epilepsy. However, a selection bias exists for epileptic patient, as STXBP1 mutated patients with ID but without epilepsy have been reported and broaden the spectrum associated with these mutations. Haploinsufficiency is regarded as the major pathogenetic mechanism, although missense mutations could instead lead to a dominant negative effect, possibly resulting in a more severe phenotype. These mechanisms in different mutation types need to be clarified, in order to develop a precision medicine approach for the treatment of this broad spectrum neurological condition.

Disclosure: No potential conflict stated.
**P05-17**

**Description of the clinical case of Cockayne Syndrome**

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**Objective:** To study the clinical and genetic characteristics of a child with Cockayne syndrome for timely medical genetic counseling.

**Methods:** Clinical and genealogical analysis, clinical case of Cockayne syndrome in a 9-year-old boy.

**Results:** Child from the first pregnancy, first birth and inbreeding marriage. His mother had rubella during the first trimester, at the age 3 years old, diagnosed with cerebral palsy. Neurological examination: patient is conscious, has microcephaly, does not hold the head, does not sit, does not turn over, does not walk. Photoreaction is absent. He has a horizontal nystagmus, dysphagia, dysphonia. Muscle hypertonia, contracture of the knee, ankle joints. Dysfunction of the pelvic organs. Phenotypically - "bird’s face", cachexia, nanism (80cm), microcephaly, sparse hair, low-setted large auricles, enophthalmos, bilateral cataract, large “eagle” nose, thin lips, micrognathia, keeled chest, scoliosis, foot deformity, bilateral cryptorchism against photosensitivity. In the dynamics, child’s condition deteriorated, the symptoms of multiple organ failure increased on the background of somatic pathology, followed by death.

**Conclusion and discussion:** The described clinical case of Cockayne syndrome from consanguineous marriage (parents are second siblings). The clinical picture presents distinctly phenotypic manifestations of Cockayne syndrome and severe neurological disorders, which coincide with the literature data.

**Disclosure:** No potential conflict stated.

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**P05-18**

**The phenotype spectrum of PURA Syndrome: report of three cases**

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**Background:** PURA Syndrome is a rare neurodevelopmental disorder, which molecular base has recently been identified. The gene PURA (Purine-Rich element-binding protein A) encodes the Pur-α protein, involved in the control of the transcription of other genes, the transport of mRNA in the cytoplasm and the DNA replication. The protein is important for brain development, neuronal proliferation and maturation of dendrites.

**Objective:** The aim of the study is to describe 3 clinical unrelated cases with PURA Syndrome, as a contribution to the knowledge of the phenotype associated to PURA gene mutations.

**Methods:** Phenotype description of 3 patients with mutations in PURA gene, identified by phenotype driven exome sequencing.

**Results:** In all the patients, a de novo heterozygous mutation in PURA-5q31.3 gene has been identified: p.Ser28GlnfsTer50 - c.81delC (pt 1), p.Ala14GlyfsTer64 - c.41delC (pt 2) and p.Met157Arg - c.470T>G (pt 3).

All 3 cases presented with hypotonia, apneas and feeding difficulties during the neonatal period, nystagmus and mild dysmorphic facies. Two of them, at last follow-up, aged respectively 11y (pt.1) and 20y (pt.2), showed severe global neurodevelopmental disorder with prevalence of intellectual over motor dysfunction; none was functionally verbal. The third case developed infantile spasms at 11 months of age and, at last follow-up at 1 year of age had developmental delay.

**Conclusions:** The availability of NGS/WES techniques is hugely expanding the power of molecular diagnosis of rare neurodevelopmental disorders and widening the knowledge of the phenotype of many genetic diseases. The non specific phenotype of the PURA syndrome underscores the importance of NGS/WES techniques early in the diagnostic work up of neurodevelopmental disorders, to avoid a diagnostic odyssey to the families.

**Disclosure:** No potential conflict stated.
**P05-19**

**Ataxia as the presenting feature of Juvenile-Onset Alexander Disease**

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**Objective:** Alexander disease is a rare neurological disease with various clinical and neuroradiological features depending on the age of onset. Most of them present as infantile-onset form with severe and progressive leukodystrophy and macrocephaly. Here we aim to report a case of juvenile-onset form with a de novo, novel mutation in GFAP who had cerebellar ataxia as the sole symptom with atypical neuroimaging features.

**Methods:** After comprehensive evaluation for cerebellar ataxia did not establish an etiologic diagnosis, whole-exome sequencing was performed and Sanger sequencing was done for validation.

**Results:** A 10-year-old boy presented with ataxic gait disturbance. He had no specific symptoms other than ataxia. His brain magnetic resonance imaging (MRI) showed abnormal signals in cerebellum. Whole-exome sequencing revealed the presence of a novel, de novo, GFAP mutation (p.T240P). During follow-up, he developed slightly progressive cognitive decline and dystarthis with cerebellar ataxia, and his brain MRI also revealed atrophic changes in cerebellum and brainstem.

**Conclusions:** This report expanded the phenotypic and genotypic spectrum of Alexander disease. Alexander disease with GFAP variants should be considered in the differential diagnosis of cerebellar ataxia, especially in case of signal changes in cerebellum.

**Disclosure:** No potential conflict stated.

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**P05-20**

**MECP2 gene anomalies are not synonymous with Rett Syndrome**

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**Introduction:** MethylCpG-binding protein 2 (MECP2) gene mutations are the cause of most cases of Rett syndrome (RTT). As new mutations in MECP2 gene are being identified, distinct non-RTT phenotypes are recognized.

**Methods:** We reviewed the phenotypes of 4 children with confirmed mutation in MECP2 gene that lacked clinical features for RTT.

**Results:**

Patient 1: 14 year-old-girl presented with psychomotor development delay and mild intellectual disability. At the age of 10, she manifested polymorphic seizures that evolved to medically refractory epilepsy and regression of cognitive skills. A MECP2 nonsense mutation (c.1452G>T) was identified.

Patient 2: 14 month-old-girl presented with delayed psychomotor development, congenital microcephaly, oculomotor abnormalities, pyramidal signs and apnoea/hypopnea episodes. Later on, auto mutilation stereotypies and growth retardation developed. A MECP2 truncating variant (70kb deletion of Xq28) was identified.

Patient 3: 8 year-old-boy presented with early hypotonia, delayed psychomotor development resulting in intellectual disability with absent speech, microcephaly, manual stereotypies, recurrent infections, bruxism, scoliosis and craniofacial dimorphisms. A duplication of Xq28 including the MECP2 locus was identified.

Patient 4: 4 year-old-girl presented with early hypotonia, delayed psychomotor development resulting in intellectual disability with absent speech, microcephaly, manual stereotypies, recurrent infections, bruxism, scoliosis and craniofacial dimorphisms. A duplication of Xq28 including the MECP2 locus was identified.

**Conclusion:** This series underlines the diversity of clinical phenotypes associated to MECP2 gene mutations, beyond RTT. Atypical features and/or later symptoms may delay the molecular diagnosis. Delayed psychomotor development was a common feature.

**Disclosure:** No potential conflict stated.
**P05-21**

**Survey concerning ultra-rare diseases and parental understanding**

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**Introduction:** During the last 10 years the possibility to diagnose patients with genetic disorders has changed dramatically because of new genomic techniques. More and more ultra-rare diseases are discovered, which poses several challenges to parents and caretakers.

**Methods:** At the Child- and Adolescent Habilitation Center in Malmö, Sweden, a survey was performed, asking 6 families with affected children the following:
1. How they generally feel after the genetic diagnosis was confirmed?
2. Are they content with the information they got regarding the diagnosis?
3. Has the information affected everyday life for them and their families.
4. Would the parents have the testing done over again, given their experiences?
Some of the families had just gotten their child\'s diagnosis, some had known it for some time.

**Results:** All the families were pleased to know the reason why their child is different, and they want to know as much as possible about the prognosis. The diagnosis did not lead to any changes in their everyday lives. The parents would do additional genetic tests if that could lead to new therapeutic options.

**Conclusion:** For the families of the survey the testing was important and seen as positive, but it was evident that they need further case reports and databases with open access. An example of such a case report can be found regarding tyrosine hydroxylase deficiency.

**Disclosure:** No potential conflict stated.

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**P05-22**

**The puzzling variability of ATP1A3-Related Disease: 5 new mutations resulting in 5 separate phenotypes**

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**Aim:** To describe the phenotype of our patients with previously undescribed ATP1A3 mutations and examine whether the phenotype of the remaining cohort fits published information on their specific mutation.

**Methods:** We searched pubmed for the keyword ATP1A3 to review all publications of patients with ATP1A3-related disease. Genotype and phenotype of our cohort was compared to available published information.

**Results:** Since 2004 110 ATP1A3 mutations have been described in 80 publications. 72 associated with classic Alternating Hemiplegia of Childhood (AHC) phenotype, 10 Rapid-Onset Dystonia Parkinsonism (RDP), 4 either AHC or RDP, 1 CAPOS, 7 Early Infantile Epileptic Encephalopathy, 2 Childhood Onset Schizophrenia and 11 intermediate phenotypes with novel combinations of symptoms typical for ATP1A3-related disease.

Of our cohort 5 patients carry previously unreported de novo mutations. Patient 1 (c.990_993+2del/splice site) presents with mild AHC. The other patients present atypically.

Patient 2 (c.2213T>G/p.M738R) fulfills AHC diagnostic criteria, however the phenotype is dominated by early onset drug resistant epilepsy characterized by apneic seizures.

Patient 3 (c.958G>A/p.A320T) presented with distal arthrogriposis and tracheomalacia at birth. Paroxysmal eye movements, dystonic, apneic episodes and epileptic seizures started in the first year of life.

Patient 4 (c.964G>A/p.V322I) presented with episodes of hemidystonia at 3 years of age. She is ataxic.

Patient 5 (c.1006C>T/p.P336S) is microcephalic and presented with paroxysmal eye movements and dystonic episodes in the first year of life. At age 8 years he developed more frequent episodes of generalized dystonia that resolve in sleep. Patients 4 and 5 have cerebellar atrophy on MRI.

**Conclusion:** Mutations in ATP1A3 result in a vast variability of phenotypes that seem to form a continuous spectrum of ATP1A3-related disease. These seem to be mutation specific to some extent.

**Disclosure:** No potential conflict stated.
A case of Early-Infantile Onset, Rapidly Progressive Leukoencephalopathy with calcifications and cysts caused by mutations in SNORD118

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Introduction: Leukoencephalopathy with calcifications and cysts (LCC) is a rare autosomal recessive genetic disorder neuroradiologically characterized by intracranial calcification, cerebral white matter disease, and multiple cysts. Although the small nucleolar RNA, C/D box118 (SNORD118) gene was identified as the cause of LCC in 2016, clinical courses are different for each patient. The clinical features of LCC have not yet been established, since the age of onset ranges from infancy to adulthood and the symptoms often progress slowly. Here, we report a case of LCC with early infantile development, rapid progression, and a mutation in the SNORD118 gene.

Methods: A three-month-old female presented with epileptic seizure. The patient was followed up over the next 4 years with clinical investigations, including computed tomography and magnetic resonance imaging. Whole exome and Sanger sequencing were performed to identify causative genetic variants.

Results: Computed tomography revealed intracranial calcifications in the basal ganglia and thalamus at 3 months. Magnetic resonance imaging showed diffuse white matter lesions on T2-weighted images beginning at 7 months. Calcifications developed in the cerebral white matter, pons, and cerebellum. Small cysts appeared in the cerebral white matter at 1 year 6 months and increased thereafter. The patient’s epilepsy was well controlled, but she exhibited severe developmental delay and was unable to speak or walk at 4 years old. Whole exome sequencing did not reveal any causative variants. However, a biallelic variant of the SNORD118 gene was identified by Sanger sequencing.

Conclusion: This is a unique case of LCC presenting with early infantile onset and rapid progression. As SNORD118 gene mutations are difficult to detect by regular whole exome sequencing, careful follow-up with neuroimaging may be necessary to diagnose LCC.

Disclosure: No potential conflict stated.
Novel Heterozygous Missense Mutation c.92A>G in the LMNA gene: a case study

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Introduction: LMNA-related disorders are provoked by mutations in the LMNA gene which encodes the nuclear envelope proteins, lamin A and C. A-type lamin-related congenital muscular dystrophy (L-CMD) is also one of them and characterized by muscle weakness and a dropped head. Here, we describe a novel heterozygous mutation in the LMNA gene leading to L-CMD.

Case: A 10-months-old girl visited our clinic for development delay. She was born at full term by spontaneous vaginal delivery. Up to 9 months, she could sit alone and hold her head 90 degrees in a prone position. However, she was not able to control her head representing dropped head sign from the age of 10-months. BSID and DDST performed at 10 months indicated a marked delay in gross motor domain and mild delay in fine motor domain. Languages and cognitive domains showed development in months. Brain MRI and EEG was also normal. Electrodiagnostic studies showed abnormal spontaneous activities in several muscles with normal nerve conduction study. Elevated serum creatinine phosphokinase levels were discovered (1085 U/L). She had normal female karyotype, and the gene related to muscular dystrophy or spinal muscular atrophy was not detected. In a next Generation sequencing (NGS) test and conventional Sanger sequencing, we found a heterozygous missense variation (c.92A>G) in the patient’s LMNA gene, which leads to an exchange of amino acids (p.Glu31Gly).

Conclusion: From other cases reporting missense mutations of the same codon and closely resembled phenotype, we could consider L-CMD as a diagnosis. This missense mutation is the first case reported in Korea and abroad. Clinical features provide the best clues for diagnosing L-CMD early in the disease, and we urge clinicians to become familiar with those phenotypes.

Disclosure: No potential conflict stated.

A first report of homozygous missense mutation in the ADCY5 gene, related to an Autosomal Dominant Dyskynesia Syndrome

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Background: ADCYS5-Related Dyskinesia is a diverse group of movement disorders, mainly characterized by dystonia, myoclonus or chorea, with variable disability. The disorder is inherited in an autosomal dominant manner; however, recently two siblings with generalized dystonia and superimposed myoclonus have been described, associated with compound heterozygous mutations in ADCY5 gene.

Patient: We describe girl, born to consanguineous parents following an uneventful delivery at 37 weeks. At some point, she was diagnosed with spastic quadriplegic cerebral palsy and severe psychomotor delay. At the age of 1 year and 9 months she was referred to our neurogenetic clinic. She presented a severe global developmental delay. Her neurologic examination showed markedly increased tonus and episodic dystonic postures in trunk, extremities and face, exacerbated by voluntary movement. In addition, spontaneous events of oculovestibular convergence spasm and orofacial dystonia were observed. She had recurrent episodes of hyperthermia and hyperhidrosis. MRI at the age of 1 year was suggestive of delayed myelination. Metabolic workup included patterns of neurotransmitters in cerebrospinal fluid, which were not specific. Further metabolic analyses were normal.

Results: Whole exome sequencing revealed a novel homozygous c.1406G>A (p. Ser469Asn) mutation in the ADCY5 gene (OMIM 600293). The variant was not found in GnomAD or ExAC browsers, was classified as damaging/disease causing by in-silico prediction programs, and the residue Ser469 was shown to be highly conserved throughout evolution. Both parents, reported as healthy, were found to be heterozygous carriers.

Conclusion: To our best knowledge, we present a second family with biallelic mutations in ADCY5 gene, associated with a severe neurologic presentation of ADCY5-Related Dyskinesia spectrum.

Disclosure: No potential conflict stated.
POSTER PRESENTATIONS > POSTER SESSION 5
Genetics

P05-27

Genetic anomalies in siblings with intellectual disabilities

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Objective: Intellectual disability (ID) is a common but extremely complex neurodevelopmental disorder with a strong genetic component. Genetic causes of ID range from microscopically visible chromosomal abnormalities to point mutations. The introduction of array-based comparative genomic hybridization (aCGH) proved instrumental in ID investigation, allowing for discrete pathological CNVs to be detected. Besides aCGH, detection of regions of homozygosity (ROH) combined with sequencing represent a new approach for the investigation of gene defects in ID.

Methods: We report on 29 families with ID, 25 with 2 affected siblings and 3 with 3 affected siblings, investigated by aCGH and CGH+SNP array using 105k and respectively 180k microarray platforms (Agilent Technologies); one family was investigated by sequencing.

Results: The sibling pairs presented complex phenotypes including ID and other clinical findings such as dysmorphic features, autism or other behavioral disorders, epilepsy or seizures etc. The genomic variants identified in our patients covered the entire spectrum of clinical significance, from benign to pathogenic. Among the pathogenic variants identified within a family we mention 4p duplication/10q deletion and 22q13.3 deletion. The heterozygosity status was investigated in seven families. Several ROH that include genes involved in neurodevelopment, were identified. In one family a mutation of NDST1 gene was identified in all three siblings.

Conclusions: The genomic investigations on our study group, although including a small number of families, has proved informative with regard to etiology and family counseling.

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Disclosure: No potential conflict stated.

P05-28

Probable dysfunction of GABA-A receptors in patients with GNAO1-Related Syndromes – An example of four clinical cases

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Objectives: Wide range of phenotypic spectrum of GNAO1-related syndromes includes early onset epileptic encephalopathy (EOEE) and a range of movement disorders (MDs) with or without epilepsy. Above clinical symptoms are associated with disturbances in presynaptic auto-inhibitory effect of several neurotransmitters on their receptors (M2/M4 muscarinic, α2-adrenergic, µ/δ opioid, GABA-B).

Methods: Clinical course of disease was evaluated in four patients of Polish origin with GNAO1-related syndromes. The diagnosis in all cases was establish on the basis of whole exome sequencing (WES) analysis on Illumina platform. All variants in GNAO1 gene occurred de novo (negative parental testing).

Results: In three patients clinically presenting symptoms of EOEE the gain-of-function (GOF) (patient 1 - c.736G>A; patient 2 - c.607G>A) or normal function (patient 3 - c.625C>T) variants of GNAO1 gene were identified. In all of them MDs co-existed with seizures (patient 1 and 3 – generalized dystonia, patient 2 – combination of choreathetosis and focal dystonia). In fourth patient MDs (combined choreathetosis with focal dystonia) without epilepsy were caused by the previously reported variant of unknown function (patient 4 - c.709G>A).

In all patients significant hypersensitivity to higher doses of benzodiazepines and in patient 4 also to higher doses of baclofen was noticed. In patient 2 early onset of EOEE (2 weeks of age) with good response of seizures to vigabatrin treatment was observed, with further development of startle response from 3 years of age with paradoxical reaction to clonazepam treatment.

Conclusions: In our series of patients with EOEE and MDs related to mutations in GNAO1 gene we identified some drug responses or hypersensitivities which could be indicative for functional disturbances not only of GABA-B, but also GABA-A receptors. Further functional studies are needed.

Disclosure: No potential conflict stated.
Can the clinical spectrum of Epileptic Encephalopathy associated with SYNGAP1 mutation be extended to include some lysosomal features? – An example of two clinical cases

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Objectives: The SYNGAP1 gene encodes a brain-specific synaptic Ras GTP-ase-activating protein, which is involved in postsynaptic regulation of glutaminergic neurotransmission. Down-stream effectors dysregulation by the SYNGAP1 mutation could be associated with impaired acidification, vesicles transport and genes expression in lysosomes.

Methods: Two patient of Polish origin with SYNGAP1-related epileptic encephalopathy with co-existing specific lysosomal features in clinical spectrum were evaluated. The diagnosis in both cases was establish on the basis of whole exome sequencing (WES) analysis on Illumina platform. All variants in SYNGAP1 gene occurred de novo (negative parental testing).

Results: In both patients, 5-year-old boys, two different types of mutation in the SYNGAP1 gene were identified – patient 1: c.3618_3619delAG (p.Lys1206fs) (variant reported for the first time), patient 2: c.1676+5G>A (variant reported in literature). In both patients congenital ophthalmologic sings, mild microcephaly with facial dysmorphic features, appendicular hypotonia, vomiting and delayed motor development after food intake and megaloblastic anemia extended metabolic evaluation was performed. Ascertained high levels of serum cyanocobalamin, normal serum folate and homocysteine, low levels of methionine in plasma and CSF and 5-Me-THF level in CSF suggested atypical intracellular resistance to cyanocobalamine. All metabolic features normalized after treatment with high doses of liposomal hydroxocobalamin. In patient 2 the macular cherry reds spots were identified with further normal enzymatic evaluation towards typical lysosomal storage diseases.

Conclusions: Some lysosomal features could co-exist with typical signs in patients with SYNGAP1 mutations. It could be indicative for dysfunction of lysosomes due to dysregulation of down-stream effectors of SYNGAP1 protein (mTOR pathway).

Disclosure: No potential conflict stated.

SCN2A mutation: different genotype and phenotype, clinical cases

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Introduction: Mutations in SCN2A a gene encoding the voltage-gated sodium channel Nav1.2, have been associated with a spectrum of epilepsies and neurodevelopmental disorders. There are many publications that are devoted to study correlation between genotype and phenotype in SCN2A.

Methods: We had 2 girls with epilepsy and development delay. They had full neurological examined, including Exome Sequencing. Both have a SCN2A mutation: first - c.3928G>C (p.Ala1310Pro), second - c.2558G>A (Arg853Gln). Girls are having a health parents without any mutations (in bough families parents had an Exome sequencing too).

Results: Girl with c.3928G>C (p.Ala1310Pro) variant had a muscle hypotonia, vomiting and delayed motor development after born; at age of 10 months began infantile spasms, epileptic encephalopathy and progressive delay of development; seizures are resistant to AED treatment (VPA, VGB, TPM, benzo, transient positive effects of ACTH and negative of prednisolone); now she is suffering of seiziers and has an arrest of development. Girl with c.2558G>A (Arg853Gln) had delay of motor and mental development along first year of life; later, at age of 18 months began frequent focal seizures: she had taken VPA, LEV, she had a negative effects of all kinds of hormones; now girl take VGB and TPM, she is free of seizures along 15 months, but she has a gross motor problems, intellectual disability and autistic features.

Conclusion: Different mutation in SCN2A gene are demonstrate a different phenotype of disease. Girl with c.3928G>C (p.Ala1310Pro) variant has a resistant epilepsy. Girl with c.2558G>A (Arg853Gln) has a controlled epilepsy with a later debut. In both cases girls have a mental and motor delay with poor prognoses of quality of life.

Disclosure: No potential conflict stated.
**P05-31**

Expanding the phenotype of PIGA variants in Early Onset Epilepsy

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**Introduction:** PIGA variants at Xp22.2 have recently been described in case reports of early onset epileptic encephalopathy (EOEE). Little has been reported about neuropathological findings in these cases.

**Methods and Results:** Here we report the case of a boy born at 34 weeks gestation by emergency caesarean section; he was breech and his mother had gone into spontaneous labour. He required some initial resuscitation but his Apgar score at 5 and 10 were 8 and 10. Surfactant was given at 7 hours of life, he was never intubated for ventilation. His weight and head circumference were above the 99th percentile. His only initial neurological finding was mild central hypotonia. He had coarse facial features, persistent jaundice, hepatomegaly, and large echogenic kidneys on USS. On day of life 13 he began having tonic seizures with cyanosis. These initially responded to phenobarbitone. His electroencephalogram showed burst suppression. Brain imaging on day 21 revealed subtle areas of white matter T2 hyperintensities. Despite treatment with antiepileptic treatment he had refractory seizures. He died at 42 days.

Post mortem Neuropathological examination demonstrated a supratentorial leukoencephalopathy characterized by posterior periventricular cysts on a background of diffuse white matter gliosis in addition to cortical disorganization and focal gliosis in the globus pallidus, a pattern very similar to that seen in infants with hypoxic ischaemic encephalopathy (HIE). An infantile epileptic encephalopathy next generation sequencing panel was sent. The result of this revealed a hemizygous variant - PIGA: c.355C>T.

**Conclusions** The post-mortem findings, which are very similar to HIE, have not previously been described in patients with a PIGA variant. This case expands the phenotype of PIGA and also increases the diagnoses to be considered when findings consistent with HIE are found at post-mortem.

**Disclosure:** No potential conflict stated.

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**P05-32**

Late-infantile Neuronal Ceroid Lipofuscinosis presenting in a child of West African ethnicity with a novel TPP1/CLN2 mutation

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**Introduction:** The neuronal ceroid lipofuscinoses (NCL) are a group of progressive neurodegenerative disorders characterised by regression of motor and intellectual function, epilepsy and visual impairment.

The late-infantile form has onset between 1-4 years of age and is typically caused by homozygous mutations to TPP1 (previously known as CLN2) leading to a marked reduction in the activity of the enzyme tripeptidyl peptidase 1. There are currently 144 mutations to TPP1 identified as causing disease, predominantly affecting children from Europe and North America.

**Case:** We report a girl presenting at 3 1/2 years with a 6-month history of speech regression, unsteadiness and frequent falling, and secondary incontinence. Her parents described that recently her hands appeared to shake and she had episodes of head-bobbing. EEG demonstrated high-amplitude spike and slow waves with frequent isolated spikes or polyspikes, some associated with negative myoclonic drops of the head, and a type IV photoparoxysmal response.

She was found to have low leucocyte tripeptidyl peptidase 1 activity and targeted genetic analysis identified a novel homozygous mutation to TPP1 for which both of her parents are carriers. This mutation (c.533del) is predicted to cause a frame-shift and premature termination of the protein, p.(Pro178Glnfs*5).

Her parents originate from the Gambia but are unrelated. While NCL has been described in most populations, to date it has not been reported in any individuals of West African origin.

**Conclusion:** This is the first reported case of a child with late-infantile NCL of West-African ethnicity, with a novel pathogenic mutation to TPP1. This therefore broadens both the understanding of genetic and ethnic variation for this rare condition.

**Disclosure:** Dr Andrew Mallick has received an educational grant from BioMarin.
**P05-33**

**Periventricular Nodular Heterotopia with genetic mutation in Filamin A; a rare case**

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**Introduction:** Periventricular nodular heterotopia is a rare disorder of neuronal migration. We describe a newborn infant with an abnormal antenatal scan showing macrocephaly and an underlying Filamin A gene mutation.

**Case description:** Patient X was born at 36+3 with antenatal diagnosis of macrocephaly. She had normal examination with normal milestones. The MRI scan was abnormal showing arachnoid cyst and sybependymal grey matter heterotopias. She had structural cardiac abnormalities including PDA and PFO with normal ventricular function. Following extensive genetic investigation she was diagnosed with a filamin A gene mutation.

**Discussion:** This is an X-linked disorder with unknown incidence. Affected individuals are almost invariably female as hemizygous males show early lethality. There is increased risk of cardiovascular disease and stroke as well as other vascular and coagulation problems. In this case, the patient had typical features on MRI scan with loss of function mutation in FLNA and normal neurodevelopment to date.

**Conclusion:** Children with antenatally diagnosed macrocephaly, cardiac involvement and MRI findings of grey matter heterotopia may benefit from genetic assessment and investigation with close follow up of neurodevelopmental progress.

**Disclosure:** No potential conflict stated.

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**P05-34**

**Clinical Heterogeneity of CACNA1A mutations in childhood including Hyperekplexia and Global Developmental Delay**

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**Objective:** CACNA1A mutations can result in diverse neurological presentations. This study reviewed the clinical presentation of all children diagnosed with CACNA1A mutations at a tertiary referral centre.

**Method:** Case series of nine children with a proven CACNA1A mutation diagnosed at a tertiary neurology centre between 2010-2018. The clinical presentation and mutation details of each child was reviewed. The study includes video footage of three cases.

**Results:** Nine children presented to our institute over an eight-year period; five were female and four male. Presentations include paroxysmal torticollis of infancy, infantile onset epileptic encephalopathy, episodic ataxia, and global developmental delay, tremors and epilepsy. The classical phenotype of episodic ataxia or migraine was seen in a third of the cases. Two children with episodic ataxia had positive family history. One patient had biallelic mutations in CACNA1A with confirmed biparental inheritance which is newly described. An emerging novel phenotype is that of hyperekplexia. Though all cases had the same channelopathy, different medications seemed to help the different phenotypes. This is thought to be related to whether the mutation leads to a gain or loss of function. CACNA1A is not a well recognised cause of hyperekplexia and global developmental delay and so should be considered when evaluating these phenotypes.

**Conclusion:** CACNA1A phenotype in childhood is expanding. Understanding the function of the mutation and whether it is a gain or loss of function, and the relationship between the gene change and the phenotype could be important in choosing the most effective treatment for patients in this group of heterogeneous conditions.

**Disclosure:** No potential conflict stated.
P05-35

RANBP2 mutation in a Turkish child with Recurrent Acute Necrotizing Encephalopathy

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Introduction: Acute necrotizing encephalopathy is a rare disorder characterized by encephalopathy following a nonspecific febrile infection. Most cases are sporadic; however, recurrent and familial cases have been linked to RANBP2 mutation.

Case: This is a description of a four and half years old boy with recurrent ANE with a pathogenic RANBP2 mutation (c.1754 C>T (p.T585M)). He had two episodes of encephalopathy, firstly 10 days after HAV vaccination and the other after febrile infection. Neuroradiologically, he had typical findings involving bilateral thalami, pons, hippocampal gyri. He was managed with intravenous gamma globulin and Prednisolone during both the episodes. He recovered significantly with residual deficits in his cognitive and language domains.

Conclusion: It is important to make early diagnosis, to prevent and avoid infectious disease in patients and their families with RANBP2 mutation.

Disclosure: No potential conflict stated.

P05-36

Brain morphologic study in Rett and Rett-Like Syndrome with MECP2 mutation

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Introduction: Rett syndrome (RTT) is a rare congenital disorder which in most cases (95%) is caused by methyl-CpG binding protein 2 (MECP2) mutations. RTT is characterized by regression in global development, epilepsy, autistic features, acquired microcephaly, habitual hand clapping, loss of purposeful hand skills, and autonomic dysfunctions. Although the literature has demonstrated decreased volumes of the cerebrum, cerebellum, and the caudate nucleus in RTT patients, surface-based brain morphology including cortical thickness and cortical gyrification analyses are lacking in RTT. Methods; We present quantitative surface- and voxel-based morphological measurements in young children with RTT and Rett-like syndrome (RTT-l) with MECP2 mutations. The 8 structural T1-weighted MR images were obtained from 7 female patients with MECP2 mutations (3 classic RTT, 2 variant RTT, and 2 RTT-l) (mean age 5.2 [standard deviation 3.3] years old).

Results and Discussion: Our analyses demonstrated decreased total volumes of the cerebellum in RTT/RTT-l compared to gender- and age-matched controls (t (22)=-2.93, p=.008, Cohen’s d=1.27). In contrast, global cerebral cortical surface areas, global/regional cortical thicknesses, the degree of global gyrification, and global/regional gray and white matter volumes were not statistically significantly different between the two groups. Our findings, as well as literature findings, suggest that early brain abnormalities associated with RTT/RTT-l (with MECP2 mutations) can be detected as regionally decreased cerebellar volumes.

Conclusion: Decreased cerebellar volume may be helpful for understanding the etiology of RTT/RTT-l.

Disclosure: No potential conflict stated.
**Novel SLC9A6 mutation in a family with X-linked Intellectual Disability, mimicking Angelman Syndrome**

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**Introduction:** Mutations in SLC9A6 gene have been reported in Christianson syndrome (CS) type of X-linked syndromic mental retardation. The disease is associated with severe to profound intellectual disability, ataxia, seizures and an Angelman-like phenotype. Here we report first Georgian family, consisting of two hemizygous brothers (aged 23 and 5) and their asymptomatic carrier mother, with novel missense mutation in SLC9A6 gene - c.1474G>A, p.(Ala492Thr).

**Methods and Results:** The diagnosis was made using NGS epilepsy gene panel (283 genes). The older brother had delayed initial psychomotor development, rare epileptic seizures starting from 2 years that completely resolved by age 9, truncal ataxia, happy demeanor, microcephaly, drooling, strabismus, wide mouth, delayed puberty, fat pads, inverted nipples, gaze aversion, autistic features and was nonverbal, with previous clinical diagnosis as Angelman syndrome (AS). His brain MRI done at various ages showed progressive cerebellar atrophy with vermis involvement. The younger brother at the age of 5 also presented with delayed psychomotor development, ataxia, strabismus, drooling, autistic behavior, hand stereotypes, facial dysmorphism, seizures starting from 3 years and was nonverbal, with normocephaly and no obvious cerebellar atrophy on brain MRI at that age. Despite the broad clinical spectrum of SLC9A6 gene mutations in the literature, the clinical phenotypes of CS and AS are similar. Progressive cerebellar atrophy, autistic behavior, milder course of epilepsy and neurodevelopmental regression should be a clue to the clinicians to differentiate between CS and AS, that is crucial in terms of genetic counseling. Moreover, we underline the importance and high diagnostic yield of expanded NGS based panels in pediatric epilepsy patients.

**Disclosure:** No potential conflict stated.
Practical implications of genetic diagnosis through Array-CGH

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Introduction and Objectives: Neurodevelopmental disorders (NDD) are a common cause of consultation in neuropsychiatrics. In recent years the use of Array-CGH (aCGH) has emerged for its etiological diagnosis, but there are not many publications that analyze the impact of these results in clinical practice.

Material and methods: Retrospective descriptive study in a tertiary hospital during 2016. Data were collected on the consequences at clinical practice level (change of therapeutic regimen, referral to other specialties, request for new tests) of patients with pathological genetic results.

Results: During the study period, 42 patients with a pathological aCGH result were observed. This discovery involved a change in medication in 4.2% of the cases (2 patients), initiation of the assessment in other subspecialties in 22% (9 patients) and, also in 22% (9 patients) the request for new complementary tests.

Conclusions: The initial diagnostic evaluation of patients with NDD should include the performance of an aCGH. In addition to the prognostic and genetic counseling implications, it involves a change in management in one in four patients studied. In our sample we have not seen significant changes in terms of modification of the treatment regimen.

Disclosure: No potential conflict stated.

Whole-exome sequencing as an early diagnostic tool in children with Progressive Neurological Disorders

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Aim: Our aim is to study prospectively the value of whole exome sequencing (WES) as early diagnostic tool in pediatric patients with severe neurological and neurodegenerative disorders, and retrospectively to compare diagnostic yield and costs with similar patients who did not undergo early WES.

Methods: A prospective cohort of 48 patients with infantile onset severe neurological disorder or childhood onset progressive neurological disorder was collected from Children's Hospital, Helsinki University Hospital. WES was performed to all patients, and parent samples were analyzed to confirm segregation of identified variants. All exome findings were confirmed by Sanger Sequencing as an independent technique. Findings were reported to treating clinicians. For cost-effectiveness calculations, patient medical records are reviewed and all diagnostic costs during the time from start of investigations to diagnosis are compared.

Results: Of our 48 patients, 18 (38%) got a definitive genetic diagnosis through WES, with a previously known disease gene in a typical phenotype. The therapy of 4 patients was modified because of diagnosis. Of confirmed mutations, 6 were de novo mutations, and 5 patients had recessive mutations. Of our control cohort of 50 patients with no early WES, 9 (18%) got a diagnosis by investigations including clinical tests (including candidate gene tests and panels). 10 patients underwent WES, that identified gene defect in 5 patients (10%).

Conclusion: Early WES outperformed other diagnostic means in a Finnish tertiary hospital setting. The cost-effectiveness analysis is ongoing. We found that most families have their own rare mutations and that de novo mutations are a common cause of early severe disorders of children even in a genetic isolate such as Finland. These results strongly promote analysis of early WES in infantile progressive encephalopathies.

Disclosure: No potential conflict stated.
Epileptic-Dyskinetic Encephalopathy caused by a mutation in the SCN8A gene: a case of neonatal onset

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Introduction: The SCN8A gene encodes the alpha subunit of the voltage-gated sodium channel in excitable neurons. Gain-of-function mutations have been associated with early-onset epileptic encephalopathy. It often appears within the first 7 months of age and it is characterized by progressive neurological impairment.

Result: A male infant was born with arthrogryposis multiplex, inquinal and umbilical hernias, hypotonia, none epileptic myoclonic startle response, blepharospasm, horizontal nystagmus and bulbar palsy. The electroencephalography (EEG) and brain magnetic resonance imaging (MRI) at neonatal period were normal. Electroencephalography, evoked potential test, metabolic test,CGH-Array 60K, SMN1, SMN2 and GLRA1 gene analyses were normal. Muscle biopsy was inconclusive and mitochondrial respiratory chain analysis in fibroblasts was normal. At 4 months he began with tonic and myoclonic seizures with a severe myoclonic epileptic encephalopathy pattern in EEG. Targeted gene sequencing panels for new-onset epilepsy identifies a previously unknown de novo heterozygous missense mutation in SCN8A gene.

Brain MRI performed at 5 and 21 months showed supra and infratentorial atrophy and severe myelination delay suggestive of hypomyelinating disorder. The patient required mechanical ventilation and gastrostomy feeding. He did not reach any development milestone and he developed a refractory epilepsy despite the treatment with several antiepileptic drugs (clonazepam, zonisamide and valproic acid, and midazolam infusion). He died at 25 months due to a status epilepticus.

Conclusion: Approximately 1% of early infantile epileptic encephalopathies are associated with missense mutations in the SCN8A gene, but the majority are de novo missense mutations. The literature had described around 50 cases, but it is uncommon to find an onset neonatal patient with hypomyelination in brain MRI as we present.

Disclosure: No potential conflict stated.

Intellectual disability associated with dysmorphism, cleft palate, congenital heart defect and behavioural anomalies due to a de novo MEIS2 mutation

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Objective: Intellectual disability (ID) has an estimated prevalence of 1.5-2%. Whole exome sequencing (WES) studies have identified a multitude of novel causative gene defects and have shown that a large proportion of sporadic ID cases result from de novo mutations in newly discovered genes.

Methods: Here, we report on a 9-year-old girl, who has been presented in our neuropediatric outpatient clinic. A median cleft palate as well as a ventricular septal defect (VSD) and a patent foramen ovale (PFO) were surgically corrected in infancy. Her psychomotor development was delayed and her speech development severely impaired. Apart from ID, she has behavioral anomalies, muscular hypotonia, scoliosis, and hypermobile joints. Her facial phenotype is characterized by arched eyebrows, mildly upslanted and long palpebral fissures, prominent nasal tip and large, protruding ears.

Results: Under suspicion of a syndromic disorder, the family was referred to our human genetics department. Trio exome sequencing was performed and revealed a de novo missense mutation in MEIS2 (c.998G>A, p.(Arg333Lys)). Haploinsufficiency of MEIS2 had been discussed as the most likely mechanism of the microdeletion 5q14-associated complex phenotype with ID, cleft palate and heart defect. Only very recently, two studies including in total 15 individuals with intragenic MEIS2 variants leading to haploinsufficiency were published (Douglas et al., 2018, Verheije et al., 2018).

Conclusion: ID, with or without other abnormalities, causes complex problems for the affected families. Establishing the exact diagnosis is often demanding. WES can be a suitable diagnostic tool which enables counselling about the course of the disease and the probability of recurrence.

Disclosure: No potential conflict stated.
A case of Eosinophilic Meningitis accompanied by Phaeohyphomycosis due to Exophiala Dermatitidis

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Objective: We report a fatal case of eosinophilic meningitis due to Exophiala dermatitidis.

Methods: Retrospectively reviewed the medical record of the patient.

Results: A 10-year-old girl was admitted because of fever and headache lasting over 2 weeks. She was reported to be healthy before and outside MRI of the brain revealed multiple small acute or subacute infarction in the right middle cerebral artery territory with suspicious narrowing of right ICA. Laboratory tests revealed CSF leukocytosis (307/μL) and eosinophilia (57% of the total CSF leukocyte). Follow ing culture and antibody screening for parasitic, fungal, bacterial, and TB infection were all negative. Immunologic tests were unremarkable and STAT3 gene test was normal. With a tentative diagnosis of eosinophilic meningitis, antibiotics, antiviral agents, anti-helminthic drug, and corticosteroid was administered and therapeutic CSF tapping was done. However, her neurological symptoms were gradually worsened and she showed stuporous mentality at hospital day (HD) 16 and underwent an external ventricular drain to control increased intracranial pressure and antifungal agents were added because of strongly positive serum and CSF f-D-glucan. Repeated culture and 16s RNA test for fungi could not prove the causative agents. At HD 32, she moved to pediatric intensive care unit due to semi-comatose mentality following a seizure and her brain MRI revealed multiple brain edema with tonsilar herniation. Despite of emergency craniectomy with brain biopsy, uncontrolled increased intracranial pressure eventually led to death at HD 34. After her death, Exophiala dermatitidis was identified from the brain abscess culture and biopsy. Subsequent whole exome sequencing revealed homozygous CARD9 mutation (c.821delinsGA).

Conclusion: Fungal meningitis due to Exophiala dermatitidis is very rarely reported but should be considered when unexplained invasive eosinophilic meningitis occurs in previously healthy children.

Disclosure: No potential conflict stated.

IRF2BP1 mutation causing a neurodegenerative phenotype with Movement Disorder and Bulbar Palsy

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Introduction: Diagnosis and management of neurodegenerative diseases is a challenge in clinical practice. Vast majority of these diseases is caused by genetic changes. Identification of new genes, using tools such as Whole Exome Sequencing (WES) has attributed significantly in molecular and clinical diagnosis aiming for individualised and targeted therapy.

Methods: We report a patient that presented with gradual regression of her skills since 18months-old and resemblance of a neurodegenerative course. We describe the diagnostic approach.

Results: A girl of 4.5years-old presented with psychomotor regression and signs of ataxia and generalised hypotonia, affecting her gait. Choreoathetosis and pyramidal signs were also impaired. The phenotype attributed to a neurodegenerative disease, although epilepsy was not present. Thorough and repeated clinical, neurometabolic and molecular testing did not reveal any specific pathology. At the end of 2018 a repeated analysis of the WES data was performed that identified a heterozygous mutation in IRF2BP1 gene, that had been reported earlier that year and was responsible for the newly described phenotype of “Neurodevelopmental disorder with regression, abnormal movement, loss of speech and seizures (OMIM#618088). IRF2BP1 gene is expressed mainly in the central nervous system and is acting as a transcriptional factor.

Conclusion: This particular case is an example of the difficult and agonizing course in diagnosing extremely rare neurodegenerative diseases. WES after 2 years gave the opportunity to review the data and identify a newly described gene that was implicated in the phenotype. Future targeted therapy is the key for treatment approach in these difficult cases.

Disclosure: No potential conflict stated.
A Williams-Beuren Syndrome with chromosome 16p12.2-p11.2 deletion or undeclared new syndrome

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Background: Williams-Beuren syndrome (OMIM 194050) is a multisystem disorder caused by hemizygous deletion of 1.5 to 1.8 Mb on chromosome 7q11.23, which contains approximately 28 genes.

Method: Clinical, genetical, radiological, pathological and survival data were gathered.

Results: The patient report presents the medical history of a Williams-Beuren Syndrome (WBS) child with unique molecular karyotype. It is a combination of chromosome 7q11.23 deletion and chromosome 16p12.2-p11.2 deletion. It is important to note that WBS is the cause of the hemizygous deletion on chromosome 7q11.23. This case tries to resolve the diagnostic issues related to the combination of different deletions simultaneously in one child. The phenotype peculiarities of the child were: a flat midface, medial eyebrow flare, periorbital fullness, epicanthic folds, thick lips, a long philtrum, strabismus, a depressed nasal bridge, kyphoscoliosis, poor balance and coordination, mental retardation, severe speech impairment, and attention deficit disorder. Child has not brain defects on MRI, organs pathology on ultrasound investigation, data of his EEG and EMG are normal. Results of blood test are without abnormalities. These peculiarities are different from standard features of WBS. The most common symptoms of Williams syndrome are heart defects, low muscle tone and unusual facial features described as "elfin", widely spaced teeth, and a flattened nasal bridge were absent in this child.

Conclusion: Therefore, the investigation continues to determine whether the child has an atypical form of WBS or a new genetic syndrome, which combines the previously noted deletions.

Disclosure: No potential conflict stated.

A new compound heterozygous mutation in Ataxia-Telangiectasia: a case report

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Introduction: Ataxia telangiectasia (AT) is an autosomal recessive multisystem genetic disorder characterized by progressive cerebellar ataxia, ocular cutaneous telangiectasia, immunodeficiency, and chromosomal instability. This disease is caused by mutations of the ataxia telangiectasia mutated (ATM) gene which is located on chromosome 11q22-q23. Specific laboratory abnormalities such increased alpha-fetoprotein levels may help in diagnostic approach. A diagnosis of AT can be confirmed by the detection of the mutations of the ATM gene and/or a deficiency ATM protein/ATM kinase activity in cultured cell lines.

Case report: A 15 month-old female patient admitted with the complaint of unbalanced walking. Her medical history was unremarkable with non-consanguineous parents. She was suffering from a mild ataxia and oculomotor apraxia.

In laboratory examination, we have noted an elevated alpha-fetoprotein level(44,55 ng/ml), decreased serum IgG and IgA (618 md/dl and 15,9 mg/dl) levels and increased serum IgM (272 mg/dl) level. Abdominal ultrasound was normal. Any clinical or laboratory signs of malignancy weren’t detected. Gene study was figured out the variant c.3102T>G/p. Tyr1034Ter on the exon 21 and the variant c.7473G>T/p. Trp-2491Cys on the exon 50. Both mutations were not previously reported in the literature, and these mutations were predicted to be pathogenic. The patient’s mother has the same mutation on the exon 21 and the patient’s father has the same mutation on the exon 50. The patient was referred to pediatric immunology and physical treatment departments and followed-up by pediatric neurology department.

Conclusion: Because certain neurological features may arise later, a diagnosis of AT should be carefully considered for any ataxic child especially in our country where consanguineous marriages are common. In this way, genetic counselling can be given to families and the protection approaches could be especially for ionizing radiation.

Disclosure: No potential conflict stated.
**P05-47**

**Rapid onset Coreodystonia without Parkinsonism due to mutation in the ATP1A3 gene**

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**Introduction:** Rapid onset dystonia parkinsonism (DYT12 or DYT-ATP1A3) is a rare disorder characterized by the abrupt onset of generalized dystonia and signs of Parkinsonism, produced by mutations in the ATP1A3 gene.

**Methods:** Case review report

**Clinical case:** A 7-year-old girl presented with acute encephalopathy, facial dyskinesias, abnormal eye movements and rapid onset dystonia at 5 years of age, triggered by scarlet fever and influenza B virus infection. She was initially treated with corticosteroids, gamma globulins, valproic acid and carbamazepine without any improvement. Metabolic tests, video-EEG and brain MRI were normal. On the physical examination she presented generalized choreo-dystonia (BFMDRS motor scale 46/120 points and disability scale 13/20 points) with predominant involvement of upper limbs leading to a lot of difficulty to perform any daily living activities. She did not show any signs of Parkinsonism. PET scan showed a discrete cerebellar hypometabolism and a decrease in the uptake in the right thalamus compared to the contralateral one. Partial exoma sequencing revealed a previously reported pathogenic mutation in the ATP1A3 gene (p.Arg769His/c.2306G>A). Treatment with L-dopa (5 mg/kg/d) and trihexyphenidyl (15 mg/day) was ineffective. She is in surgery plans for deep brain stimulation.

**Conclusion:** Mutations in the ATP1A3 gene produce three different clinical phenotypes: 1) alternating hemiplegia of childhood, 2) dystonia-rapid onset Parkinsonism and 3) CAPOS syndrome (cerebellar ataxia, arreflexia, cavus feet, optic atrophy and sensorineural deafness). Unfortunately, dystonia-Parkinsonism does not respond to L-dopa or trihexyphenidyl. Deep brain stimulation could be an optional treatment possibility.

**Disclosure:** No potential conflict stated.

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**P05-48**

**PTEN-related Disorders. Phenotypic description in a series of paediatric patients**

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**Objective:** Describe neurological phenotype and genotype in a series of patients with pathogenic variants in PTEN.

**Material and Methods:** Retrospective clinical review of paediatric patients who exhibited pathogenic variants in PTEN. Age, gender, type of genetic variant; family background; neurologic phenotype; presence of tumors and type, biochemical alterations (serum taurine and cysteine and urinary aspartic acid), and neuroimaging findings will be described.

**Results:** We included in the study 6 patients with confirmed PTEN mutations. 50% were females. Mean age: 9.6 years (6-18). No relevant family background. 100% of patients have macrocephaly (>4.5SD). Autism spectrum disorder was confirmed in 4 out 6 cases. Motor delay and hypotonia were present in 4/6. One patient was diagnosed with Lhermitte-Duclos syndrome, with macrocephaly and ASD associated. 3 patients presented with tumors, related with Cowden Syndrome (2 of them did not present neurologic symptoms except for macrocephaly). Amino acid’s profile and neuroimaging were normal. All variants were de novo (4 missense and 2 deletions). Deletions were associated with oncologic phenotype.

**Conclusion:** We recommend to rule out a PTEN-related disorder in patients with macrocephaly associated to ASD and/or motor delay. Long-term follow up is essential in these patients in specialized units for risk of tumor development, and provide adequate genetic counselling.

**Disclosure:** No potential conflict stated.
**P05-49**

**CACNA1A mutation presenting as early onset Developmental Encephalopathy without Epilepsy: presentation of two cases**

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**Objectives:** Heterozygous variants in the CACNA1A gene are known to lead to a broad clinical spectrum including episodic ataxia type 2, spinocerebellar ataxia type 6, familial hemiplegic migraine, and more recently developmental encephalopathy with severe epilepsy.

We report two cases presenting a de novo mutation in the CACNA1A gene, one with a clinical presentation compatible with alternating hemiplegia of childhood (AHC) and the other with developmental encephalopathy without epilepsy.

**Methods:** This first girl was born after a normal twins’ pregnancy. In the first year of life, she was irritable, presented paroxysmal nystagmus and developed a static and dynamic ataxia. At the age of 2, she presented an acute episode of loss of consciousness with vomiting, left hemiplegia and tonico-clonic movements of the right hand. Several 24 hour EEG performed when she felt faint failed to show any ictal or interictal abnormalities and AHC was diagnosed. Sequencing analysis showed a de novo variant resulting in missense substitution p.Ala712Thr in the CACNA1A gene. Aged 2 years, she presents a developmental encephalopathy with ataxia and daily migraine unresponsive to carbamazepine, valproate, channel calcium blockers, acetazolamide and flunarizine.

The second girl was born after an uneventful pregnancy. She experienced feeding difficulties and had severe axial hypotonia with developmental delay. Head control was acquired at 9 months and is unable to sit alone at 19 months of age. At 13 months, a 24-hour EEG showed diffused slow waves but no seizure was reported so far. At 16 months, a severe scoliosis was diagnosed. Sequencing analysis revealed a missense de novo variant p.Asp668Ala in the CACNA1A gene.

**Conclusion:** These cases expand the phenotype of CACNA1A mutation that can present with AHC and developmental encephalopathy without epilepsy.

**Disclosure:** No potential conflict stated.

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**P05-50**

**New mutation CACNA1A and its clinical manifestations**

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**Introduction:** CACNA1A mutation presented phenotypic heterogeneity: ataxia, familial hemiplegic migraine, epileptic encephalopathy, cognitive disfunction and development delay, nystagmus, autism, and other. We reported patient four year old, who had generalised hypotonia with ataxic episodes, sporadic nystagmus and strabismus bilateralis from birth. We noticed at four years age global development delay (motoric, speach, visual, cognitive).

**Methods and Results:** With molecular DNA analysis we identified the following genetic variant(s) related to the clinical presentation of the patient: The variant c.5422G>T (NM_00112722.1) in gene CACNA1A. Present the variants excluding in both parents of the child. This variant has not previously been reported.

**Conclusion:** That is the novo heterozygous, missense variant in CACNA1A gen, considered with clinical manifestation in our patient.

**Disclosure:** No potential conflict stated.
P05-51

Two siblings with a novel mutation in RIN2 gene associated with Epilepsy, further expanding the clinical spectrum
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Introduction: RIN2 syndrome which is previously named as MACS syndrome is a rare autosomal recessive inherited disorder. RIN2 syndrome’s main features are macrocephaly, alopecia, cutis laxa and scoliosis in association with progressive coarsening of face, a distinctive appearance of protruding lips, sagging chin, upper eyelid fullness and severe joint hyperlaxity. The disease mutations were identified in RIN2 gene.

Methods: Here, we report two Turkish siblings with novel RIN2 mutation associated with epilepsy.

Results: The index patient, a 20-year old male and similarly affected 13-year-old sister was born to consanguineous parents. Family history was unremarkable. The boy first presented with focal epileptic seizures at the age of 13. On the examination, he had dysmorphic features including macrocephaly, long coarse face with upper eyelid fullness, infra-orbital folds, downsloanted palpebral fissurs, epicanthus and full cheeks. He also had mild scoliosis, umbilical hernia, rectal prolapsus, short stature, joint hypermobility and hyperextensibility. His sister also had similar phenotypic features without seizure. EEG of index patient showed focal epileptic focus. Brain MRI of both patients revealed dilatation of Virchow-Robin spaces. The patients were preliminary diagnosed as mucopolysaccharidosis or Sener syndrome. Since the screening of metabolic test was negative, we performed genetic testings with TruSight Inherited Disease Sequencing Panel which showed homozygous a novel RIN2 mutation.

Conclusion: RIN2 syndrome must be considered in the differential diagnosis of children presenting with macrocephaly, dysmorphic features and dilatation of Virchow-Robin spaces. We report, for the first time to the best of our knowledge, epilepsy occurring in a patient with RIN2 syndrome, further expanding the clinical spectrum of RIN2 syndrome.

Disclosure: No potential conflict stated.

P05-52

A very early-onset Isolated Dystonia associated with DYT1 gene
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Introduction: Early-onset isolated dystonia (EOID) which usually begins in a leg or the arm, often as inversion of the foot or arm typically presents in childhood or adolescence. Although the dystonia might be triggered only by vigorous physical activity initially, over time, the posturing becomes susceptible to triggering by minimal physical activity and will progress to generalized dystonia in over 50 percent within five years of onset. Disease severity varies considerably even within the same family and no other neurologic abnormalities are present.

Methods: Here, we report a three-year-old Turkish boy with an EOID.

Result: A three-year-old boy referred to our child neurology department with tremor in his hands and head. His parents first noticed this irregular tremor at the age of 2 while he was holding toys. His medical and family histories were normal. On neurological examination, he had tremor and mild dystonia on both hands and head during action. Brain magnetic resonance imaging and medical laboratory investigation did not show any abnormal findings. Genetic test for DYT1 gene was performed which showed a mutation. During the follow up, inversion of the foot during running was started at 4 years.

Conclusion: Children who presented with tremor and dystonia with normal neurodevelopmental features and neuroimaging findings should be considered to perform genetic testing for mutation in DYT1 gene.

Disclosure: No potential conflict stated.
P06-01

Expanding the neurological spectrum of Seipin Deficiency (BSCL2), a complex lipid defect

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Introduction: BSCL2 mutations disrupt seipin, an endoplasmic reticulum membrane protein that modulates lipid droplets. Clinical phenotypes include congenital lipodystrophy 2, progressive encephalopathy with or without lipodystrophy (recessive), distal motor neuropathy type V, and Silver spastic paraparesis (SP) (dominant).

Methods: Clinical, electrophysiological, biochemical, neuroimaging and genetic data were reviewed in a cohort of BSCL2 patients.

Results: Eight patients from four families were identified. Onset age was before 6 months in all but 3 patients (SP group). Onset symptoms include: -failure to thrive (1); -seizures (2); -psychomotor delay (4); abnormal upper limb postures (1) and gait difficulties (2). Three patients carried homozygous BSCL2 variants presenting a severe progressive encephalopathy with spastic-dystonic features. Five patients showed heterozygous BSCL2 variants presenting SP and peripheral neuropathy. Periphereral neuropathy was found in all patients with nerve conduction studies. In one patient CSF analysis found low levels of homovanillic and 5-hydroxy-indolacetic acid. Neuroimaging showed pallidum hypointensity and caudate atrophy in one lypODYSTROPHIC patient.

Discussion: Seipin defects disturb lipid droplet biosynthesis and belong to the recently described category of complex lipid disorders. Prominent motor and cognitive symptoms, neurodegeneration, early refractory epilepsy, axonal neuropathy were core features. Neuroimaging showing pallidum hypointensity was not previously described in this disorders. Hypertriglyceridemia as biomarker was found in only one patients with lipodystrophy.

Disclosure: No potential conflict stated.

P06-02

Sanfilippo Syndrome Type B: a continuum spectrum of clinical phenotypes

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Introduction: Mucopolysaccharidosis type III (MPS III; also known as Sanfilippo Syndrome) belongs to a group of rare, genetic lysosomal storage disorders and is characterized by a deficiency in 1 of 4 enzymes involved in the degradation of heparan sulfate, resulting in progressive cell damage and multisystem disease. Four subtypes of MPS III (A–D) have been identified based on the enzyme deficiency, along with their underlying genotypes and biochemical pathways.

Methods: Clinical, biochemical and radiological data retrospective analysis of 10 Brazilian MPS III type B patients.

Results: Symptoms generally begin between the ages of 2 and 6 years in 9 patients and include developmental and language delays, hyperactivity unresponsive to medication, “aggressive” behavior and sleep disorders. Hepatomegaly was seen in 5 patients. All the patients – but two – showed the the typical progression of the disease, divided roughly into 3 phases: phase I with developmental and language delays, frequent ear and respiratory infections, and diarrhea (not present in 4 patients who showed no apparent gastrointestinal features); phase II with progressive cognitive deterioration, behavioral difficulties, and sleep disturbances was present in 7 patients; phase III with dementia, motor function decline, swallowing difficulties, and spasticity was seen in 8 patients (all of them older than 10 years of age). Autism spectrum disorders were diagnosed in 9 patients. One of the patients showed early onset sensorineural deafness as first manifestation.

Discussion: Patients with Sanfilippo B can also present with symptoms that masquerade as a behavioral disorder. Several reports have shown patients to present with symptoms consistent with a variety of behavioral disorders, including autism, attention deficit disorder, and pervasive developmental disorder, which have resulted in misdiagnoses or delayed diagnosis.

Disclosure: No potential conflict stated.
Long-term effectiveness of Enzyme Replacement Therapy (ERT) in paediatric patients with Mucopolysaccharidosis Type II

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Introduction: Mucopolysaccharidosis type II (MPSII) is a lysosomal disorder caused by deficiency of iduronate-2-sulfatase (I2S). Few clinical trials have assessed the effect of enzyme replacement therapy (ERT) for this condition and the results has been variable.

The aim of this study is to analyze the clinical response of ERT with I2S in patients with MPSII who have been in treatment for more than 1 year.

Methods: Retrospective and prospective-comparative study. Description of clinical changes observed during ERT treatment. Evaluation period 12 to 36 months with ERT. Patients with genetic diagnosis of MPS II, with 18 years or less at the start of ERT were included. Echocardiography, sleep study with polysomnography, hepatic and splenic size evaluation, 6-min walk test (6MWT) and cognitive evaluation was performed and compared before ERT and after 12, 24 and 36 months after ERT.

Results: 6 males (4-19 years). Average diagnosis age 35 month (5 months-5 years). All patients presented neuroopathic form. Echocardiography: Pre-ERT 4 presented valvulopathies that were not modified with ERT and 2 slight left ventricular hypertrophy that reversed. Polysomnography: After-ERT respiratory events decreased in all patients, with normalization of the minimum saturations, the only patient with initial AVNI, stopped needing it. Hepatic and splenic size: Pre-ERT 5 patients presented mild hepatomegaly and 3 mild splenomegaly, After-ERT 4/5 hepatomegaly and 3/3 splenomegaly reversed. 6MWT: 5 patients were evaluated, After-ERT 2 maintained and 3 improved their age expected walking percentage. Cognitive evaluation: After-ERT no changes was observed.

Conclusions: These data provide some further evidence on the long-term effectiveness of ERT, improving cardiac, sleep, gastrointestinal and walking parameters. No cognitive changes was observed.

Disclosure: No potential conflict stated.

Stuttering as a prominent clinical feature in an adolescent patient with CLN3 Disease

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Introduction: CLN3 disease presents with rapidly progressing visual loss, followed by cognitive decline, epilepsy, speech disturbances, behavioral problems and movement abnormalities. Neurological speech impairment is considered a common feature of CLN3 disease (ORPHA: 228346 -Human Phenotype Ontology Database); however data for the type and timing of its appearance are limited. Stuttering is recently reported as a feature of CLN3.

Methods: The patient (aged now 16y) had lost vision by the age 4y and has been erroneously diagnosed as Leber congenital amaurosis. At the age 10y, he presented to our department with epilepsy. He was attending school for visually impaired children and no other neurological or behavioral problems were reported at that time. In the next years his epilepsy has been partially controlled (5-7 brief episodes /year on 3 antiepileptics). Stuttering was presented at the age 12y and has gradually become a major problem. His speech became unintelligible because of disruptions in the production of speech sounds, involuntary repetitions of words, prolongations of speech sounds or complete blockage of speech for several seconds. Intensive speech therapy was totally ineffective. His gait has also mildly deteriorated and the neurological examination revealed mild dystonic features, without significant change in his behavior and academic performance.

Results: Genetic testing using WES revealed homozygosity for the common 1.02-kb deletion [NM_000086.1: c.460+1_461-1_(677+1_678-1)] in the CLN3 gene (OMIM 607042). Mutations in this, as well as other neuronal ceroid-lipofuscinosis (CLN) genes, cause neurodegenerative diseases collectively known as neuronal ceroid lipofuscinoses (NCLs).

Conclusion: Though CLN3 disease has distinctive clinical features patients may remain undiagnosed or misdiagnosed. Stuttering was a distinctive clinical feature in this patient with CLN3 that presented at the early stages of neurological/neuropsychological decline.

Disclosure: No potential conflict stated.
P06-05

AXO-AAV-GM2 for the treatment of GM2 Gangliosidoses: programme overview

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Introduction: Tay-Sachs disease (TSD) and Sandhoff disease (SD) are ultra-rare, autosomal recessive, uniformly fatal neurodegenerative lysosomal storage diseases (LSD) resulting from a deficiency of lysosomal enzyme β-hexosaminidase A (HexA), which is a heterodimer comprised of α and β subunits and responsible for monosialoganglioside 2 (GM2) degradation. The toxic accumulation of GM2 leads to cell ballooning and death, primarily in neurons of the central nervous system (CNS) where gangliosides are most abundant. HEXA (encoding for HexA α subunit) or HEXB (encoding for HexA β subunit) mutations result in TSD and SD, respectively. TSD and SD are characterized by progressive nervous system dysfunction, resulting in seizures along with marked cognitive and physical impairment. TSD and SD result in approximately 50% mortality by 3.5 years of age and 75% mortality by 5 years of age. Currently there are no disease-modifying treatment options available for these diseases. As these are monogenic disorders, they are ideal targets for gene therapy to restore function, prevent neurodegeneration, and slow disease progression.

Methods: AXO-AAV-GM2 is a novel gene therapy product that utilizes an adeno-associated virus (AAV) vector delivering the HEXA and HEXB transgenes directly to the CNS to correct HexA enzyme activity to levels sufficient to stabilize or reverse disease progression. AAV vectors have emerged as a potent platform for efficient and stable in vivo gene transfer to the CNS for the treatment of genetic diseases. HEXA and HEXB transgenes are delivered directly to the CNS where gangliosides are most abundant. In a phase 1/2A study, AXO-AAV-GM2 was well tolerated and demonstrated a significant and sustained increase in HEXA enzyme activity in the brain and no evidence of vector toxicity.

Results: AXO-AAV-GM2 will be evaluated under a comprehensive clinical development program, with the first patient having been dosed in November 2018. AXO-AAV-GM2 is a novel gene therapy product that utilizes an adeno-associated virus (AAV) vector delivering the HEXA and HEXB transgenes directly to the CNS to correct HexA enzyme activity to levels sufficient to stabilize or reverse disease progression. AAV vectors have emerged as a potent platform for efficient and stable in vivo gene transfer to the CNS for the treatment of genetic diseases. HEXA and HEXB transgenes are delivered directly to the CNS where gangliosides are most abundant. In a phase 1/2A study, AXO-AAV-GM2 was well tolerated and demonstrated a significant and sustained increase in HEXA enzyme activity in the brain and no evidence of vector toxicity.

Conclusion: This abstract provides an overview of the AXO-AAV-GM2 development program, including a summary of relevant preclinical information to support evaluation in patients with TSD and SD.

Disclosure: All Axovant Gene Therapies authors are employees of the same.

P06-06

Asparagine Synthetase Deficiency – A rare neurometabolic disorder with Congenital Microcephaly, early speech delay and Drug Refractory Epilepsy – Experience from Oman

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Objective: Asparagine synthetase deficiency (ASNSD, OMIM #615574) is an extremely rare but relatively recently known neurometabolic condition. To date only 26 cases have been reported in literature. We report first case series of genetically confirmed cases of ASNSD from Oman. Methods: This was a retrospective case review of cases confirmed to have pathogenic mutation in the Asparagine synthetase gene.

Results: Eight cases were identified from four Omani families. 2/8 patients were born preterm (35 week). Three siblings from a single family had severe phenotype and died in the neonatal period. All had jitteriness, neonatal seizures and thin corpus callosum on MRI brain. Among the survivors (5/8) the reported seizures were Myoclonic (1), generalised convulsive (4), focal motor seizures (5). Age of onset of epilepsy ranged between 4 to 12 months among the survivors (5/8). Recurrent complex febrile seizures in the first year of life was reported in two patients. Microcephaly at birth, drug refractory Epilepsy and early speech delay was seen in all survivors. One Patient has shown promising early results with Vagal Nerve Stimulation. Only one patient completed 6 month trial of Oral Asparagine with no change in the baseline clinical sate.

Conclusion: Microcephaly with predominant speech delay in infancy is followed by Motor regression in late childhood in our patients with ASNSD. Replacement with exogenous oral arginine supplementation does not seem to benefit. Vagal Nerve stimulation could be a potential option to help control refractory epilepsy in this group of patient and can be considered an early option.

Disclosure: No potential conflict stated.
Molybden Cofactor Deficiency Type B presenting with Guillain-Barré Syndrome-like flaring of Chronic Peripheral Neuropathy, Intellectual Disability and Dysmorphism

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Introduction: Molybden cofactor deficiency (MCOD) is a rare autosomal recessively inherited neurometabolic disorder. MOCS1, MOCS2 and GPHN gene mutations are responsible for this disease. Neonatal-onset severe psychomotor retardation, refractory seizures, dysmorphism, cystic white matter involvement on brain MRI and low serum uric acid level are the classic findings. Peripheral neuropathy was not defined in MOCS2 gene mutations. We present two siblings with Guillain-Barre syndrome-like flaring of chronic peripheral neuropathy and intellectual disability who had MOCS2 gene mutation.

Methods: Four and 2.5-year old boys were reported to the hospital with acute weakness, and diagnosed as Guillain-Barre syndrome. They have both delay of neuological development since early infancy, and have dysmorphic features. Acute weakness improved in a few month. In the acute phase of the disease, EMG showed loss of motor and sensory potentials, axonal and demyelinating involvement could not be evaluated. Serum uric acid level was low in both siblings. Purine nucleotide phosphorylase deficiency was excluded by enzymatic analysis. Inborn errors of metabolism screening tests were uneventful. Cranial MRI showed dysgenetic corpus callosum. Whole exome sequencing for targeting MOCS genes was planned due to low serum uric acid levels.

Results: Whole exome analysis showed c.1A>G (p.Met1Val) variant in the MOCS2 gene. Parents were heterozygous for the same variant. In silico analysis showed that this variant was pathogenic.

Conclusion: There is no patient in the literature with peripheral neuropathy and Guillain-Barré syndrome-like acute flaring of chronic neuropathy due to MOCS2 mutation. Our patients widen the clinical spectrum of molybden cofactor deficiency.

Disclosure: No potential conflict stated.

Succinic Semialdehyde Dehydrogenase Deficiency – A case report

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Introduction: Succinic semialdehyde dehydrogenase (SSADH) deficiency is a rare metabolic disorder marked by an inborn error in the metabolism of GABA, resulting in accumulation of γ-hydroxybutyric acid (GHB), which can be detected in bodily fluids. SSADH is inherited as an autosomal recessive trait and is characterized by early-childhood-onset non-specific symptoms of slowly progressive encephalopathy, most commonly delayed acquisition of developmental milestones, behavioral problems and motor dysfunction.

Methods: A 13-year-old girl presented with late-infantile-onset general psychomotor retardation and behavioral issues, mainly hyperactivity and impaired social interaction. During clinical examination, hyporeflexia, hypotonia and ataxia were also discovered. She was an IUGR newborn with normal APGAR score and had surgically corrected congenital strabismus. She has non-consanguineous parents and a healthy older brother with normal psychomotor development. Basic labs, CPK, ammonia and lactic acid tests were performed, as well as basic CSF analysis, karyotype, urine organic acid and aminoacid analysis. Furthermore, an EEG and a brain MRI scan were done.

Results: There was absence of metabolic acidosis. The karyotype was that of a normal female. The aminoacid analysis showed an increased glycine concentration, while the organic acid analysis showed high concentration of GHB. The MRI scan and CSF analysis were normal. The EEG presented diffuse background slowing. Following the metabolic tests’ results, molecular genetic testing was ordered, which showed biallelic mutations in the ALDH5A1 gene and the diagnosis of SSADH was established.

Conclusion: Due to the non-specific symptoms associated with the disorder, it is believed that SSADH deficiency is likely underdiagnosed. It is important to suspect the disease in the presence of the aforementioned features and perform the suitable paraclinic testing to avoid misdiagnosis.

Disclosure: No potential conflict stated.
**P06-09**

**Neuroimaging spectrum of GM1 Gangliosidosis with description of novel imaging phenotypes**

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**Introduction:** GM1 gangliosidosis is an autosomal recessive lysosomal storage disorder due to GLB1 mutations leading to deficient b-galactosidase enzyme activity and accumulation of monosialogangliosides. Three clinical types have been defined, the age of onset correlating inversely with the level of residual enzymatic activity; these include infantile, juvenile/late infantile and chronic/adult types. Previous neuroimaging in GM1 gangliosidosis has suggested delayed and demyelinating patterns; we cohered six cases to see if there were any characteristic features to aid diagnosis.

**Methods:** We looked retrospectively at the imaging of six diagnosed cases of GM1 between Great Ormond Street Hospital (UK) and Christian Medical College & Hospital (Vellore, India). Cases were analysed by two expert Paediatric Neuroradiologists whom identified characteristic features in these cases.

**Results:** Our imaging findings showed delayed and demyelinating patterns seen in our late-infantile and infantile forms respectively. It highlighted a common feature in our chronic GM1 cases of bilateral globus pallidus hypointensity with one case showing blooming on SWI in a wishbone pattern with a comma shaped putamen.

**Conclusion:** Imaging of storage disorders in children shows significant overlap with dark thalami with hyperdensity and white matter abnormalities described in other lysosomal storage disorders. Globus pallidus hypointensity also often leads to a diagnostic confusion with neurodegeneration with brain iron accumulation (NBIA). Ventral and dorsal striatum, though lack an anatomical boundary, are functionally different. This could account for different enzymatic activity and resultant differences in ganglioside deposition. Our cases add to the small cohort of previously reported changes in GM1 gangliosidosis. It also highlights predeliction for the putamen (the wishbone sign), which may help differentiate from the usual pattern of NBIA disorders.

**Disclosure:** No potential conflict stated.

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**P06-10**

**A rare case presentation: a novel mutation in GTPBP3 gene**

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**Introduction:** Mutations in nuclear and mitochondrial genes cause mitochondrial dysfunction and cause clinical abnormalities such as neuromuscular disorders, respiratory failure and cardiomyopathy. GTPBP3 gene is one of the genes that affecting to function of mitochondria. The main clinical findings identified in patients with homozygous mutation in GTPBP3 are cardiomyopathy, cardiac failures, delayed psychomotor development, lactic acidosis and hyperintense lesions in the thalamus, basal ganglia, and brainstem.

**Methods and Results:** We report A 11-year-old girl patient with mental -motor retardation, tetraparesis and generalized tonic seizures. She had no lactic acidosis and cardiomyopathy. She experienced status epilepticus due to prolonged generalized tonic seizures. The seizures were mainly controlled by valproate although phenytoin, levetiracetam, carbamazepine, topiramate and clonazepam were used. Whole exome sequencing (WES) was performed. As a result of WES, homozygous c.932C>T (p.Pro311Leu )mutation was detected in the GTPBP3 gene. We emphasize the rare case with mental-motor retardation, tetraparesis and epilepsy but no lactic acidosis and cardiomyopathy with homozygous mutation in GTPBP3 gene.

**Disclosure:** No potential conflict stated.
**P06-11**

**Fatal Neonatal Onset of Mitochondrial DNA Depletion Syndrome due to novel MPV17 gene variants in two sisters**

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**Introduction:** The MPV17 gene encodes a mitochondrial inner membrane protein and mutations have been described to cause mitochondrial DNA depletion syndrome. Fewer than 50 patients have been reported worldwide. We report two sisters of Filipino and Indian descent with hepatocerebral syndrome who are compound heterozygous for novel variants c.375G>A and c.408+1G>A.

**Methods:** We describe the clinical presentation, various investigations and outcomes for this pair of siblings.

**Results:** Both siblings presented on Day 2 of life with significant hypoglycemia and lactic acidosis. The elevated lactate levels responded well acutely to intravenous dichloroacetate. They had global developmental delay, hypotonia and muscle weakness. Definitive diagnosis of mitochondrial DNA depletion syndrome was clinched on both muscle biopsy and genetic testing. Despite conservative treatment, both had progressive liver failure and demised in early infancy.

**Conclusion:** These two cases illustrate the very early onset of mitochondrial DNA depletion syndrome due to novel MPV17 gene variants. Genetic analysis is able to provide the etiology of liver disease in a timely manner in acutely and progressively ill infants. The definitive diagnosis enables prognostication and reproductive genetic counselling.

**Disclosure:** No potential conflict stated.

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**P06-12**

**Differential diagnosis for X-linked Adrenoleukodystrophy**

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**Introduction:** X-linked Adrenoleukodystrophy belongs to orphan diseases (lipidosis, peroxisomal disease). It requires a complex differential diagnosis between lymphomas of the central nervous system, gliomas, demyelinating diseases, encephalitis. The atypical course of the disease can lead to erroneous treatments.

**Methods:** Neurological examination, immunological and virological studies, lumbar puncture and cerebrospinal fluid examination, determination of very long chain fatty acids. MRI and MRS.

**Results:** During a neurological examination, we identified apathy, cognitive deficits, dysarthria, asymmetry of the face, left arm and leg weakness, inability to walk independently. The neurological deficiency was progressing within the last three months. Cerebrospinal fluid studies results excluded subacute sclerosing panencephalitis (Van Bogaert disease), Lyme disease, viral encephalitis. Blood tests showed a decrease in cortisol levels, an increase in very long chain fatty acids. MRI findings were characterized by white matter hyperintensities with the more intense rim on the periphery in T2 and FLAIR modes, mainly in deep and superficial parts of the temporal, parietal and occipital lobes at the level of the posterior horns of the lateral ventricles, with the involvement of corpus callosum. MRS results showed a sharp increase in the choline peak with decreased levels of other metabolites, a moderate increase in lipid-lactate peak was seen as well.

**Conclusion:** So, we had diagnosed one of the most severe diseases of childhood - X-linked leukodystrophy. This pathology requires doctors vigilance and timely diagnosis. Since at the stage of marked clinical manifestations the treatment is already ineffective.

**Disclosure:** No potential conflict stated.
**P06-13**

**AXO-AAV-GM1 for the treatment of GM1 Gangliosidosis: programme overview**

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**Introduction:** GM1 gangliosidosis is a rare, inherited neurodegenerative lysosomal storage disorder caused by mutations in the GLB1 gene located on human chromosome 3p. The GLB1 gene codes for lysosomal acid β-galactosidase (β-gal), an enzyme which catalyzes the hydrolysis of GM1 ganglioside and keratan sulfate. GLB1 gene mutations cause impaired β-gal activity, leading to accumulation of GM1 ganglioside predominantly in the central nervous system (CNS), where its rate of synthesis is the highest, but also in the periphery. The toxic accumulation of GM1 gangliosides lead to the progressive destruction of nerve cells in the brain and spinal cord and early death.

GM1 gangliosidosis is uniformly fatal, and there are no disease-modifying treatment options currently available. As this is a monogenic disorder, it is an ideal target for gene therapy to restore function, prevent neurodegeneration, and ameliorate symptoms.

**Methods:** AXO-AAV-GM1 is an investigational gene therapy utilizing an adeno-associated virus (AAV) vector to deliver a functional copy of the GLB1 gene with the goals of improving neurological and neuromuscular function and extending survival by restoring β-gal activity and reducing GM1 ganglioside buildup in the CNS and periphery.

**Results:** AXO-AAV-GM1 is being evaluated under a comprehensive clinical development program.

**Conclusion:** This abstract provides an overview of GM1 gangliosidosis as well as the rationale for the AXO-AAV-GM1 development program, including a summary of relevant preclinical information to support evaluation in patients with GM1 gangliosidosis.

**Disclosure:** All Axovant Gene Therapies authors are employees of the same.

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**P06-14**

**Quality of life in patients with Morquio A Syndrome treated in a Paediatric Neurology reference centre**

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**Introduction:** Mucopolysaccharidosis IV-A (MPS IV-A) is a lysosomal storage disorder manifests mainly as short stature and skeletal dysplasia resulting in significantly impaired functional capacity, mobility and quality of life (QoL).

**Methods:** We evaluated the QoL among adults with MPS IV-A (≥18 years, N=5) using the general Health-Related Quality of Life (HRQoL) questionnaire EuroQol EQ-5D-5L.

**Results:** All the patients showed the classic phenotype. The QoL evaluation showed that all patients had pain from mild to severe, 4 patients had a reduce in mobility from mild to moderate, 3 patients had mild problems to perform their usual activities, 2 patients had moderate problems to wash or get dressed and no patient manifested anxious or depressive symptoms. The HRQoL utility values were from 0.887 in an male not using a wheelchair to 0.462 in a female always using a wheelchair. The analysis of the questionnaire showed that HRQoL was more negatively affected in the domains of mobility and pain.

**Conclusions:** The QoL of MPS IV-A patients is affected mainly by pain, discomfort and a reduce mobility. Greater attention to this problems in order to keep patients pain free, active and independent for as long as possible, may help maximize overall QoL.

**Disclosure:** No potential conflict stated.
P06-15

Neuronal Ceroid Lipofuscinoses Type 6 and impaired autophagy system

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Introduction: A 7 years old male, the sole child of non-consanguineous parents had shown psychomotor deterioration at 3 years of age. He lost his ability to walk and speak at 5 years old. Focal impaired awareness seizures were treated with Carbamazepine, Topiramate, Levetcaramab, and Clobazam from 4 years old. Myoclonic seizures and gelastic seizures occurred at 5 years old and Lamotrigine and Perampanel were added. Cerebral and cerebellar atrophy with decreasing white matter volume were demonstrated by MRI. Interictal electroencephalogram showed frequent, diffuse, spike-wave bursts evoked by photic stimuli (PS). Myoclonic seizures were also induced by PS. The bilateral median nerves showed giant somatosensory evoked potential (SEP). We derived lymphoblastoid cell lines (LCL) from his peripheral blood lymphocyte. Autophagic molecules, for example, LC3, and p62 were evaluated by RNA and protein extracted from LCL respectively.

Results: Whole-exome sequencing (WES) and Sanger sequencing revealed that he had compound homozygous mutations in the CLN6 gene (NM_017882.2: c.794_796del, p.Ser265del). The expression of LC3A/B was reduced compare to control LCL, p62 was elevated slightly in qRT-PCR. Whereas, the expression of LC3A/B were elevated compare to control LCL, whereas p62 was similar to control in western blot.

Conclusion: We reported a case of NCL6 and autophagic activity of NCL6. The accumulation of LC3A/B might be suggest-ed disturbing fusion between autophagosomes and lysosomes that is, insufficiency of autophagy in LCL of CLN6 mutation.

Disclosure: No potential conflict stated.

P06-16

Twenty years’ follow-up of Bone Marrow Transplantation (BMT) in two patients with Adrenoleukodystrophy (ALD)

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Introduction: Hematopoietic stem cell transplantation (HSCT) including BMT is the most realistic treatment of ALD even in the age of gene therapy. We report 2 patients (A;33y and B;26y) with childhood ALD who have been followed up more than 20 years and we describe their clinical course and their thought about their quality of lives (QOL).

Case reports: They received BMT at 10 and 6 years of age, respectively. Main lesion on MRI at BMT was frontal in patient A and occipital in patient B. Donors of BMT were their younger sisters. One (patient A) is a quiet person with slight attention deficient. He works daily at a cookhouse. Another (patient B) is a member of an ambulatory social welfare facility. He has a cheerful character despite of his limited visual and worsening physical function due to adrenomyeloneuropathy. They have been followed up yearly with full workup of their clinical status after their acute stage of the treatment. Intelligence decline is mild (Full IQ 64, VIQ59, PIQ76 by WAIS-III) in patient A and severe (5years-old level of DA by Binet test) in patient B. Recent evaluation of standardized Japanese QOL scale of both patients was good with no special concerns. But their parents had physical concern.

Discussion and Conclusion: They were pioneers who could obtain the benefit of the leading-edge treatment of their era. Earlier treatment if they could have, surely bring better prognosis. However, the patients now can spend their lives with enough satisfaction while their parents have of course more concern in their children. Realization of successful gene therapy at the newborn period should be considered in the very near future.

Disclosure: No potential conflict stated.
The 7th Greek case of Tyrosine Hydroxylase Deficiency: even stronger evidence for a founder effect

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Introduction: Tyrosine hydroxylase (TH) deficiency is a rare autosomal recessive disorder mapped to chromosome 11p15.5. Its clinical expression varies with presentations as dopa-responsive dystonia (recessive Segawa’s disease), dopa-responsive infantile parkinsonism, dopa-responsive spastic paraplegia, progressive infantile encephalopathy or dopa-non-responsive dystonia.

Methods: We describe a 10-month-old boy with infantile encephalopathy and partial responsiveness to dopamine. The patient demonstrated generalized hypotonia with delayed motor milestones, pyramidal tract dysfunction, macrocephaly and temperature instability after the second month of life. Dystonia, tremor and oculogyric crises complicated the clinical picture during the following months.

Results: Neurotransmitter analysis in CSF disclosed low levels of HVA and MHPG, whereas serum prolactin was profoundly increased. Subsequent molecular analysis revealed homozygosity for a missense mutation (c.707T>C) in the TH gene. L-Dopa therapy in progressively increasing doses resulted in a moderate beneficial effect. Today, at the age of 2 years, the patient demonstrates severe developmental retardation with trunkal hypotonia, and occasionally dystonic crises.

Conclusion: He is the seventh Greek patient with TH deficiency to be reported. Since all six previously reported patients carry the same pathogenetic mutation, a founder effect is strongly suspected. It is noteworthy that all 7 patients demonstrated a rather severe clinical course.

Disclosure: No potential conflict stated.

Leigh Encephalopathy in patients with valine metabolism defects due to mutations in HIBCH and ECHS1 genes

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Objectives: To delineate the phenotype of patients with Leigh syndrome and pathogenic variants in HIBCH and ECHS1.

Methods: We analysed 28 patients with Leigh syndrome with whole exome sequencing and performed phenotypic characterization in those with HIBCH and ECHS1 mutated variants. Results: Pathogenic variants in valine catabolism related genes were found in 4/28(14.3%) patients from our cohort. Eleven more patients were included form other centers. We describe biallelic mutations in 14 (HIBCH, n=5; ECHS1, n=9) patients, including missense (n=11), frameshift (ECHS1: c.123_124del) and splicing (HIBCH c.517+1G>A) variants. Age at onset was similar to both defects 9 (1-28) months. The majority of patients developed episodes of acute encephalopathy, hypotonia, dystonia and seizures. ECHS1 patients had a more severe phenotype which involved bulbar dysfunction (6), respiratory failure (4), optic atrophy and nystagmus (7), hearing loss (6), microcephaly (6), parkinsonism (4), ventricular hypertrophy (4), leading to early death in three cases. A characteristic feature of HIBCH was cerebellar ataxia. Plasma lactate was elevated in 90% (ECHS1) and 60% (HIBCH). 2-Methyl-2,3-dihydroxybutirate was elevated in 2/4 ECHS1 patients. RCC I deficiency was observed in 3 patients, multiple complex deficiency in 2 patients and aPDH was low in one. Brain MRI showed signal abnormalities in globus pallidus (GP) (9, including cavitation in three HIBCH patients), putamen (9), caudate (7) and dentate nucleus (3), cerebellar atrophy (6) and white matter hypomyelination (5).

Conclusion: Patients with ECHS1 and HIBCH defects present in infancy with basal ganglia dysfunction and lactic acidosis. They evolve into a phenotype with diffuse brain involvement,
neurosensorial deficits, seizures and cognitive impairment. Prognosis is poor for ECHS1 patients. Valine catabolism defects should be suspected in Leigh syndrome patients with basal ganglia neurodegeneration, especially if GP is involved.

Disclosure: No potential conflict stated.

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**P06-19**

**Severe MTHFR Deficiency with Hyperhomocysteinemia, Demyelinating Leukodystrophy and Psycho-Motor Retardation**

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**Introduction:** Methylenetetrahydrofolate reductase (MTHFR) is a cytoplasmic enzyme that catalyzes the physiologically irreversible reduction of 5,10-methylenetetrahydrofolate (methyleneTHF) to 5-methyltetrahydrofolate (methylTHF). Severe 5,10-methylenetetrahydrofolate reductase (MTHFR) deficiency results in hyperhomocysteinemia and varying severity of disease, ranging from neonatal lethal to adult onset. We present a case of severe MTHFR deficiency presenting with severe psycho-motor retardation, prominent cerebral atrophy and demyelinating leukodystrophy, and to discuss the value of early diagnosis in this rare disease.

**Methods:** An 11-month-old girl was presented for delay of development. She had hypotonia, loss of head control and eye contact. There was no dysmorphism. Head circumference was 41.5 cm (3-10 percentile). Other system findings were uneventful. Parents were first degree cousins. One of her brother dies at 2 years of age with similar clinical and laboratory findings without any diagnosis. She had two healthy siblings.

**Results:** Cranial MRI showed generalized cerebral atrophy and demyelinating leukodystrophy. Tandem MS/MS was normal. Methylmalonic acid excretion was found in urine organic acid analysis. Plasma homocysteine level was >50 micromol/L, and methionine was low. There was no megaloblastic change on peripheral smear. Laboratory findings were compatible with MTHFR deficiency, and we ordered MTHFR gene analysis to confirm the diagnosis. Sanger sequencing of the MTHFR gene showed a known homozygous mutation. Betain, hydroxycobalamine and folic acid were ordered and at follow-up the neurological status of the patient improved.

**Conclusion:** Plasma homosistein level should be investigated in the patients who have demyelinating leukodystrophy and psycho-motor retardation for the diagnosis of cobalamin metabolism defects and MTHFR deficiency. Early diagnosis of MTHFR deficiency is important because of the positive effect of betain, hydroxycobalamine and folic acid replacement on neurologic prognosis.

Disclosure: No potential conflict stated.
Glucose Transporter Type 1 (Glut-1) Deficiency Syndrome: a single centre case series

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Objective: Glucose transporter type 1 deficiency syndrome (GLUT-1 DS) is a metabolic disorder, characterized by impaired glucose transport across the blood-brain barrier and manifests as seizures, developmental delay, episodic movement disorders, spasticity, acquired microcephaly and ataxia. Gold standard treatment is the ketogenic diet (KD).

Methods: We describe the clinical features, molecular findings, treatment and outcome of patients with GLUT-1 DS in our department.

Results: There were two girls and a boy aged 3 to 15 years, with an age of onset symptoms at 3 to 6 months. Seizure was the first presenting symptom in all cases. The main other clinical manifestations were ataxia, global developmental delay and acquired microcephaly. All children had ataxia; one had spasticity, one had oculomotor apraxia and stereotypic hand movements. EEG demonstrated interictal focal epileptiform discharges in all cases and mild intermittent diffuse background slowing in two cases. Cranial magnetic resonance imaging results were normal in all cases. Lumbar puncture was performed in two cases after a four-hour fasting period and the cerebrospinal fluid vs. blood glucose ratio was determined low (0.35 and 0.40). Two patients had heterozygous mutation (c.389G>A and c.734A>C ) and one had microdeletion (1p34.2) of SLC2A1 gene. All children were treated with a ketogenic diet (3:1) and achieved remission in ataxia and seizures within 4-8 weeks.

Conclusion: We described a case series of patients with GLUT1DS presenting with a heterogenic phenotypic and genotypic features. We also suggest that early diagnosis and treatment with KD can increase the chance of better outcome.

Disclosure: No potential conflict stated.

Metacromatic Leukodystrophy – Rare and serious progressive disease

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Introduction: Metacromatic leukodystrophy (MLD) is a rare metabolic disease caused by the deficiency of arylsulfatase A or lack of SAP-B (saposin B) sphingolipid activator protein, which normally stimulates the degradation of sulphate by ARSA. Not recognized or appropriately treated, leads to severe neurological degradation and early death in children. Treatment modalities include stem cell transplantation, bone marrow transplantation along with genetic engineering and gene therapy. Despite the development of gene therapy, the treatment of infantile MLD is still limited.

Case report: A 2 years old boy came with gradual regression in development which started at the age of 15 months with inability to sit and stand. Prior neurological and somatic developments as well as medical history were uneventful. The family history was negative for neurological diseases. Mother noticed weakness in lower limbs and he was taken to orthopedist who found no problems. Upon our examination he had bilateral horizontal nystagmus, ataxic movements with inclined head to the left side, broad-based walking with adherence, lower extremity hypotonia with absent reflexes and negative Babinski sign. MRI scan of brain was abnormal, likely suggestive of dysmyelination/demyelination sequelae to MLD. Arylsulfatase A enzyme activity in leukocytes was tested and found to be decreased. The genetic test was done to the whole family. He has two heterozygous pathogenic variants in the ARSA gene and parents have one of the two known pathogenic ARSA variants in a heterozygous state. Over time he has developed epileptic seizures, with progression of severe neurological disability.

Conclusion: It is important to recognize this rare disease in timely manner to be able to offer potential treatment in certain cases. For our patient unfortunately, only symptomatic support is available.

Disclosure: No potential conflict stated.
Leukodystrophy and differential diagnosis of Arylsulfatase Deficiency

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Objective: Progressive neurological dysfunction with leukodystrophy and arylsulfatase A (ARSA) enzyme deficiency suggest metachromatic leukodystrophy (MLD) but differential diagnosis may be complicated.

Methods: We reviewed 17 patients (7 girls, 10 boys) aged 22 mo–38 years (mean 6.5 yr) from 14 families presenting with neuropsychiatric or gastrointestinal findings and leukocyte ARSA activity <10% of normal.

Results: Three cases are neurologically asymptomatic (one infant detected because of symptomatic sibling and one 4-year-old diagnosed with gallbladder papillomatosis). Others had symptoms starting between 2mo–28yrs: delayed walking and ataxia (n=11); cognitive and speech problems (n=6); motor-mental delay (n=2); recurrent vomiting, abdominal pain and jaundice (n=1). MRI findings ranged from normal to severe leukodystrophy. With detailed metabolic and genetic tests, 15 patients were diagnosed with MLD (10 late infantile, 3 juvenile, 1 adult, 1 neurologically asymptomatic). Of 2 patients diagnosed with multiple sulfatase deficiency (MSD), one had ichthyosis, hypertrichosis and coarse face noticeable after 2 months but the other had subtle systemic features. Two MLD patients had associated ARSA pseudodeficiency. Two MLD cases underwent bone marrow transplantation (BMT) from fully matched siblings. Leukocyte enzyme levels reached normal levels (50–250 µmol/g protein/hr); one has been stable for one year while the other has only 2 months' follow-up yet.

Conclusions: Diagnosis can be challenging even in well-known neurodegenerative diseases. ARSA deficiency and increased urinary sulfatides may not always represent MLD: systemic examination, family history, and clinical correlation are important. Early MLD presents with motor delay while older children manifest cognitive and speech problems. Early diagnosis of MLD is important for BMT and future enzyme replacement and gene therapies.

Disclosure: No potential conflict stated.

Congenital Disorder of Glycosylation (CDG) Type II associated with a SLC39A8 gene variant: description of two siblings with variable phenotype

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Introduction: The SLC39A8 (MIM: 608732) gene encodes the manganese and zinc transporter located in the cellular and mitochondrial membrane. Its defect has been reported as a cause of type II CDG, which would be explained due to the reduced activity of the alfa-galactosidase enzyme, which requires manganese as a cofactor.

Methods: Clinical, biochemical and neuroimaging description of 2 siblings carrying SLC39A8 variants.

Results: The patients described here were 13 and 27 years-old at the time of assessment and were borned after an uneventful pregnancy from consanguineous parents.

Case 1: Child with psychomotor delay from the first months of age. Follow-up showed severe cognitive impairment associated with behavioral disorder, stereotypes, ataxia and peripheral neuropathy. Physical examination showed peculiar phenotype with gynoid distribution of adipose tissue. Gait ataxia limited autonomous gait.

Case 2: Girl with initial symptoms of psychomotor retardation and congenital cataract. Follow-up showed mild cognitive impairment and mild ataxia. Autonomous gait was preserved until its last assessment. Physical examination showed a peculiar phenotype with small palpebral fissures and keloid scarring in the skin.

In both, neuroimaging studies showed a progressive cerebellar atrophy. The glycosylation profile pattern showed increased amounts of trisialotransferrin. Initially the exome study direct-ed to ataxias and CDG was negative. The extended study detected the SLC39A8 gene variant: c.113G>A in a homozygous status.

Conclusions: We report the case of two siblings with variable severity of cognitive impairment and ataxia, associated with cerebellar atrophy. Although other unidentified variants that could explain the differences in their clinical features cannot be excluded, the SLC39A8 transporter dysfunction would explain the clinical symptoms, based on recently reported cases.

Disclosure: No potential conflict stated.
**P06-24**

**Metachromatic Leukodystrophy: a case report of a new mutation**

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**Introduction:** Metachromatic leukodystrophy (MLD) is an autosomal recessively inherited disorder caused by a deficiency of the lysosomal enzyme arylsulfatase A. Disease course is highly invariable and stereotypic and the initial signs include irritability, diminished muscle tone, and gait disturbance accompanied by mental regression. Demonstrations of reduced nerve conduction velocity and of demyelination by magnetic resonance imaging (MRI) are the major laboratory findings. On MRI central white matter is easily affected with typically butterfly-shaped confluent white matter hyperintensities on T2w with a characteristic tigroid pattern. Regardless of the type of disease, corpus callosum is involved early. White matter changes on MRI clearly precede the onset of clinical symptoms in juvenile and adult MLD. As the disease progresses, there is increasing white matter involvement including U-fibers and involvement of cerebellar white matter as well as cerebral atrophy. The gene that regulates the activity of arylsulfatase A has been located on the long arm of chromosome 22 (22q13.33). We present herein a case of 3 year-old boy suffered from gait disorder, peripheral neuropathy in ENMG, leukodystrophy with specific pattern, and consanguinity marriage of parent, the diagnosis of MLD should be considered. The mutation was found to be reported for the first time in MLD patients and may provide critical information for MLD families.

**Disclosure:** No potential conflict stated.

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**P06-25**

**Clinical and genetic aspects of Progressive Myoclonus Epilepsy: experience in a cohort of 48 children**

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**Objective:** To evaluate the clinical course of different progressive myoclonus epilepsy (PME) in children.

**Methods:** The retrospective study included children with PME, aged 1m - 18 y treated in Institute (1998-2018). Clinical, neurophysiological, ophthalmological, neuroradiological, psychological evaluations were done in all cases. Diagnosis was proved by enzyme, genetic and/or histopathology analyses. We evaluated: the age of onset, course of disease, neurological and physical satatus, clinical and EEG features of epilepsy, response to treatment.

**Results:** The retrospective study included 48 children: neuronal-ceroid lipofuscinosis (NCL) (28), Gaucher disease (GD) (5), Niemann-Pick C (NPC) (4), mitochondrial disorders (4), Lafora (3), Krabbe (2), Sialidosis (1), KCNC1 (1). Focal or generalized seizures were among initial manifestations in 26 patients: in all cases had neurological and cognitive impairment, ten had visceromegaly. Photoparoxysmal EEG response had patients with NCL and LD at the early phase of disease, while slow, low-amplitude background activity persist in later phase in almost all cases. All patients had pharmacoresistant epilepsy and 22 suffered one or more status epilepticus. Enzyme replacement was given in five cases (GD, CLN2).

**Conclusion:** PME is heterogeneous group of diseases with different clinical course. NCL is the most frequent etiology. Progression, myoclonus, neurological and cognitive abnormalities are not obvious at early stage and contribute to late diagnosis. Genetic tests have to be considered early in all children with unexplained cause of seizures associated with systemic, neurological and/or cognitive abnormalities. Early diagnosis is helpful for adequate genetic council, prenatal diagnosis and new treatment possibilities.

**Disclosure:** No potential conflict stated.
Clinical characteristics and inherited metabolic or genetic aetiologies of Homocystinemia; a single centre experience

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Objective: Homocysteine is a non protein amino acid, which is an intermediate compound of methionine degradation, is remethylated to methionine. Elevations in the plasma homocysteine concentration can occur because of genetic defects in the enzymes involved in homocysteine metabolism, nutritional deficiencies in vitamin cofactors (folate, vitamin B6, or vitamin B12), or other factors including some chronic medical conditions and drugs (methotrexate). Inherited homocystinemia occurs through mutations in genes that encoded cystathionine beta-synthase (classic homocystinuria) and 5, 10 methylenetetrahydrofolate reductase (MTHFR), as well as inherited disorders of folate and cobalamin metabolism.

Materials and Methods: This study retrospectively evaluated 10 consecutive children with homocystinemia with different etiologies other than nutritional deficiencies from a single institution in Adana, Turkey. Extensive workup for homocystinemia was performed for all patients including genetic and metabolic screening.

Results: From December 2011 to December 2018, seven boys and three girls (age range 2 to 17 years) diagnosed with homocystinemia. The presenting diagnosis were stroke due to homozygote MTHFR mutation.

Conclusion: The clinical manifestations and etiologies of the patients with inherited homocystinemia would be extremely variable. We suggest evaluating homocysteine levels in children with unexplained neurologic disorder in children

Disclosure: No potential conflict stated.

Phenotypic spectrum of Short-Chain enoyl-CoA Hydratase-1 Deficiency

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Introduction: ECHS1 encodes for the enzyme Short-chain enoyl-CoA hydratase, a key component of fatty acid β-oxidation and involved in isoleucine and valine catabolic pathways. Biochemical markers are elevated blood methacrylyl-CoA and acrylyl-CoA on and urine 2-methyl-2,3-dihydroxybutyrate acid and N-acetyl-L-cysteine. In literature a few scattered patients are described with a wide clinical spectrum.

Methods: We report two new ECHS1-mutated patients and we provide a systematic literature revision of clinical, biochemical and neuroradiological features.

Results: Our patients presented different clinical severity and MRI features, which reflects the differences reported in literature. We were able to distinguish 3 main phenotypes: a severe prenatal-neonatal onset presentation with rapid and fatal course and significant white matter abnormalities, an intermediate infantile onset variant with slower neurological deterioration, developmental delay, pyramidal, extrapyramidal signs, optic atrophy, feeding difficulties, mild white matter abnormalities and neostriatal and/or pallidal involvement and a mild phenotype presenting with recurrent episodes of neurologic impairment triggered by infections or energetic failures, only slight chronic neurological signs and mainly nuclear pallidi degeneration. Biochemical analysis documented 2-methyl-2,3-dihydroxybutyrate aciduria as the most consistent biochemical marker. Secondary multiple respiratory chain complexes and PDH activity deficiency are inhomogeneously detected.

Conclusions: We reported two new ECHS1 mutated patients and we present the first systematic literature revision. ECHS1 mutations cause a metabolic encephalopathy which can present with three main phenotypes: an early onset severe presentation, an early infantile intermediate variant and a later mild intermittent form. Blood and urine metabolic evaluations are essential in the diagnostic work up in allowing a rapid diagnosis.

Disclosure: No potential conflict stated.
P06-28

Advances in the natural history of an underdiagnosed group of Neurometabolic Disorders: the International Niemann-Pick Diseases Registry (INPDR)

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Background: Niemann-Pick diseases (NPD) are a group of rare inherited Lysosomal Storage Disorders (LSDs) that can affect both children and adults. Niemann-Pick type A/B is caused by acid sphingomyelinase deficiency (ASMD), presenting with both neurological and/or visceral finding with varying effects on other organs including the lungs. Niemann-Pick Type C disease (NP-C) is a trafficking lipid disorder caused by two different genes NPC1 and NPC2, leading to an accumulation of non-sterified cholesterol and sphingolipids in the liver, brain and spleen.

Materials: Clinical, biochemical, neuroradiological data are collected, including the following items: demographic characteristics, genetic profile, clinical manifestations, quality of life assessment, among others.

Results: Patient registries can fulfill a number of roles, including collating data regarding disease natural history data, post-marketing surveillance tool and patient quality-of-life register. The International Niemann-Pick Disease Registry (INPDR) contains two linked, but separate, databases, one holding clinician entered data and the other containing patient recorded outcomes (PRO). Data from 236 patients, entered from 6 countries is presently held within the Registry. 74% of the patients entered in the Registry so far have NPC and 26% are diagnosed with ASMD. Most of the patients with NPC (71%) and ASMD (74%) were diagnosed below 12 years of age; in contrast, 15% of ASMD patients and 10% of NPC patients had their diagnosis after 30 years of age.

Conclusions: INPDR is a single, rare disease-specific registry collating Niemann-Pick data on a global basis. It was created by professionals and patients for worldwide use. It collects clinical data and patient reported data with separate datasets for ASMD and NP-C. It will replace the need for multiple registries and offer a single, effective data resource for NPD.

Disclosure: No potential conflict stated.

P06-29

Neuronal Ceroid Lipofuscinosis Type 2: when the “atypical” phenotypes may be the typical ones

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Introduction: Late-infantile neuronal ceroid lipofuscinosis (NCL), also called neuronal ceroid lipofuscinosis type 2 (CLN2), is caused by the deficiency of lysosomal enzyme tripeptidyl peptidase-1 (TPP1) due to mutations in the CLN2 gene and is the most common form of NCL in children. The classic phenotype is late-infantile presenting with language development delay, with its clinical signs usually appearing between the ages of 2 to 4 years with seizures and a rapid decline of psychomotor functions. Most children are bedridden at 5 years and die around the age of 10 years. Nevertheless, atypical phenotypes have been reported in the literature, creating a clinical challenge to avoid diagnosis without significant delay.

Methods: Clinical, biochemical and neuroradiological data retrospective analysis of five CLN2 patients showing atypical/protracted phenotypes

Results: All four patients (3 males; 2 females) showed an atypical late onset phenotype. First symptoms started around 5 – 10 years of age being cerebellar ataxia the most prominent feature. Abnormal findings in brain MRI were found in all patients (cerebellar atrophy and periventricular white matter changes). Seizures were present in three patients, starting after 6 years of age. Cognitive decline was seen in 4 patients and mild learning disabilities in one. TPP1 enzyme was decreased in all patients, although not in the typical range found in “classical” CLN2 patients. Only one patient developed visual loss around 9 years of age.

Discussion: The protracted CLN2 phenotype was previously considered globally rare. In South America, the frequency is approximately 50% of affected individuals. Recently with the recent approval of intraventricular enzyme replacement therapy (ERT) with cerliponase alpha for CLN2 disease, early diagnosis is essential to start treatment before disease progression.

Disclosure: No potential conflict stated.
**P06-30**

**Ethylmalonic Encephalopathy: a rare inborn error of metabolism with a unique constellation of clinical-radiological features**

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**Introduction:** Ethylmalonic encephalopathy (EE) is a rare inborn error of metabolism which affects the brain, gastrointestinal system and peripheral blood vessels and is characterized by a unique constellation of clinical and biochemical features. It is due to a mutation in the ETHE 1 gene, located on chromosome 19 (19q13). Patients with EE exhibit symptoms in neonatal period or infancy mainly from the CNS, such as seizures, hypotonia, dystonic movements and psychomotor regression. In addition, they often manifest hemorrhagic rash, orthostatic acrocyanosis and chronic diarrhea.

**Patients and Methods:** A 12 month old boy presented with seizures, hypotonia, growth retardation, and hemorrhagic rash. Episodes of diarrhea were also reported. EEG was abnormal and suggestive of a metabolic encephalopathy. Brain MRI revealed bilateral and symmetrical atrophy in the fronto-temporal areas and hyperdensities on T2 sequences at the basal ganglia, midbrain,pons, cerebellum and white matter. Urinary organic acid analysis revealed markedly increased excretion of ethylmalonic acid. Acylcarnitine analysis in dried blood spots showed increased butyrylcarnitine. Further course was downhill with the patient exhibiting severe respiratory distress and deterioration of his neurological status. He was admitted to the PICU where intubated; however, despite all necessary actions he succumbed three days later. Results of the mutation analysis of the ETHE1 gene delivered post mortem, demonstrated homozygosity for the mutation p.Glu44fs, confirming the diagnosis of EE at a molecular level.

**Conclusions:** EE although rare is a clinically-recognizable disorder with typical clinical features and no specific therapy up to date. The diagnostic confirmation by molecular studies is very important for the family, since prenatal counseling can be provided timely, thus leading to prevention of further recurrences.

**Disclosure:** No potential conflict stated.

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**P06-31**

**The natural history of renal manifestations in patients with Mitochondrial Disease**

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**Objective:** We aimed to study the renal manifestations in patients with mitochondrial disease and its associated morbidity and mortality. Further, we aimed to identify prognostic biomarkers which help to access the severity of renal manifestations.

**Methods:** In this retrospective study, patients were recruited from eight European centres specialising in mitochondrial disorders; Gothenburg, Rotterdam, Helsinki, Copenhagen, Stockholm, Bergen, Oulu and Barcelona. Detailed clinical, laboratory and genetic data have been collected.

**Results:** Thirty six patients were included. The majority had mt-DNA associated disease (23/36). Median age at onset of mitochondrial disease was two years, while the onset of the renal manifestations was 12 years. Renal involvement was captured on routine laboratory examination in 18 patients, nine of them showing isolated increased creatinine or cystatin C in serum. Hypertension was the first sign in four patients. The majority developed chronic kidney disease, while acute kidney injury was found in seven patients. Sixteen patients developed tubulopathy, predominately Fanconi syndrome (7/16). Acute kidney injury was significantly associated with inferior overall survival. Arterial hypertension and diabetes mellitus were among the most common comorbidities, other than nervous system involvement.

**Conclusion:** Our data showed that there was a clear delay in identification of the renal involvement in patients with mitochondrial disease. In most cases, renal involvement was identified on routine control late in the disease course. It is therefore important to develop a standardized protocol for assessing renal function at an early stage and systematically throughout the disease course.

**Disclosure:** No potential conflict stated.
P06-32

Progressive Demyelinating Neuropathy after hematopoietic cell transplantation in Metachromatic Leukodystrophy: a case series

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Purpose: Metachromatic leukodystrophy (MLD) is a neurometabolic disorder caused by arylsulfatase A (ASA) deficiency, leading to sulfatide accumulation and subsequent demyelination of both central and peripheral nervous system. Hematopoietic cell transplantation (HCT) can provide both clear benefits for asymptomatic and early-symptomatic MLD patients. However, peripheral neuropathy may cause major residual disease burden, despite otherwise successful HCT. This case series illustrates progressive severe peripheral neuropathy after HCT in two patients with the late-infantile and one with the adult form of MLD.

Methods: We performed a retrospective patient record review of three MLD patients who experienced progressive peripheral neuropathy after HCT. Pre-HCT myeloablative conditioning regimen consisted of anti-thymocyte globulin, busulfan and fludarabine, with cyclosporine for prophylaxis of graft-versus-host disease (GVHD).

Results: The three patients had demyelinating polyneuropathy before HCT, performed at the ages of 2 years in two patients and 23 years in one. Progression of peripheral neuropathy after HCT correlated with tapering immunosuppression. Differential diagnoses included disease progression, steroid use, neurological GVHD or an (auto-) inflammatory cause. Laboratory and pathology investigations were not conclusive. In two patients, treatment with distinct immunosuppressive drugs led to partial improvement/stabilization, but not the halt of peripheral neuropathy progression, which in the end became quite debilitating despite immunosuppressive therapy. The third patient showed no response to immunosuppressive treatment. He died ten months post-HCT due to respiratory failure.

Conclusion: The extensive diagnostic and therapeutic attempts highlight the challenge of characterizing progressive peripheral neuropathy after HCT: is it linked to disease progression and MLD subtype, neurological GVHD or an otherwise immune mediated demyelinating process? The three cases described here provide a good starting point for discussion and further research.

Disclosure: No potential conflict stated.

P06-33

Neurodegeneration with Brain Iron Accumulation (NBIA) – Two cases in Bosnia and Herzegovina

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Introduction: Neurodegeneration with brain iron accumulation (NBIA) is a group of inherited neurologic disorders in which iron accumulates in the basal ganglia resulting in progressive dystonia, spasticity, parkinsonism, neuropsychiatric abnormalities, optic atrophy or retinal degeneration. An estimated prevalence of NBIA is 1-3/1 000 000. Brain MRI image shows iron deposits in the basal ganglia, the so-called eye-of-the-tiger sign (T2w GRASE sequence). Clinical findings and molecular genetic testing establish the diagnosis of specific types.

Case reports: We have presented two cases with two different types of NBIA, pantothenate kinase-associated neurodegeneration (PKAN) and mitochondrial membrane protein associated neurodegeneration (MPAN).

The first patient, girl, with PKAN died at the age of 9 years. The brain MRI at the age of 6 years was normal, but at the age of 8 years on brain MRI typical „eye of the tiger sign“ in basal ganglia was present. Molecular genetic analysis has been done out of Bosnia and Herzegovina, due to diagnostic insufficiency and mutation of the PANK2 gene was confirmed.

The second patient, girl at the age of 22 years, has MPAN. The first brain MRI at the age of 8 years was normal, but at the age of 9 years typical „eye of the tiger sign“ in basal ganglia was present. She is now wheel chaired. Molecular genetic testing has been done also out of Bosnia and Herzegovina and mitochondrial membrane protein associated neurodegeneration, with biallelic pathogenic variants in C19orf12 (MMIN gene) was confirmed.

Conclusion: Clinical course and brain MRI follow up may help in the diagnostic process of NBIA. In the countries with limited resources genetic testing is not available, so final diagnosis is rather postponed.

Disclosure: No potential conflict stated.
Delays in diagnosis are associated with poor clinical outcomes in patients with Arginase 1 deficiency

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Introduction: Arginase 1 Deficiency (ARG1-D) is an inherited metabolic disease with elevated plasma arginine and prominent neurological manifestations (spasticity, seizures, and intellectual disability). Although diagnostic testing by plasma arginine is widely available, the variable presentation and rarity of the condition may lead to delayed or mis-diagnosis. Given the known impact of plasma arginine reduction with diet and recent therapeutic advances, prompt diagnosis is important in optimizing patient outcomes. The aim of this study was to review the clinical presentation of patients with ARG1-D, including the magnitude of delay in diagnosis.


Results: Lower limb spasticity was present in 84% of 117 patients. Intellectual disability was noted in 82% of 97 patients with available data and was moderate or severe in 39% of them. Seizures and upper limb spasticity were present in 70% and 50% of patients respectively and 56% had failure to thrive. Maximal plasma arginine exceeded 4.5x ULN (n=112, ULN=115µM) in >50% of patients. Despite disease management, arginine values remained elevated beyond 200 µM in most patients (n=33). Median age at presentation was 2 years (n=81). Delays in diagnosis by ≥2 years were reported in 39% of patients and by ≥5 years in 24% of patients; median age at death was 17 (n=20).

Conclusions: ARG1-D presents with prominent neurological manifestations with significant delays in time to diagnosis. Patients are at risk of progression to develop more severe complications with early mortality. Plasma amino acid analysis to assess arginine levels in patients presenting with spasticity, seizures and cognitive impairment lead to early diagnosis and interventions that reduce morbidity and mortality risk in this patient population.

Disclosure: No potential conflict stated.

Difficulties in the differential diagnosis of convulsions in Spinal Dysraphies: a clinical case

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Introduction: Spina bifida is a formidable congenital condition in which a hernial protrusion is formed; types range from a simple defect in 1 or more vertebral arches (spina bifida occulta) to myelomeningocele (spina bifida cystica). The frequency of spina bifida ranges from 1 to 2 per 1000 newborns.

Clinical Case: Boy, 6 years 10 months old, entered in ICU into City Children’s Hospital No. 2, Astana with complaints on apnea, blueing, convulsions and hyporesalivation. At the age of 6 days of life, he was operated for correction of Spina bifida. Examination: Spina bifida lumbar spine. Lower flaccid paraparesis. Paresis of nervous facialis. Congenital dislocation of the hips; neurogenic bladder; convergent strabismus. MRI: Arnold-Kiyari malformation type 2. Surgery was performed to decompress the brainstem. In the postoperative period- the positive dynamics.

Discussion: Thus, the case presents the congenital malformations of the central nervous system spina bifida with the development of Arnold-Chiari syndrome with the median medulla oblongata. Rehabilitation of such children may accompanied by complications for periods of prolonged apnea or cardiac arrhythmias, which can lead to sudden death due to brain stem compression. Convulsive syndrome does not require standard anticonvulsant therapy, as apnea is not a cortical origin but situationally induced. As a result, their resolution occurs after decompression of the brain stem.

Disclosure: No potential conflict stated.
**P07-02**

**Magnetic Resonance Spectroscopy (MRS) in Neonatal Hypoxic Ischaemic Encephalopathy (HIE)**

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**Introduction:** HIE affects around 1.5/1000 live births. Prognostication relies on clinical progress, neurophysiology, neurological examination, and Magnetic Resonance Imaging (MRI). There is limited information on the relationships between MRS brain results and visual appearances of the brain on MRI and clinical features. This work studied the use of MRS in this cohort.

**Methods:** MRS is used routinely in all neonates with HIE in our unit, so approval for this service evaluation was obtained from our Clinical Governance Department. We identified neonates with HIE between Jan 2010 and March 2016 who had MRI and MRS in the first 7 days of life. Medical notes were reviewed and MRI results categorised as normal or abnormal. MRS results and clinical features were compared between MRI groups using parametric or non-parametric testing. Correlation and regression analyses studied relationships between clinical features and MRS results. P values of <0.05 were assumed to be significant.

**Results:** 76 participants were identified, 20 were excluded because they did not meet our inclusion criteria. Data from a total number of 57 neonates were analysed using R studio. Babies with abnormal MRI scans had higher levels of lactate in their basal ganglia (p=0.03) and parieto-occipital white matter (p=0.01), and higher levels of N-acetylaspartate in the parieto-occipital white matter (p=0.008). Multiple linear regression showed the following variables contributed significantly to the MRS results: Apgar scores, cord gases, Sarnat score and the highest lactate recorded.

**Conclusion:** This study demonstrated that abnormal MR spectroscopy markers, particularly those including lactate, differ in neonates with normal and abnormal standard MRI, and were associated with a number of clinical features.

**Disclosure:** No potential conflict stated.

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**P07-03**

**Application of ketogenic diet to alleviate symptoms of Autism in children – Case series**

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**Introduction:** Ketogenic diet (KD) has been applied successfully for over 100 years to treat epilepsy. In many countries there are guidelines determining the obligatory place of KD in drug-resistant epilepsy treatment. Recently, there is accumulating evidence of possible efficacy of the KD in the treatment of autism spectrum disorders (ASD). The aim of the study is to present a history of three consecutive children with ASD successfully treated with KD.

**Case reports:** We observed for 12 months, 3 children (2M, 1F) in the mean age of 4.5 years with mean CARS score of 45 and mean IQ=70 treated with the application of classical KD slowly liberalising the dietetic regime towards LGIT (low-glycaemic index diet) but still maintaining the ketosis. All 3 children had severe glucose metabolism alterations detected in a non-invasive positron emission tomography (PET) with 18 fluoro-deoxyglucose (18FDG PET) examination. At 3, 6 and 12 months we observed significant improvement in behavior and intellect of all the children by mean decrease of CARS score by 12 points and increase of IQ by 12. Main improvements were observed in speech and the reduction of hyperactivity. Along with clinical improvements in children behavior, parallel changes in 18 FDC-PET occurred.

**Conclusion:** KD is extremely promising therapy to alleviate symptoms of autism, especially in the subgroup of patients with brain glucose hypometabolism detected in 18 FDG PET.

**Disclosure:** No potential conflict stated.
**P07-04**

**Progression of neurophysiological changes in a child with Subacute Sclerosing Panencephalitis**

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**Introduction:** Subacute sclerosing panencephalitis (SSPE) is classically associated with characteristic electroencephalogram (EEG) features of periodic and stereotyped high-voltage discharges. We present the electroclinical evolution in a case where these changes were not initially evident.

**Methods and Results:** The patient is a fully immunized seven-year old boy with a six-month history of increasingly frequent atonic drops with behavioural change and cognitive decline. His initial EEG showed continuous high amplitude 1-2 Hz sharp and slow wave activity, which were frontally dominant with little change on midazolam infusion. Eight days later, the EEG had a diffusely slow background with anterior sharp waves in a periodic/semi-periodic fashion, with complexes every 1-2 seconds.

A rapid neurocognitive decline ensued, characterised by fluctuating consciousness, visual impairment, aphasia and dystonia, rendering him non-ambulant within weeks of hospital admission. The EEG evolved with a diffusely slow background with no periodic sharp waves, except occasionally in the temporal regions. MRI brain showed asymmetrical T2-weighted signal change in sub-cortical and deep white matter. Serial imaging demonstrated increasing widespread signal abnormality. SSPE was confirmed by CSF measles PCR. His EEG at ten weeks progressed to typical periodic sharp and slow wave complexes, occurring every 6-7 seconds.

**Conclusion:** The clinical course and EEG add weight to the growing body of evidence of SSPE occurring in a younger than expected cohort across Europe. SSPE is a neurodegenerative disorder where early illness is known to have higher association with development of sequelae. At a time when vaccination uptake is at an all-time low, increased awareness of the burden of measles is crucial to facilitate improved vaccination uptake worldwide. SSPE should be considered in any child presenting with regression and seizures even if the EEG and neuroimaging are not initially supportive.

**Disclosure:** No potential conflict stated.

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**P07-05**

**Alternating Hemiplegia of childhood – 17 years follow-up and genetic testing**

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**Introduction:** AHC is a rare disease with recurrent episodes of temporary paralysis, affecting one side of the body.

**Methods:** The course of AHC diagnosed clinically 17 years ago is presented.

**Results:** 13 months old girl with slightly delayed development started to have daily episodes of one-sided weakness with dystonia and tremor, eyes and head deviation, irregular breathing without loss of consciousness, lasting 30min-2h. The episodes made her suffer and cry. Sleep usually helped, paroxysms never happened just after awakening. Exercises, unexpected stimuli, emotional factors, hot bath usually provoked episodes. Interictal EEG was non-epileptic. MRI did not show any abnormalities. Benzodiazepines reduced the frequency of events temporary. The girl was put on Flunarizine. She was admitted to our department for re-evaluation of the diagnosis several times. Her symptoms always were the same. Now she is 18 years old. During interictal periods she walks independently, but the gait is ataxic, she can speak. She has cognitive defect and needs individual care. Dystonic episodes happen 1-3 times per week, during them the girl cannot move neither speak. Sometimes diazepam is needed.

Sequence analysis and deletion/duplication testing of the 181 genes (Invitae Epilepsy Panel) had been performed during her last follow-up visit. A variant, c.2415C>G (p.Asp805Glu), heterozygous was identified in ATP1A3, Exon 17. This variant has been observed before in individuals affected with AHC (PMID: 24523486). Parental testing had been also performed. Videos of events at different age will be presented.

**Conclusion:** AHC is a differential diagnosis of epilepsy. AHC significantly worsens quality of life of the patient and the family. In our case medication were of poor help. Genetic testing is crucial for understanding the condition by family and prognosis.

**Disclosure:** No potential conflict stated.
Clinical and radiological features of Myelitis associated with Non-Polio Enterovirus Infections in the Western Cape Province of South Africa

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Introduction: With the eradication of poliomyelitis, reports of cases of acute flaccid paralysis due to other non-polio enteroviruses are on the rise, globally. Outbreaks of enterovirus 71 and D68 have been reported in the literature in the past decade. The spectrum of neurological disease affects the whole or variable parts of the neuraxis. Here we describe the clinical and radiological features of myelitis associated with non-polio enterovirus infections in our institution.

Methods: A retrospective analysis of the paediatric neurology database of patients seen at the Red Cross War Memorial Children’s Hospital. The case records of all patients admitted with acute flaccid paralysis and radiological myelitis from February 2012 to February 2019 were reviewed. Demographic, clinical, laboratory and neuroimaging data were analysed.

Results: An average of 3-6 patients per year presented paralysis and myelitis, in keeping with enteroviral disease. There were distinct patterns of involvement of the spinal cord with or without involvement of the brainstem and spinal roots. Acute flaccid paralysis with bulbo-respiratory weakness, requiring paediatric intensive care management was frequently seen. Some cases with brainstem involvement presented in precipitous shock, not explained by either sepsis or hypovolaemia. Neuroimaging with classical dorsal brainstem and anterior cord grey matter involvement was seen. More than 90% had preceding respiratory or diarrhoeal illness. Non-polio enteroviruses were isolated in stool or respiratory secretions in the majority. Residual paralysis was found in survivors.

Conclusion: Besides Guillain Barre’ syndrome, enteroviral myelitis, with or without radiculitis, is the most common cause of acute flaccid paralysis in our institution. The clinical and neuroimaging features are similar to poliomyelitis. Non-polio enteroviruses are beginning to replace poliomyelitis as a cause of acute flaccid paralysis with serious neurological morbidity globally.

Disclosure: No potential conflict stated.
**Approaches to utilising simulation-based-education in Paediatric Neurology training**

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**Introduction:** Simulation-Based-Education (SBE) is becoming increasingly used in Paediatric medical education. It provides a safe learning environment in a time of limited training hours and complex rotas which potentially limit exposure to crucial topics (Cleriheu, 2016). It is a useful tool in the teaching of human factors and rehearsal of non-technical skills. This could involve high- or low-fidelity manikins, or simulated patients. Despite concerns including difficulties demonstrating nuances of neurological examination findings SBE has previously been used successfully in neurology teaching in this way (Ermak et al. 2013, Gaitrey et al. 2017)

**Simulation:** We have facilitated bi-weekly teaching sessions for Paediatric doctors, nurses and Emergency Department staff. Scenarios have included febrile seizures, status epilepticus and raised intra-cranial pressure amongst other Paediatric emergencies in the curriculum. Alongside this there are regular courses for registrar level doctors which incorporate managing a range of conditions, as well as twice yearly regional teaching days for new Paediatric trainees.

Both Likert-scale and free-text feedback has been extremely positive, highlighting learning outcomes including the need for anticipation of upcoming management steps and communication among teams. Many trainees reported having not encountered the scenarios frequently in ‘real-life’ – supporting the need for the opportunity to rehearse these skills.

**Conclusion:** SBE may aid in the teaching of many topics in Paediatric neurology. This may improve management via reinforcement of human factors, i.e. anticipation of required medications during status epilepticus. There may even be scope to utilise SBE for more complex neurological scenarios and communication events, for example for higher specialty trainees in Paediatric neurology, and in novel ways to teach other relevant skills such as ultrasound guided lumbar puncture via task trainers.

**Disclosure:** No potential conflict stated.

**Herpes Simplex Virus-1 as a rare aetiology of Isolated Acute Cerebellitis**

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**Introduction:** Acute cerebellitis is one of the most common cerebellar disorders and occurs due to para-infectious, post-infectious, or post-vaccination cerebellar inflammation. Cerebellar involvement of HSV-1 is rare and almost always associated with meningoencephalitis. To date, HSV-1 has been identified as the cause of acute isolated cerebellitis in only two patients. Here we report another case of isolated acute cerebellitis caused by HSV-1.

**Methods:** A 20-month-old boy presented with moderate fever and inability to walk beginning 4 days before admission to our hospital. Neurologic examination revealed normal mental status but hypotonia, ataxia, truncal titubation, and nystagmus. Cranial MRI showed T2-weighted hyperintensities of the cerebellum consistent with cerebellitis. Examination of cerebrospinal fluid (CSF) showed mild pleocytosis and protein elevation. Treatment with intravenous immunoglobulin (1 g/kg/day for two days) was started on day 5 of symptoms, day 1 of hospitalization. Significant clinical recovery was observed, with marked improvement in truncal titubation and ataxia. CSF cultures were bacteriologically sterile. Herpes simplex virus-1 DNA was detected in CSF. After two weeks of treatment with acyclovir, PCR analysis of the second CSF sample was negative for HSV-1 DNA.

**Results:** He received acyclovir treatment for 21 days and was discharged with a wide-based ataxic gait. After 1 year of follow-up with physical therapy, he walks independently with a wide-based gait and has poor fine motor coordination. Follow-up MRI at 1 year showed cerebellar atrophy.

**Conclusion:** Acute cerebellitis is rarely seen in pediatric patients. Although HSV-1 is an uncommon cause, it should be considered during etiological investigation of patients with acute cerebellitis.

**Disclosure:** No potential conflict stated.
P07-10

4-year-old girl with Horizontal Gaze Palsy with Progressive Scoliosis (HGPPS): investigation with MRI Imaging including DTI Tractography Sequence

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Introduction: HGPPS (Horizontal gaze palsy with progressive scoliosis) is a rare autosomal recessive disorder, characterized by congenital absence of conjugate horizontal eye movements, preservation of vertical gaze and convergence, and progressive scoliosis. MRI diagnostic key features consists of: 1) reduced volume of pons with midline cleavage at the tegmentum (split pons sign), 2) hypoplastic medulla oblongata with a butterfly or rhomboid configuration, 2) absence of facial colliculi with subsequent tent shaped fourth ventricular floor 3) lack of prominence of the gracile and cuneate nuclei on the posterior aspect of the medulla, 4) scoliosis. GPPS is caused by mutations in ROBO3 gene that is related to cell migration, decussation of pyramids and hindbrain formation. Maldevelopment of hindbrain structures suggests an explanation to imaging and clinical features.

Method: Investigation of a patient with clinical signs of HGPPS with MRI and DTI tractography.

Results: A 4 years old girl, born at term to healthy nonconsanguineous parents after an uneventful pregnancy, was noted to have conjugate horizontal eye movement limitation with preservation of vertical gaze since the age of 4 months. At clinical examination dextroscoliosis was observed. MRI imaging with DTI tractography revealed: 1) fourth ventricular floor was tent shaped due to absence facial colliculi, 2) hypoplastic pons and medulla, 3) split pons sign, 4) absence of decussation of pyramids, 4) medulla oblongata with a butterfly formation, 5) cerebral peduncle atrophy, 6) dextroscoliosis.

Conclusion: Clinical signs in combination with imaging features establish the diagnosis of HGPPS. Further investigation includes ROBO3 sequencing. Therapeutic goal is the proactive intervention for scoliosis.

Disclosure: No potential conflict stated.

P07-11

A follow-up study of clinical characteristics, disease course, disability, quality of life and psychological difficulties in children and adolescents with Migraine

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Objective: The aim of the study was to determine the association between the headache frequency, severity, and course with disability and quality of life (QOL) in children and adolescents with migraine.

Methods: Fifty children and adolescents with migraine aged 7-17.5 years were followed-up for six months. The Pediatric Migraine Disability Assessment tool – PedMIDAS and KIDSCREEN-27 were used.

Results: The PedMIDAS score highly correlated with the number of headaches in the month before the assessment (p < 0.01). Magnesium prophylaxis in 32 subjects led to a statistically significant decrease in numbers of headaches (F (df) = 28.99 (1.15), p <0.01). In relation to the first estimate, after six months of monitoring, a significant reduction in PedMIDAS scores (F (df, dferror) = 11.10 (1.63, 50.49), p <0.001) was registered. Considering the KIDSCREEN-27, scores for physical and psychological well-being and social support domain significantly increased from baseline to end-point (p ≤ 0.01).

Conclusion: The headache frequency was the only consistent factor that significantly affected the disability due to migraine and QOL. The prophylactic use of magnesium led to a decrease in the headache frequency, degree of disability and improvement in some QOL domains.

Disclosure: No potential conflict stated.
P07-12  
Quality-of-life evaluation of healthy siblings of children with Cerebral Palsy and Epilepsy

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Background: Chronic childhood illness can cause changes in the health-related quality of life (HrQoL) of the individual’s family members. This study aimed to evaluate the HrQoL among healthy siblings of children with cerebral palsy (CP) and epilepsy.

Method: We administered the Pediatric Quality of Life Inventory questionnaire to healthy siblings of 60 children with CP and epilepsy, and siblings of 100 healthy children. The physical health, psychosocial health and total QoL scores were calculated using individual sibling and parent responses.

Results: According to the self-reports of healthy siblings, the psychosocial health scores were lower in the CP group comparing to controls (p<.05). Total QoL scores were also lower in the CP group than the controls (p<.05). According to the parent reports, the psychosocial health score and total QoL score were lower among the CP and epilepsy groups than the controls (p<.01). According to self-reports of healthy siblings, the global impact on HrQoL for CP and epilepsy groups were significantly higher than the controls (42.1% and 30.7% vs. 14.1%; p<0.05). According to the parent reports, the global impact on the HrQoL for CP and epilepsy groups were significantly higher than the controls (26.9% and 14.7% vs. 0%; p<0.01).

Conclusion: In healthy siblings of children with CP and epilepsy, we observed a global impact on the HrQoL, especially in CP group and for psychosocial scores, and a low level of parental awareness about this situation. This might increase the risk of emotional neglect and abuse in these children and special support programs are needed for these families.

Disclosure: No potential conflict stated.

P07-13  
Arachnoid Cyst in children: the relationship of clinical features and neuroanatomical location

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Background: Arachnoid cysts is defined as the most common congenital lesion of the brain and are often an incidental finding. This study aimed to evaluate the relationship of clinical features and neuroanatomical location in children with arachnoid cyst.

Method: In this study, the clinical and radiological features of pediatric patients with arachnoid cysts were investigated retrospectively between 2010 and 2017.

Results: A total of 5360 patients aged between 1 month - 18 years underwent brain neuroimaging. Arachnoid cyst was detected in 309 children and the prevalence of arachnoid cyst was found to be 5.7%. The male / female ratio was 2:1. Headache was the most common indication for neuroimaging. Most of the arachnoid cysts were located in the middle fossa. The cyst was on left hemisphere in 54.7% and bilateral in 20.4% of children. The mean size of cyst was larger in children with positive findings in neurological examination. In children with epilepsy, the size of cyst was larger than in children presented with headache. During follow up the size of cyst increased in 9% and only 12.9% of children were operated, mostly located in the posterior fossa. Two children died because of complications of surgery.

Conclusion: The result of present study showed that arachnoid cysts are common intracranial lesions in children. The size of cyst might change according to the presenting compliant of patient. Patients must be followed up.

Disclosure: No potential conflict stated.
P07-14

The clinical profile and outcome of children with Tuberous Sclerosis in Durban South Africa

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Objective: To determine the clinical profile and outcome of children diagnosed with Tuberous Sclerosis in Durban, South Africa. Neurodevelopment, behaviour, seizures and clinical signs were assessed at the initial and the last clinic visit. The pharmacological management of the children was also reviewed.

Methods: A retrospective chart audit of patients diagnosed with Tuberous Sclerosis between January 2003 and December 2018 at Inkosi Albert Luthuli Hospital a quaternary hospital in Durban, South Africa was done.

Results: 27 patients were diagnosed with TSC. 19 (70.4%) were males and 8 (29.6%) were female. The median age was 5 years with an interquartile range of 7.5 years. 66.7% (N=18) had generalised tonic-clonic seizures and only one patient had infantile spasms. 2 patients did not have seizures at presentation. 26% (n=7) had hemiplegia with 6 out of the 7 patients being right sided. 7 patients had aphasia and 6 patients (60%) presented with associated abnormal neuro-behaviour. Sodium Valproate was used in 81.5% of the patients and Vigebratin was used in the patient with infantile spasms. 2 patients had renal angiomyolipomas and 6 (22%) had cardiac rhabdomyomas.

Conclusion: Most the patients from our regional population had aphasia, abnormal neuro-behaviour with hemiplegia on follow up. Majority of patients had seizure remission. mTOR inhibitors should be strongly considered in view of the poor clinical outcome and SEGAs noted in this population.

Disclosure: No potential conflict stated.

P07-15

Recurrent Hemiplegic Migraine induced by Exertion: a singular presentation of en Coup de Sabre Sclerodermia

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Introduction: Localised scleroderma en coup de sabre (ECS) is a rare disorder of unknown etiology characterized by band-like fibrotic lesion over the frontoparietal area. Neurological involvement is rare, however there is growing evidence for associated autoimmune dysfunction.

Case Report: Fifteen-year-old girl diagnosed with ECS at 6 years of age, involving the left frontoparietal region. At thirteen, she presented right hemibody seizures, which were easily controlled with levetiracetam. MRI revealed multiple left subcortical T2/FLAIR hyperintense lesions. AngioMRI and angioCT were normal. CSF analysis showed lymphocytic pleocytosis (18 cells/mm3) and IgG oligoclonal bands. In the following year, recurrent episodes of left hemiparesis progressively evolving to severe migraine lasted for 1-2 days and reverted with intravenous analgesics and methylprednisolone. Each event was invariably preceded by moderate physical exertion like walking long distances. Video-EEG monitoring of these events was unremarkable. Repeat MRI disclosed prominent extension of the lesions. Due to neurological progression, immunosuppressive treatment with methotrexate combined with oral prednisolone was started. However, prolonged and abundant relapses occurred in several attempts to reduce or discontinue corticosteroids. Methotrexate was then switched cyclophosphamide. The patient remains stationary clinical and radiologically. She presents cognitive deterioration in school performance.

Conclusions: We report a case of ECS with a singular presentation of exertion-induced hemiplegic migraine with an explosive progression. Therapeutic guidelines for this condition are currently not available in literature, being of major importance in future management of these patients.

Disclosure: No potential conflict stated.
**Meningococcal Septicaemia presenting as Acute Brachial Plexus Neuritis**

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**Introduction:** Isolated acute brachial plexus neuritis is rare in children/young people. We report for the first time to our knowledge, a child with meningococcal sepsis presenting with brachial neuritis.

**Method:** We describe an unusual clinical presentation of a 15-year old boy with symptoms of acute brachial neuritis as the first presentation of meningococcal septicaemia.

**Results/Case Presentation:** A previously well left-handed 15-year old boy presented with sudden onset right arm pain and swelling. Several hours later, he developed fever, headache, vomiting and a non-blanching rash. This was treated as meningococcal septicaemia with intravenous antibiotics and fluid resuscitation. Blood cultures confirmed Neisseria meningitidis serotype B. He recovered systemically within 24 hours. Right shoulder area/upper arm swelling persisted. Right arm motor weakness, pain and burning sensation became increasingly problematic, requiring intensive pain relief. Neurological examination revealed motor impairment on the right side involving the myotomes from C4 to T1, consistent with brachial plexus distribution. Sensation was impaired over the right C6 dermatome with hyperesthesia, impaired temperature sensation and burning sensation. The remainder of the neurological examination was normal. MRI of the right brachial plexus region showed inflammation in the right supraclavicular region, as well as thickening and enhancement involving the right brachial plexus trunks. He was treated with a 4-week oral prednisolone course after antibiotics. He needed ongoing pain management and physical therapy. At 2-month follow up, he had significant improvement in motor ability with minimal residual weakness and sensation impairment.

**Conclusion:** Acute brachial neuritis is a rare inflammatory complication of meningococcal septicaemia. Prognosis is variable, therefore guarded. Further data is needed to explore the efficacy of steroids in management.

**Disclosure:** No potential conflict stated.

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**Unilateral Facial Erythema following food chewing**

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**Statement of the Problem:** A 3 yrs old girl presented with unilateral facial erythema and sweating after gustatory stimuli. She had history of mycoplasma and Brucella infection.

**Methods and Results:** She developed left facial palsy that has been resolved. She received antibiotics and corticosteroids. CT scan and MRI brain were normal. Interestingly, the child fulfilled the clinical diagnosis of Frey syndrome. Frey’s syndrome is characterized by unilateral sweating and flushing of the skin in the area of the parotid gland, occurring during meal, or on salivary stimulation. It is a common complication following surgery/injury in the parotid gland region/temporomandibular joint surgery; however, very few cases had been reported following herpetic infection. The condition may be misdiagnosed as contact dermatitis or food allergy, but these can be excluded by the normal skin texture and typical unilateral distribution on the pre-auricular area and cheek. The diagnosis is made on clinical grounds, and further testing is not needed. It is important for the clinician to recognize its unusual symptoms as early as possible to prevent its potential negative social and psychological effect on the patient. Mycoplasma infection, as in this case, is a rare cause of Frey’s syndrome. Here we highlight the importance of considering Frey syndrome in these cases as Patients can be reassured of the benign nature of the condition and that symptoms usually resolve spontaneously in children.

**Disclosure:** No potential conflict stated.
P07-18

Acute Ataxia in children: common causes and yield of diagnostic work-up in the post-Varicella vaccine era

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Abstract: Objective: To identify the most common causes of acute ataxia in children in the era of post-varicella vaccination, and the diagnostic yield of commonly used diagnostic work-up.

Methods: This retrospective study reviewed the medical records of children who presented with ataxia of less than 72 hours’ duration, over the last 12 years. Associated signs and symptoms, laboratory, EEG and neuroimaging studies, final diagnosis and clinical findings at discharge and during follow-up were studied.

Results: A total of 58 patients (35 boys, 23 girls), mean age 4.9±3.8 years, were enrolled. The most common etiology of acute ataxia in our study was post-infectious acute cerebellar ataxia (50%). These children were significantly young (3.6±3.1 vs. 6.2±4.1 years, p=0.01) and 86% were younger than 5 years of age. In these children, extra cerebellar neurological signs were absent. The abnormality yield of work-up studies performed in our cohort was 39% for lumbar puncture, 36% for EEG, 7% for CT scan and 14% for MRI.

Conclusions: Post-infectious acute cerebellar ataxia remains the most common cause of acute ataxia in children. Although lumbar puncture and neuroimaging should be considered in all children with acute cerebellar ataxia, younger children with a history of previous viral illness and no extra cerebellar signs and symptoms may benefit from watchful waiting.

Disclosure: No potential conflict stated.

P07-19

Cosyntropin mediates Melanocortin Microglial Inflammation and improves outcomes in rodent TBI

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Objective: Traumatic brain injury (TBI) is a leading cause of mortality and morbidity and is associated with chronic neuroinflammation. Melanocortin receptor (MCR1–5) agonists (e.g., ACTH or adrenocorticotropic hormone) that target MC3R/4R ameliorate central and peripheral neuroinflammatory responses and provide a novel therapeutic approach. In this study, we examined the role of Cosyntropin (synthetic ACTH) in reducing microglial activation in a rodent TBI model.

Methods: We used a controlled cortical impact TBI model in adult Sprague-Dawley rats, randomized to 4 groups: sham, sham-cosyntropin, CCI-vehicle, and CCI-Cosyntropin. Subcutaneous (SC) injections were given 30 minutes after CCI (every 12 hours for 7 days following injury). Cosyntropin (120U/kg/day) was supplied by West Therapeutic Development (Grayslake, IL). We examined the effect of Cosyntropin (synthetic ACTH) administration on microglial activation through quantification of microglia morphology. Sectioned brains were immunostained (Iba1) and visualized with diaminobenzidine. Image processing and quantification were conducted with FIJI and FracLac for ImageJ resulting in 15 morphological values/cell. Parameters included cell area, fractal dimension, circularity, and cell perimeter and density.

Results: CCI animals exhibited increased microglia in the lesion site with no difference in cell count between vehicle and treated. Microglia from CCI animals exhibited no change in cell area, decreased cell perimeter and increased density and circularity compared to sham animals. Cosyntropin treatment altered CCI-induced microglia changes in cell area, cell perimeter, and cell density.

Conclusions: Cosyntropin-treated CCI animals showed reduced morphological changes in microglia suggesting a reduced activation state. Decreased activation may decrease long-term deleterious neuroinflammatory effects and may be mediated by Cosyntropin effects on melanocortin receptor signaling.

Disclosure: No potential conflict stated.
P07-20

Critical role for the thalamus, corpus callosum and basal ganglia in paediatric TBI: results of a longitudinal imaging study

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Objective: MR spectroscopic imaging and DTI are useful in assessing injury location/severity after TBI to predict neuro-psychological (NP) outcomes. Attention has focused on the thalamus, corpus callosum and basal ganglia as mediators of cognitive impairments because of their role in brain connectivity. We correlated acute/long-term imaging with 12 mo. NP data.

Methods: We examined 63 mod/sev TBI (6-17d and 1yr) and 64 controls with 3D proton MRSI (NAA/Cr et al) from 7 regions (BG, ant/post CC, frontal, parietal, temporal white matter, thal). A subset (30 mod/sev TBI; 38 controls) were imaged with DTI (FA/MD/AD/RD). Measures of memory, attention, FSIQ/PIQ were done at 3mos and 1yr.

Results: In mod-TBI, metabolites normalized to control levels at 12 mos. DTI initially showed decreased FA and increased MD/AD/RD that increased regionally at 12 mos. In sev-TBI, early reduced NAA/Cr was seen in most regions and remained reduced subcortically (TH/CC) at 12 mos. FA/MD/AD/RD showed changes in sev-TBI in most regions at 12 mos but few changes initially. Acutely, in sev-TBI, reductions in NAA/Cr, FA/AD from all regions correlated with 12 mo. memory deficits, FSIQ, and PIQ; only a reduction in BG NAA/Cr correlated with 12 mo. memory in mod-TBI. Early reduced NAA/Cr from BG/TH/CC strongly correlated with 12 mo. DTI in multiple white matter regions.

Conclusions: Early NAA reductions in TH/CC/BG that persisted suggest that early and prolonged metabolic dysfunction contribute to long-term white matter axonal abnormalities. As mitochondria play a role in regulating NAA synthesis and neuronal metabolism, our findings suggest that mitochondrial dysfunction in central brain structures may be a pivotal abnormality as they are major hubs for many brain networks.

Disclosure: No potential conflict stated.

P07-21

A paediatric case of Lyme Neuroborreliosis presenting with abdominal Radiculitis

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Introduction: Lyme disease is a tick-borne infection with a wide spectrum of clinical manifestations. The most common presentation of Lyme neuroborreliosis in European children is facial nerve palsy and lymphocytic meningitis.

Methods: A 10-year-old male was referred to our department with a 1-year history of abdominal pain, anorexia and poor scholar performance. He first presented severe continuous abdominal pain. A computed tomography (CT) scan of the abdomen, a gastroscopy and a colonoscopy were performed but no abnormalities were revealed. After 2 months the pain gradually remitted. Subsequently he presented loss of appetite and loss of attention. The physical examination was unremarkable. Magnetic Resonance Imaging (MRI) showed leptomeningeal, cranial nerves and cauda equina contrast enhancement. A lumbar puncture was performed and a lymphocytic pleocytosis with increased cerebro-spinal-fluid (CSF) protein level and hypoglicorrachia were found. Lyme neuroborreliosis was considered and specific antibodies against Borrelia were positive in both serum and CSF.

Results: Intravenous ceftriaxone treatment 3 gr daily was given for 21 days. 8 weeks later a lumbar puncture was performed showing normalised cell count and reduction of protein concentration in the CSF. MRI was repeated revealing a remarkable improvement. At the follow-up, 10 weeks after the end of the treatment, the patient gradually regained appetite and a slight improvement of the attention was observed.

Conclusion: The early clinical symptoms of Lyme neuroborreliosis may be nonspecific and can point to a wide spectrum of disease. Although extremely rare in children, abdominal pain due to radiculitis could be the starting symptom of the infection.

Disclosure: No potential conflict stated.
Scurvy. An autistic boy refuses to walk: the comeback of an ancient disease

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Introduction: A severe vitamin C (ascorbic acid) deficiency, also known as scurvy, is relatively unknown in developed countries. This disease has a heterogeneous presentation including fatigue, malaise, bleeding gums, petechiae/purpura, and musculoskeletal symptoms.

Methods: We describe a 3 year old boy presenting with an inability to walk or stand, without previous trauma. In the past, he was diagnosed with autism spectrum disorder. Clinically, he had normal tendon reflexes and a subtle symmetrical muscle weakness of the lower limbs (4/5). There was an anal fissure, severe obstipation and a sacral hematoma. Due to the unexplained hematoma, anal fissure and unexplained neurologic presentation, we suspected child abuse.

Results: Complet blood count, electrolytes, creatine kinase and markers of inflammation were checked. Only the sedimentation rate was elevated (40 mm/h). An inflammatory or auto-immune disease had to be excluded. The analysis of liquor was negative, including antibodies against Mycoplasma, Epstein Barr, Cytomegalovirus and Borrelia. Antiganglioside and paraneoplastic antibodies were negative. MRI of the brain and spine showed a subacute subdural hematoma. Radiograph evaluation showed multiple non-traumatic fractures and a hypodensity located on the metaphysis of multiple bones, which has been described as the Frankel line. A bone scintigraphy showed no lesions. Metabolic screening showed severe vitamin C deficiency (<0.5mg/dl).

Food intake was evaluated, showing a very restrictive eating pattern (as part of his autistic behavior) consisting out of chocolate milk and white bread with chocolate spread. Substitution of vitamin C was started. We observed a rapid recuperation of his muscle tone and he regain the ability to walk within 2 weeks.

Conclusion: Vitamin C deficiency (or scurvy) has to be considered in children with a restrictive eating pattern and unexplained neurological and gastrointestinal symptoms.

Disclosure: No potential conflict stated.

Critical illness Polyneuropathy and Myopathy in children: case reports and literature review

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Background: Critical illness polyneuropathy (CIP) and myopathy (CIM) occurs approximately one-third of adult patients who require intensive care treatment and impair the short and long term outcome. One prospective-based study of critically ill children reported that the incidence of the CIP/CIM was much lower (1.7%) than adults (20 to 76%).

Aim: To elucidate etiology and mechanism, we report two pediatric cases of CIP/CIM and review the medical literature.

Case 1: A 6-year-old girl with rhabdomyolysis induced by viral infection developed severe circulatory failure, and was admitted to the intensive care unit (ICU) in our hospital. On the convalescent phase, she exhibited weakness with her limbs, without complications of consciousness level or cranial nerves' dysfunction. Nerve conduction study revealed that she had severe axonopathy especially in her lower extremities.

Case 2: A 12-year-old boy with myocarditis developed severe circulatory failure. He was admitted to the ICU, requiring mechanical ventilation. He exhibited weakness of his four limbs, and the consciousness level and facial muscles were spared during the recovery period. The nerve conduction study showed axonal dysfunction and/or myopathy in the upper and lower extremities.

Conclusion: The two cases developed severe circulatory failure in their acute phase, and required the intensive care including hemodialysis, extracorporeal membrane oxygenation (ECMO), mechanical ventilation, intravenous steroid pulse therapy and high-dose intravenous immunoglobulin. We noticed their muscle weakness during the recovery period, and the nerve conduction study was useful for the diagnosis. Though CIP/CIM is relatively rare in children, we need to pay attention to axonal neuronal damage as a sequel of severely critical illness.

Disclosure: No potential conflict stated.
Scoliosis in children and young people with Ataxia Telangiectasia (A-T)

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Background: Ataxia Telangiectasia is a rare, life-shortening, autosomal recessive, multisystem disease caused by mutations in ATM. Scoliosis has occasionally been observed in children attending the UK national A-T clinic.

Aim: To identify factors leading to scoliosis, the effects of scoliosis on the progression of other impairments in A-T, and the management outcomes including referral to spinal teams.

Methods: Retrospective clinical data was reviewed from 2011 to 2017.

Results: 34/98 patients had scoliosis. 29/34 records have been analysed. 28/29 with scoliosis had been using a wheelchair, and 18/29 had wheelchair postural support issues, at or before scoliosis diagnosis. 5/29 with scoliosis were recommended respiratory support compared to only 1/69 without scoliosis. 4/5 had restricted FVC and 1/5 had kyphosis in addition. 21/29 had seen a spinal surgeon; 11/21 were advised annual monitoring, 1/29 had a spinal jacket, and 2/29 were discharged to GP “as skeletal growth was complete”. 6/29 underwent spinal surgery (age 14–17 years), with good short-term outcomes: improved sitting balance, respiratory function, and overall quality of life. Poor lung function at a year post-op was noted in 1/6 patients.

Discussion: Most children with scoliosis were wheelchair dependent. Prolonged sitting periods and poor seating postures may contribute to the development of scoliosis. Proactive physiotherapy may help delay or prevent spinal deformity in A-T. Scoliosis in A-T can affect lung function and cough effectiveness, as in other neuromuscular disorders, due to a combination of factors such as reduced FVC, muscle weakness, and loss of ambulation. Progressive scoliosis has an adverse effect on lung function.

Early detection with well-defined screening criteria, using objective methods e.g. a scoliometer, and monitoring may enable timely referrals to spinal units and secure favourable outcomes.

Disclosure: No potential conflict stated.

Multidisciplinary management of Neurofibromatosis Type 1 (NF-1): the experience from two (2) paediatric hospitals in Greece

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Introduction: Neurofibromatosis type 1 (NF-1) belongs to neurocutaneous syndromes, a group of congenital disorders that include abnormalities of neuroectodermal and, sometimes, mesodermal development. The clinical spectrum is heterogeneous, involves multiple organ systems, with a predisposition to develop tumors. A multidisciplinary approach to care has been advocated in order to provide optimum care for this complex disorder.

Methods: Patients with NF-1 were evaluated by a multidisciplinary team of specialists, including pediatric neurologist, dermatologist, oncologist, ophthalmologist, geneticist, orthopedist, neuroradiologist from January 2011 until February 2019. Patients underwent regular follow-up visits that included: physical examination, developmental assessment, growth and blood pressure monitoring, skin examination, ophthalmologic examination, MRI, hearing evaluation and other additional studies were performed based on clinically signs or symptoms.

Results: During the study period 185 patients (age 5 months–17 years, 78 girls and 107 boys) were assessed. The median age of diagnosis was 4 years old. All patients fulfilled diagnostic criteria of NF-1. Molecular testing was performed in 95 patients. 73 patients (10 de novo mutations), in 5 patients molecular testing was negative and in 17 patients evaluation is still ongoing. Among the 185 patients, there were 10 families with 2 or 3 affected children. The main clinical findings in patients with NF1 were: cafe-au-lait spots (100%); lentigines (70%); UBO’s (84%); Lisch nodules (54%); cutaneous and plexiform neurofibromas (30%); optic-pathway-gliomas (30%); scoliosis (26%); pseudoarthritis (3%); short stature (21%); hypertension due to vascu-
lar stenosis (10%); seizures (3%); pilocytic astrocytomas (3%) and sarcoma (1.7%). Learning disabilities and ADHD was detected in 63% of patients.

**Conclusion:** Establishment of a multidisciplinary center for neurofibromatosis can improve clinical care by providing multidimensional approach and contributing to early diagnosis and timely therapeutic intervention.

**Disclosure:** No potential conflict stated.

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**P07-26**

**Validation of the use of WhatsApp as a method of communication with families**

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**Introduction:** WhatsApp is the main instant messaging application. There is a growing interest in the study of this and other forms of communication in the patient-doctor relationship. The objective of this study was to evaluate patterns of whatsapp use by families and determine their degree of satisfaction with this method of communication.

**Material and Methods:** Descriptive and qualitative research study in a pediatric primary care / neuropediatric clinic. The clinic provided access to direct communication with pediatricians and child neurologist via whatsapp (WhatsApp Business) to a consecutive series of families, after signing an informed consent. Data about the variables of the messages and the degree of acceptance of the families was collected.

**Results:** Most of the consultations were received on weekdays (88.3%) and in the morning (53.7%). 70% of the consultations were satisfactorily resolved without the need for face-to-face assessment. The response time was less than one hour in 80% of the cases. A satisfaction survey was sent, proving a great acceptance by the families.

**Conclusions:** The patterns of use of this form of communication and the comments of the families that used the service show that it is a method that can improve communication with patients. Given the nature of family-based care and the chronic nature of most pathologies in neuropsychiatric, neuropediatricians are specialists well positioned to transform health care in this regard.

**Disclosure:** No potential conflict stated.
Children and adolescents with disabilities and the first three years of experience from the first hospice for children and adolescents in Denmark

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Introduction: Lukashuset (respite care, symptom relief and hospice for children and adolescents) is the first of its kind in Denmark. In Denmark paediatric palliation is under development. Before 2015 no formal services in this field existed. Since 2015 Lukashuset and home based palliative teams for children and adolescents have been established in Denmark. Children and adolescents with life-threatening and life-limiting conditions and a need for specialized palliative care from a multidisciplinary team can be admitted.

We want to give an overview of the characteristics of the children and adolescents admitted to Lukashuset in the first three years.

Methods: Data was collected from the records of patients admitted to Lukashuset between 01.11.2015 and 31.01.2019 and then included in a descriptive analysis.

Results: 42 patients were admitted to Lukashuset. Age distribution: 43% < 1 year, 33% 1-12 years, 24% >13 years. The distribution of diagnoses were 26% with neurological disorder, 31% with metabolic disorders, 17% with congenital disorders, 17% with oncological disorders and 10% with other diagnoses. 88% had a physical disability as part of their illness or due to complication to treatment. At the end of the study period 60% still lived, 29% died in Lukashuset and 12% died at home or hospital.

Conclusion: 42 children and adolescents were admitted to Lukashuset during the first three years. All children had a life-limiting or life-threatening condition. 43% of the children were under the age of 1 year. 88% of the patients had a neurological illness or neurological complication due to the illness or side effects from the treatment. The results show that a high percentage of patients in Lukashuset have a neurological disability.

Disclosure: No potential conflict stated.

Idiopathic Intracranial Hypertension: a paediatric case series

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Introduction: Idiopathic intracranial hypertension (IIH) is a rare condition with unknown etiology. The majority of patients present headache, sixth cranial nerve palsy, double vision, normal neurological examination (except palsy of the sixth cranial nerve or visual field limitations), papilledema, elevated lumbar CSF pressure with normal CSF composition. The primary aim of this study was to characterize the cases of IIH in terms of symptomatology, diagnosis, treatment and follow-up.

Methods: Retrospective study of clinical files of 17 children (4 infants and 13 adolescents) with IIH followed at a Portuguese Neuropediatric Department between 2006-18.

Results: Symptoms began at a median age of 13 years [4-17]. The commonest symptom was headache (12/17), followed by visual symptoms (6/17) and diplopia (6/17). On examination papilledema was the most frequent finding (12/17), followed by sixth nerve palsy (5/17). Concerning the risk factors: none of the infants present any risk factor;7 adolescents were obese, 1 had iron deficiency anemia and 1 was using tetracycline. CSF pressure showed a range of 250-500 mm of H2O (median CSF pressure 350 mm of H2O). CSF biochemistry and cytology were normal. A neuroimaging study was done in all patients. All patients were treated with acetazolamide during a median average period of 8 months. Due to lack of response in one patient it was necessary to add furosemide and subsequently was placed a ventriculoperitoneal shunt. A recurrence of symptoms occurred in 3 patients.

Conclusions: IIH is a challenging disease that can present at any age group and can lead to a significant morbidity. Since IIH in childhood may be less specific, especially in younger children, a high degree of suspicion is required. An early diagnosis and prompt treatment can prevent visual loss.

Disclosure: No potential conflict stated.
Brainstem beaklike. A case report

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Introduction: Pontine Tegmental Cap Dysplasia (PTCD) is a recently described, rare disorder characterized by a peculiar cerebellar and brainstem malformation. The diagnostic signature of PTCD stems from a peculiar constellation of hindbrain malformations, including cerebellar vermis hypo-dysplasia, absence of inferior olives and near absence of middle cerebellar peduncles, lateralized superior cerebellar peduncles, flattened ventral pons, and vaulted pontine tegmentum (‘tegmental cap’). Patients present with neonatal hypotonia, piramidal and cerebellar signs, multiple cranial neuropathies and extracranial malformations comprising cardiac, gastrointestinal, genitourinary and skeletal defects.


Conclusions:
- PTCD is a non-progressive disorder that we should suspect in patients with developmental delay and multiple cranial neuropathies.
- Characteristic MRI: hindbrain malformation.
- Suspected physiopathology due to neuronal migration and genetic source.
- There is a clinical correlation between the degree of brainstem malformation and grade of disability.

Disclosure: No potential conflict stated.
Characterization of speech and voice abnormalities in a cohort of GLUT1DS patients

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Objective: Glucose transporter type 1 deficiency syndrome (GLUT1DS) encompasses a broad clinical spectrum including different movement disorders. Speech impairment in GLUT1DS patients has been reported but not thoroughly described. The aim of this study is to analyze speech and voice abnormalities in a cohort of GLUT1DS patients and evaluate the correlation between the clinical profile and the voice motor function.

Methods: Patients with confirmed GLUT1DS followed in Sant Joan de Déu Children’s Hospital, Spain, were included. Speech and voice were analyzed using a voice and video-recording protocol, supervised by speech therapists. The ‘Robertson dysarthria profile guideline’ and ‘Consensus Auditory-Perceptual Evaluation of Voice’ (CAPE-V) scales were applied. Acoustic voice analysis was performed using the ‘Praat’ computer program. Clinical assessment was performed with a video-recording protocol. Child neuropsychologists evaluated the patient’s cognitive function. Descriptive analysis of the results was performed. Written informed consent was obtained for the procedures.

Results: A total of 13 patients (6 male and 7 female) were evaluated, ranging from 5 to 21 years. Speech analysis showed perceptual abnormalities, with an unstable voice and frequent voice breaks. Acoustic parameters analyzed with ‘Praat’ showed an abnormal jitter, shimmer and intensity profile, more evident on the adolescent patients with dystonic features. One patient showed significant clinical speech and voice improvement following adjustment on dietary treatment.

Conclusion: GLUT1DS patients show speech and voice abnormalities suggesting a distinct dysarthria profile, which seems to correlate with age and the presence of dystonic features. Specific speech and voice markers in GLUT1DS patients may prove useful for the treatment and intervention monitoring. Further studies in larger cohorts with controls are needed to confirm this hypothesis.

Disclosure: No potential conflict stated.

A case of cutis Verticis Gyrata associated with intellectual disability and Epilepsy

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Objective: Cutis verticis gyrata (CVG) is a rare disease characterized by excessive formation of scalp skin formation mimicking cerebral gyri. It may be congenital or acquired. An increased prevalence of cutis verticis gyrata is described in patients with mental retardation. In this report we described a patient with cutis verticis gyrata associated with intellectual disability and epilepsy.

Method: 20 years old male patient was administered with complaints of folds developing in his scalp over the last 2 years. He was firstly evaluated at 6 months-old complaints of, microcephaly, focal epilepsy and motor retardation. He could sit without support at 4 years old and walk with support at 5 years old. He was seizure free last 6 years after discontinuation of therapy. On physical examination there were irregular furrows on the vertex of the scalp in a variable direction that were non-reducible with traction, nystagmus and spastic quadriparesis. A diagnosis of cutis verticis gyrata was made.

Result and Conclusion: The periodically scalp evaluation is very important for intellectual disability patients.

Disclosure: No potential conflict stated.
**P07-33**

**Tuberous Sclerosis: evaluation of 115 patients, single centre study, Turkey**

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**Objective:** The aim of this study is to evaluate the clinical and radiological findings and complications of 115 patients with tuberous sclerosis (TS).

**Materials and Methods:** 115 TS patients who were diagnosed before the age of 18 years between January 2002 and December 2017 in Erciyes University Pediatric Neurology Clinic were scrutinized in this study. The findings of all patients were evaluated with a pediatric neurologist, radiologist, child psychologist. Each patient was evaluated by a pediatric cardiologist and a pediatric nephrologist for the complications.

**Results:** Regarding 115 tuberous sclerosis patients, hypopigmented macules were detected 90.4%, angiofibroma was 48.2%, Shagreen patch was 17.5%, fibrous plaque at forehead was 3.5% andungal fibroma was 3.5%. Epilepsy was observed in 84.3% of patients and epileptic waves in EEG were observed in 78.8%. Regarding brain MRI; the most common lesions were cortical tuber (84.3%), subependymal nodule (78.3%) and subcortical tuber (75.5%). SEGA was detected in 8 patients (7%). Mental retardation was found in 52.9% of the patients and border intelligence level was found in 22.5% of the patients. Epilepsy was detected in 95.5% of patients with mental retardation and a meaningful relationship was found between epilepsy and mental retardation in patients with tuberous sclerosis (p <0.05). Autism was frequently found in 32.2% of the patients, and ADHD was found in 22.5% of the patients. Cardiac rhabdomyomas were detected in 32.7% of all patients. Renal angiomyolipoma was detected in 37.4% and renal cysts in 25.2%. Retinal hamartoma frequency was 6.6% and retinal hypopigmented patches were 6.6%.

**Conclusion:** TS is relatively common in childhood and due to systemic findings multidisciplinary management is required. New investigations are needed to develop new therapeutic approaches.

**Disclosure:** No potential conflict stated.

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**P07-34**

**Neurofibromatosis Type 1: evaluation of 124 patients, single centre study, Turkey**

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**Objective:** The aim of this study is to evaluate the clinical and radiological findings and complications of 124 patients with neurofibromatosis type 1 (NF1).

**Materials and Methods:** 124 NF1 patients who were diagnosed before the age of 18 years between January 2002 and December 2017 in Erciyes University Pediatric Neurology Clinic were scrutinized in this study. The clinical, radiological and EEG findings of all patients were evaluated with a pediatric neurologist and radiologist. The psychometric situations of the patients were examined by the Child Mental Health department. Each patient was evaluated by an ophthalmologist and a pediatric cardiologist for the complications.

**Results:** Cafe au lait spots were detected in all patients, whereas skinfold freckling was 39.5%, cutaneous neurofibromas were 20.2% and plexiform neurofibromas were found in 15.3%. Regarding brain MRI of patients, T2-weighted hyperintense lesions were detected in 80%. Optic tract glioma was 22.4% and Lisch nodules were 27.6%. 46.8% of the patients had intellectual disability. Seizures were observed in 17.7% of the patients and epileptic waves were observed in 22.1% of EEG. Sphenoid wing dysplasia was detected in 3 patients (2.7%), tibial pseudoarthrosis in 1 patient (0.9%) and kyphoscoliosis in 14 patients (12.4%). Vascular changes were observed in 9.7% of cases, most commonly in aneurysms. Various malignancies were detected in 16 patients (12.9%); including 8% glial tumor, 2.4% MPNST, 1.6% JMML, 0.8% medulloblastoma and 0.8% T-cell lymphoma.

**Conclusion:** NF 1 is relatively common in childhood and due to systemic findings multidisciplinary management is required.

**Disclosure:** No potential conflict stated.
Sturge-Weber Syndrome: evaluation of 15 patients, single centre study, Turkey

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Objective: The aim of this study is to evaluate the clinical and radiological findings of 15 patients with Sturge-Weber syndrome (SWS).

Materials and Methods: 15 SWS patients who were diagnosed before the age of 18 years between January 2002 and December 2017 in Erciyes University Pediatric Neurology Clinic were scrutinized in this study. Patients’ data up to 2016 were retrospectively reviewed. Patients diagnosed in 2016 and 2017 were followed up prospectively. The findings of all patients were evaluated with a pediatric neurologist, radiological findings and EEG findings were also evaluated. Each patient was also examined by an ophthalmologist.

Results: In 15 SWS patients, unilateral port-wine stain was detected in 14 patients (93.3%) and bilateral in 1 patient (6.7%). In 3 cases (20%) the stain was spreading through the trunk, and 2 cases (13.3%) had tongue involvement. Glaucoma was found 53.3% and buphthalmos was found in 6.7% of the patients. Epileptic seizures were observed in 93.3% of the patients, focal epileptiform anomaly was observed in 66.7% and multifocal epileptiform anomaly in 6.7% of the EEG. Headache was found in 26.7% of the patients, hemiparesis was 46.7%. Mental retardation was detected at 73.3%. Cerebral hemiatrophy (86.7%) and gyral calcification (73.3%) were the most common findings in brain imaging.

Conclusion: Sturge-Weber syndrome is a rare condition in childhood and due its infrequency mutual experience is valuable.

Disclosure: No potential conflict stated.

Significant hidden socio-emotional problems in children with neurological disorders revealed by sentence completion test

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Introduction: In children with neurological disorders (ND) different socio-emotional problems exist, which often remain undetected. The purpose of the study was to identify the patients’ attitudes, desires, beliefs, and motivations, for better understanding children’s every-day social difficulties.

Methods: Children with ND (epilepsy, TBI, tic disorder) aged 8-13 participated. 29 children (M=11.10 yrs, SD=1.543; 20 boys and 9 girls) filled the Sentence Completion test, which included 35 unfinished sentences in four categories: relationships, behaviour, self-perception, and emotions. Participants completed the sentences in ways that were meaningful to them.

Results: Sentence Completion test revealed the individual socio-emotional problems in patients. Results in relationships category revealed that 85% of boys and only 67% of girls had best friends. In behavior category, the most noticeable indication was bullying- being a problem in 90% of boys and 67% of girls. Additionally, 45% of boys and 56% of girls brought out the fear of potentially dangerous or unknown situations. In self-perception category, 75% of boys and 44% of girls could name their individual characteristics making them special. Emotion category showed that 50% of boys were happy spending time with friends and family. 50% of boys and 44% of girls were happy if their wishes were fulfilled, and 56% of girls were happy without major worries.

Conclusion: The study revealed noticeable socio-emotional problems in children with ND. Sentence Completion test is an important part of a neuropsychological assessment battery as it encourages children to reveal their hidden feelings and real relationship problems. These difficulties need intervention to better the patients’ social capital and quality of life.

Disclosure: No potential conflict stated.
Social scenarios for virtual reality platform for remediation of Social Communication Disorder in children

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Introduction: Neurological disorders (ND) often affect children’s social skills and lead to emotional disturbances. Virtual Reality (VR) introduces attractive method by giving children a chance to train in simulated real-world situations. The aim was developing VR metaphors/scenarios to improve children’s social skills and decrease anxiety in social situations.

Methods: 10 different metaphors for VR were created. In trainings, therapist observed scenarios from computer and chose different difficulty levels and reactions for characters based on patients’ individual feedback. HTC Vive VR device was used with software created by authors. 19 children aged 8–13 participated (13 with ND: epilepsy, TBI; or tic disorder- and 6 healthy controls). Vital signs: blood pressure and heart rate (HR) were monitored during sessions.

Results: In artificial VR environment children practiced communication skills with other people in socially and emotionally challenging situations. Examples:
1. Patient spills cake onto other’s plate. Patient has to explain, apologize, ask back.
2. Patient goes to cinema, sees that someone has taken his place.
3. Boy has put his shirt on backwards. Patient has to tell him appropriately.
4. Students bully patient in class. Patient has to explain to teacher why exercises were not done.
5. Boy has lost his phone. Patient has to comfort, offer solutions.

The most challenging situation for children was cinema (average max HR 102), followed by cafeteria (HR 98). Therefore, HR peaked in metaphors where children had to repeatedly confidently request in interactions when other characters argued with them.

Conclusions: An interactive VR platform with specifically constructed real-world metaphors was designed as a targeted social learning tool in varying contexts. VR appears effective, suitable and motivating for children, with advantages being flexibility, safe environment and precise measurement.

Disclosure: No potential conflict stated.

Continuous EEG monitoring in cases with Acute Non-Traumatic or Non–Opera Traumatic Encephalopathy

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Introduction: Acute encephalopathy is one of the urgent problems of childhood. According to the studies, the frequency of seizures in acute encephalopathy was found to be between 19–28%. However seizures are common in cases with acute encephalopathy, most of them are nonconvulsive (NCS). These seizures can be easily overlooked without continuous video–EEG monitoring (cEEG).

In this study, the prognostic value of cEEG in determination during early period in acute encephalopathy cases followed in Pediatric intensive care unit (PICU).

Methods: This prospective study was carried out in Ege University PICU. Twenty-four patients with GCS ≤8 who were diagnosed with acute non-traumatic/non-operative traumatic encephalopathy were included in the study. The patients were monitored for at least 24 hours. In the presence of electrographic seizures, cEEG was extended till 48–72 hours.

All patients were evaluated with Modified Pediatric Cerebral and Overall Performance Category Scale (PCOPCS) in terms of morbidity before discharge from hospital.

Results: Of the 24 patients, 14 were female. From the point of the etiology, head trauma was found in six patients, The other causes were asphyxia, intoxication, uremic encephalopathy, hepatic encephalopathy, metabolic disease. During 24-hour monitoring, eleven NCS were observed in four cases. Eighteen percent of NCS was detected during the first hour of cEEG and 82% of them developed within 24 hours. NCSE was not observed in any patient. It was concluded that the cEEG with 24 hours duration may be sufficient in cases with encephalopathy.

In accordance to PCOPCS, 11 and 13 patients had good and bad prognosis respectively.

Conclusion: cEEG is still gold standard for the detection of nonconvulsive seizures. On the other hand there are some difficulties for application of cEEG in intensive care units. Multi-disciplinary approach and cooperation are essential.

Disclosure: No potential conflict stated.
Radial Nerve Injury in the newborn. Case series

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Background and aim: Radial nerve injury is a very rare occurrence in the neonate. We present two cases of transitory radial nerve injury in neonates admitted in the neonatal intensive care unit.

Methods: We present two cases of transient radial nerve injury: one case of a premature SGA (small for gestational age) neonate and the other of a LGA (large for gestational age) newborn. Both cases were diagnosed clinically during the first week of life; the investigations consisted in radiography of the affected limb and head ultrasound. The patients were treated by the physical therapist with passive movements, stimulation and constraint in an orthosis.

Results: Case number one: a 33 weeks preterm SGA neonate, birth weight 1200 grams, with asphyxia, respiratory distress and mechanical ventilation for 72 hours. After extubation, when spontaneous movements were present, there was observed a wrist drop with flexion, extension and abduction of the forearm and arm present. The x-ray and head ultrasound were normal. The treatment began immediately The evolution was favorable. At two months the posture and the movement of the hands was normal. The etiology was probably ante or postnatal compression in the context of weak muscular mass.

Case number two: LGA neonate that presented with a wrist drop from the delivery. There were no signs of asphyxia or brachial plexus injury. The x-ray and head ultrasound were normal. The treatment began after the diagnosis. The normal movements of the hands were obtained at 6 months. The etiology was probably intrauterine compression.

Conclusion: The injury of the radial nerve could occur in the neonates in the context of prolonged ante or postnatal compression. The outcome is favorable, with complete recovery after physical therapy.

Disclosure: No potential conflict stated.

Difficulties in diagnosing of SSPE in Kazakhstan presenting at three cases

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Introduction: Main infections in this category are progressive multifocal leukoencephalopathy, cytomegalovirus encephalitis, and subacute sclerosing panencephalitis caused by measles virus. The disease is called because it typically develops over a period of less than 9 month (subacute), because of the nature of the pathological lesions (sclerosis), and from the fact that the whole brain in affected (i.e. panencephalitis).

Methods: We would like present three cases of SSPE, which observed from July to December 2018. It were boys, 3.5-4.5 y.o. One of them had a measles at 4 months of life; other two were vaccinated at 18-24 months. They were healthy until stated to have myoclonic seizures and drop attacks and one had persistent clonic seizures at right extremities and drop attacks. They were admitted to hospital with diagnosis as myoclonic-astatic epilepsy.

Results: The epileptic condition was lasting 4-5 month until they developed somnolence, autonomic failure, rigidity, akinetic mutism, decortication posture. At beginning their were no suspicious on SSPE despite on EEG picture as slow waves activity with periodical high voltage complexes. First MRI were no suggestive to SSPE too. Then 5 months later they developed somnolence, decortication posture, akinetic mutism, on MRI corical, subcortical asymmetrical hyperintense leasons on T2 with involvement of thalamus, corpus callosum and basal ganglia. Measles antibodies in blood and CSF (at one case) where positive.

Conclusion: SSPE could be misdiagnoses as epilepsy. We need suspect SSPE at affected patents presented with myoclonus, seizures progressing, eventually to akinetic mutism and decortication. The diagnosis should base on clinical presentation, blood and CSF antibodies confirming antimeasels virus response and demonstration of periodic complex on EEG.

Disclosure: No potential conflict stated.
**P08-06**

Can neonatal staff site EEG leads in the correct location? A pilot study

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**Background:** Most neonatal seizures are electrographic, so electroencephalography (EEG) is required to detect seizures in research studies. This is not available 24 hours a day, limiting research design.

**Aims:** To study whether neonatal staff could site EEG leads on a resuscitation doll after a video training session.

**Methods:** Neonatal staff watched a training video on siting EEG leads using a modified neonatal montage and a commercially available Braun template. A member of the neurophysiology team measured the distance each lead was sited from the ideal location. Clinical training of neurophysiology technicians assumes EEG positions 5mm or less from the ideal location is satisfactory. Permission was obtained from the University of Sheffield Ethics Committee and consent obtained from participants.

**Results:** 24 staff enrolled: 7 ST1-3 trainees, 6 ST4-8 trainees, 3 Consultant Neonatologists, 3 Advanced Nurse Practitioners and 5 Nurses. EEG leads were sited within 5mm of the ideal locations between 79.2-100%. Specific results for each lead were: 95.8% FP2; 100% FP1; 95.8% F8; 91.7% F7; 91.7% T4; 91.7% T3; 79.2% T6; 91.7% T5; 87.5% O2; 85.5% O1; 95.8% C4; 95.8% C3; and 95.8% Cz. The median distances from the ideal location and interquartile range for each lead were: 3.5mm(1.5,5) FP2; 2mm(0.75,5) FP1; 5mm(0.5,5) F8; 5mm(1.75,5) F7; 2mm(0.5) T4; 5mm(0.5) T3; 0mm(0.5) T6; 0mm(0.5) T5; 5mm(0.5) O2; 5mm(3.5) O1; 0mm(0.5) C3; 0mm(0.5) C3; and 0mm(0.5) Cz.

**Conclusions:** With minimal training and a commercially available template, neonatal staff can site EEG leads near the ideal location in the majority of cases. Further work is needed to determine whether they can sit the leads on a baby, whether the leads can be attached securely, and good quality EEG data can be recorded.

**Disclosure:** No potential conflict stated.

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**P08-07**

What Epilepsies are seen following moderate to severe Neonatal Hypoxic-Ischaemic Encephalopathy (HIE)

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**Background:** Epilepsy is one of several adverse neurological outcomes following perinatal hypoxic-ischaemic encephalopathy (HIE). The literature on neurodevelopmental outcome following HIE focuses on cognitive skills / impairment and cerebral palsy, with most studies reporting epilepsy as a binary outcome; i.e. “yes” or “no”. Few studies describe the types of epilepsy that follow HIE. Most of the published data was collected before therapeutic hypothermia became standard treatment for all neonates with moderate to severe HIE.

**Aims:** To determine the proportion of children with moderate to severe HIE in the age of therapeutic hypothermia who develop epilepsy and to classify the epilepsies seen.

**Methods:** A retrospective cohort study of neonates with HIE treated with therapeutic hypothermia between June 2010 and December 2013 in Sheffield. Follow-up data on the same children was accessed.

**Results:** In total 76 neonates with HIE had their amplitude-integrated encephalography (aEEG) and follow-up data reviewed. 2.4% subsequently developed epilepsy. Of the two children who had a documented epilepsy diagnosis one had multifocal epilepsy and the other polymorphic epilepsy - both were associated with severe functional motor disability (GM-FCS level 5). There was no significant correlation between non-normalisation of CFM at 48 hours and later development of epilepsy (p=0.19).

**Conclusions:** Our study reports a lower rate of epilepsy than other studies of neonates with HIE. This may be a methodological problem in missing follow-up data but could represent a lower burden of disease in this group in the modern era. Epilepsy is associated with more severe disabilities and can still occur if the aEEG normalises by 48 hours of age.

**Disclosure:** No potential conflict stated.
Role of the deprivation of liberty process in Paediatric Neurorehabilitation practice

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Introduction: In adult neurorehabilitation practice, demonstrable understanding of the legislation underpinning Deprivation of Liberty is a quality standard for specialist services. However, consultant paediatricians involved in neurorehabilitation may be unfamiliar with this concept, since consent issues in paediatric practice are usually addressed with parents. We present the case of a 16-year-old girl who sustained severe cognitive impairment following a traumatic brain injury, who received neurorehabilitation care, for whom Deprivation of Liberty legislation was highly relevant.

Case description: Our patient had sustained multiple injuries in a road traffic accident, including severe traumatic brain injury (TBI) with diffuse axonal injury (DAI). Prior to the accident she was fit and well, with above average cognition. However, she had a history of self-harm, oppositional behaviour and substance abuse and was in local authority foster care under Section 20 of the Children’s Act at the time of admission. Three months after sustaining TBI, she had made a good physical recovery but had severe cognitive impairment, particularly in the domains of attention, memory and executive function. She was deemed extremely vulnerable and therefore, was not allowed to leave the hospital premises except under close supervision.

In view of the age of the patient and the significant restrictions placed upon her, Deprivation of Liberty safeguards were considered applicable. Despite evidence of improvement in her cognitive functioning, she continued to lack capacity in this regard throughout her prolonged in-patient stay, and an application was therefore made to the Court of Protection to sanction Deprivation of Liberty.

Conclusion: We propose that awareness of the Deprivation of Liberty process and local protocols for management of such cases should be made a quality standard for specialist paediatric neurorehabilitation units.

Disclosure: No potential conflict stated.

Infantile spasms following Acquired Brain Injury – A tertiary Neuro-Rehabilitation centre experience

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Introduction: Infantile spasms (IS) is a devastating type of epileptic encephalopathy, associated with poor developmental outcome. Epidemiological studies have shown a symptomatic etiology in about 68% of children diagnosed with IS. We describe 4 children who developed IS following acquired brain injury (ABI), with an aim to highlight the diagnostic difficulties and the positive impact on rehabilitation with appropriate treatment.

Results: The age range at the time of brain injury varied between 80 days to 1 year. Two children had widespread ischaemic brain injury following pneumococcal meningitis, one child had extensive hypoxic damage following an out of hospital cardiac arrest (cause unknown) and one child had extensive subdural haematoma following a non-accidental injury. Onset of infantile spasms was between three to six months following ABI. Three of them were in-patient at the time of diagnosis and had a time lag of 1 week to 10 days from symptom onset to treatment initiation. One child had been discharged home and the time lag to treatment initiation was approximately 1.5 months. Steroid treatment based on ICISS protocol was initiated following EEG confirmation of hypsarrhythmia. Complete clinical cessation of spasms was noted between 7 to 21 days. Two of them had recurrence of spasms which was treated successfully and the other two children had evolution of different seizure types.

Conclusion: It is challenging to diagnose IS in patients with ABI, particularly with associated neurological symptoms like dystonia. We noted a positive impact on their rehabilitation following successful treatment of IS and strongly recommend a low threshold for initiation of investigations and treatment for IS in this patient subset.

Disclosure: No potential conflict stated.
Management of Neonatal Seizures in a Level 2 Neonatal Unit in the United Kingdom

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Introduction: Neonatal seizures are one of the most common neurological conditions in newborn infants. There are myriad potential causes and sequelae. Management can be variable as significant evidence for various strategies can be limited. The aim was to evaluate current investigation and management of seizures in a local Level 2 Neonatal Unit.

Methods: A retrospective cohort study was conducted. Included were all neonates admitted to the Neonatal Unit with a diagnosis of seizures (of any type) over a five year period (2014-2018). Data was collected from written and electronic medical records, including BadgerNet. Variables evaluated included gestation, timing of seizures, investigation and management of seizures, length of admission and outcomes.

Results: 90 infants were admitted to the Neonatal Unit during the five year period. These comprised 9.5% of the total 944 admissions during this time. 56.7% were male, and 67.8% were term infants. Related disorders included IVH, HIE and infection although cause was not always identified. Approximately 3/4 infants with seizures were treated with at least one anti-epileptic medication. In all cases this included Phenobarbitone. The subsequently most commonly used drugs were Levetiracetam (16%) and Phenytoin (11%) respectively. Other agents given more rarely included Midazolam, Paraldehyde, Lorazepam and Pyridoxine. 22% of infants required more than one anti-epileptic agent to control seizures.

Conclusion: Neonatal seizures remain a relatively common yet serious neurological event whose management can be variable. Our management was in keeping with existing data.

Disclosure: No potential conflict stated.

Correlations among functional classification systems in Cerebral Palsy: a study using the Surveillance of Cerebral Palsy in Europe (SCPE) Database

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Objective: To correlate functional classification systems (FCS) used in Cerebral Palsy (CP) and to define the functional levels in types of CP.

Methods: We evaluated patients entered into our registry system using the SCPE database format (n=126) and the following FCSs: Gross Motor FCS (GMFCS), Manual Ability Classification System (MACS), Communication FCS (CFCS) and Eating and Drinking Classification System (EDACS). Spearman’s Test was used to examine the correlations among the FCSs.

Results: The clinical types were spastic (n=93; 34 hemiplegic, 33 diplegic, 26 quadriplegic), dyskinetic (n=21; 13 dystonic, 8 choreoatetoid), ataxic (n=4) and unclassified (n=8). According to GMFCS, the majority of spastic children (36%) were level 1, and of ataxic children (75%) level 2, while dyskinetic children’s functional levels were distributed almost evenly. According to MACS, level 1 was the largest group in spastic and ataxic children (34% and 50% respectively), while the majority of dyskinetic children (38%) were level 3. According to CFCS, the majority of all 3 types (spastic: 63%, dyskinetic: 48%, ataxic: 50%) were level 1. For eating and drinking skills (EDACS), the majority of children (spastic:78%, dyskinetic:7%, ataxic:75%) were level 1. Correlation between FCSs was significant, strong between GMFCS and MACS (r=0.779), GMFCS and CFCS (r=0.792), and between CFCS and EDACS (r=0.765) followed by GMFCS and EDACS (r=0.696), MACS and CFCS (r=0.718), and MACS and EDACS (r=0.696).

Conclusion: Functional levels were better in spastic compared to ataxic and dyskinetic CP. Fine motor function was most impaired in dyskinetic children, while communication and eating skills were mildly impaired in the majority of all types. Significant relationships were found between FCSs, strongest between gross and fine motor, and between communication and eating skills. These results support the accuracy and reliability of FCSs frequently used in clinical practice.

Disclosure: No potential conflict stated.
Two phase 1 healthy volunteer trials investigating the potential effects of CYP3A4 and CYP2C19 inhibition or induction on Cannabidiol (CBD) Pharmacokinetics

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Objective: GW Pharmaceutical’s formulation of cannabidiol (CBD; Epidiolex®) is approved in the U.S. for seizures associated with Lennox–Gastaut or Dravet syndromes in patients aged ≥2 years. Cytochrome P450 (CYP3A4 and CYP2C19) enzymes mediate CBD oxidative metabolism. Two phase 1 trials investigated the effects of potent CYP3A4 and CYP2C19 inhibition or induction on CBD pharmacokinetics (PK) and safety.

Methods: These open-label, fixed sequence trials (n=48; 16/arm) investigated how multiple oral doses of itraconazole (CYP3A4 inhibitor), fluconazole (CYP2C19 inhibitor) or rifampicin (CYP3A4/2C19 inducer) impacted single-dose oral CBD PK. On Day 1 (both trials), subjects received 750 mg CBD within 30 min of starting a high-fat breakfast. On Day 8 (inhibitor trial), subjects received 2×200 mg itraconazole doses (fed) or 400 mg fluconazole, then 200 mg itraconazole or fluconazole once daily (OD) between Days 9–21. On Day 15, an hour after itraconazole or fluconazole, subjects received 750 mg CBD per Day 1 conditions. Between Days 5–24 (inducer trial), subjects received 600 mg rifampicin QD. On Day 20, subjects received 750 mg CBD concomitantly per Day 1 conditions. CBD plasma concentrations were determined, and safety was monitored throughout.

Results: All subjects completed both trials. The mean age was 36.4 y, 60% were female, and 28 (93.3%) subjects completed the trial. CBD exposure (Cmax and AUCt) increased when administered with food/drink vs fasted, and safety/tolerability of CBD were assessed.

Conclusions: CBD exposure was unaffected by itraconazole and not markedly affected by fluconazole or rifampicin, suggesting dose adjustment may not be warranted when CBD is co-administered with potent CYP3A4 or CYP2C19 inhibitors/inducers. Most treatment emergent adverse events were mild.

Disclosure: GM, JC, SG and BT own shares/share options in GW Research Ltd.
**Evaluation of the electroclinical phenotype in Pallister-Killian Syndrome: preliminary results**

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**Introduction and Aim:** Pallister-Killian Syndrome (PKS) is a rare genetic disorder caused by a mosaic distribution of a chromosome 12’s short arm (p) tetrasomy. Neurological involvement is always present and epilepsy is a frequent concern in PKS patients. The aim of our study is to better define epilepsy and EEG phenotype in children with PKS.

**Methods:** In 2018 we started a prospective study. 30 patients have been engaged with the aid of «PKS Kids Italia» association. To date we performed video-EEG registrations in 9 patients at Child Neurology and Psychiatry Unit of Sant’Orsola Hospital of Bologna: for each patient we analysed anamnestic data, focusing on epilepsy onset, evolution, seizure type, treatment, and neuroimaging.

**Preliminary Results:** Age ranges from 8 months to 10 years and 3 months, mean age 30 months, sex ratio 4/5 (M:F). 9/9 (100%) have slowing and paroxystic EEG discharges in temporo-occipital regions. 6/9 (66%) patients have epilepsy: age at onset 5 months-8 years and 6 months, mean age 28 months, 3 males/3 females. In 4/6 cases, epilepsy onset was before 18 months of age. 4/6 (66%) present focal seizures and 3/6 (50%) have myoclonic seizure with myoclonic jerks at low frequencies of intermittent light stimulation. 5/6 started an antiepileptic treatment.

**Conclusion:** Our preliminary experience confirms that epilepsy is a frequent concern in PKS: early-onset myoclonic seizures and focal seizures are possible clinical manifestations. Epileptic spasms are often reported in PKS: a differential diagnosis between clusters of myoclonic seizures and epileptic spasms has to be considered. Interestingly, photosensitivity was frequently observed in our patients. Further data are needed to better define which genes on 12p are potential candidate contributing in epileptogenesis (e.g. GRIN2B, ERC1, GEFS+, GABRB3, SLC6A12-13, EPM1).

**Disclosure:** No potential conflict stated.

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**Idiopathic Infantile Spasm with a good outcome**

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**Introduction:** Infantile spasms are one of the most critical issues in neurology, because of their refractive nature and a propensity to psychomotor disability. Early diagnosis and proper treatment are important to preserve development. Infantile spasms are movements of acute flexion, extension or a mixture of both. During clinical practice, especially extensor spasms may be overlooked.

**Case:** A four-month-old male with a history of normal prenatal, natal and postnatal period, presented with sudden extension of the arms for 2 days. His developmental milestones were normal for age. Home videos revealed extensor type infantile spasms. EEG showed bursts interspersed with 2-second-long attenuation periods. Cranial MRI and metabolic screening were normal. There was no family history or consanguinity. He received a course of tetracosactide (ACTH) of 14 doses. He has been seizure-free since the fourth dose, and is now on phenobarbital. Follow-up EEGs were improved. He is now developmentally normal at 1 year of age.

**Discussion:** Infantile spasms should be recognized and treated as soon as possible. Although additional developmental delay is seen in nearly all, early treated idiopathic cases could lead a normal developmental path.

**Disclosure:** No potential conflict stated.
**P08-16**

Febrile Infection–Related Epilepsy Syndrome (FIRES): clinical presentation, treatment and outcome in a series of patients

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**Introduction:** Febrile infection-related epilepsy syndrome (FIRES) presents with refractory multifocal status epilepticus (SE) in healthy children after a febrile infection. The etiology remains mostly unknown, but a genetic predisposition and an inflammation-mediated process are thought.

**Methods:** Three case studies of FIRES and follow-up were analyzed retrospectively at the Gregorio Marañon Hospital of Madrid between 2005 and 2018. We evaluated: main clinical features, neuroimaging findings, treatment and outcome.

**Results:** Median age of disease onset: 5.6 years. All patients were previously healthy with normal psychomotor development. Febrile illness prior SE lasted (median 3.6 days). Two of them related to pharyngitis and the other to flu illness (Influenza B). Investigations for other infectious, autoimmune and metabolic etiologies were normal. All of them presented a focal status epilepticus with motor seizures and a sensitive aura, with a median duration of one hour. Median duration of hospitalization in intensive care unit (ICU): 30 days. All patients needed ventilatory support (median 6 days). Main findings in MRI were hyperintensity in both hippocampus and cerebral atrophy. Patients were treated with steroids, IVIG, and several antiepileptic drugs. Only one child accepted ketogenic diet, which had a better outcome. All patients had an overall poor outcome, recurrent and refractory seizures, and moderate to severe neurocognitive difficulties.

**Conclusions:** It is important to identify FIRES, and then to begin an early treatment; antiepileptic drugs, IG intravenous and ketogenic diet. It is important to begin ketogenic diet in the first week when status epilepticus is refractory to antiepileptic medications, although we don’t have the definitive diagnosis of FIRES, in order to minimize cognitive impairment. MRI might be helpful to diagnosis and follow-up.

**Disclosure:** No potential conflict stated.

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**P08-17**

Longitudinal trajectories of self-reported depressive symptoms in children with Epilepsy

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**Aim:** Longitudinal examination of self-reported depressive symptoms in children with epilepsy.

**Methods:** Prospective cohort study of children with epilepsy treated at six Canadian tertiary-care centers and followed over 28 months (N = 506) with repeated assessment of child self-reported depressive symptoms using the Children’s Depression Inventory Short-Form (CDI-S). Trajectories of depressive symptoms were estimated using linear mixed effects (LME) modeling.

**Results:** Mean age was 11 years 5 months, and 234 participants were female. Mean CDI-S T-score at baseline was 45.7 (SD=7.5) and at 28 months was 44.9 (SD=8.2), both within “average” range. Results from LME modeling revealed mean raw CDI-S score corrected for age 10 of 1.81 (corresponding to T-scores slightly below the normed mean of 50), with no significant change over three measurements (slope=-0.046, p =0.189), indicating that CDI-S scores were stable over 28 months. Children with high initial CDI-S scores had lower subsequent scores, as demonstrated by the correlation of -0.66 between intercept and slope. The depression scores did not correlate with the seizure severity scores.

**Significance:** Self-reported depressive symptoms were generally low and stable over an extended follow-up period. Even in children reporting higher depression scores at one point, normalization of scores was seen upon repeated assessment. These findings speak to the importance of repeated assessment over time.

**Disclosure:** No potential conflict stated.
Febrile Infection-Related Epileptic Syndrome (FIRES) case report presentation: a challenging medical event with ominous outcome

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Introduction: FIRES, refers to a life-threatening epileptic encephalopathy connected to an underlying febrile infection, with unclear etiology, in the absence of existing neurological disorder. The aim is the description of a first appeared Status Epileptic episode, resistant to the indicated treatment, in a 12 month old infant due to FIRES and the necessity of immediate therapeutic intervention.

Methods: On July 2016, the infant admitted to the Emergency Department due to seizures lasting approximately 1 hour.

Results: The episode was characterized by tonic-clonic seizures and staring. Fever, 39oC, was observed a few hours ago and an episode of gastroenteritis 10 days earlier (Family history of psychokinetic retardation-cousins). Oxygen therapy was administered as well as 2 doses of IV Midazolam, followed by IV Phenytoin but due to the unresponsiveness to the treatment and an episode of cardiac arrest, it was urgently intubated by anesthesiologist and transferred to the closest ICU of a tertiary hospital. Blood results showed increased inflammatory markers, liver enzymes, CPK and severe acidosis with normal CT Brain scan. After an intubation period of 12 days, MRI scan showed ischemic encephalopathy. Even though it was discharged with triple antiepileptic treatment, the child exhibited frequent seizures, characterized mainly by opisthotonus and abnormal eye movements. Progressive psychokinetic disorders were also developed. The diagnosis of FIRES was set in a quaternary hospital based on its clinical history.

Conclusion: FIRES is a rare, potentially fatal epileptic syndrome with poor prognosis, which requires a multifocal approach. The quick hospital admission and staff coordination is crucial for early therapeutic interventions, establishment of differential diagnosis and transfer to executive center if needed.

Disclosure: No potential conflict stated.
## P08-20

**Transient elevation of TSH following seizures in children**

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**Background:** Seizure is a common neurologic disorder in children and adolescents. Seizure affected by pituitary hormonal change and hormone influenced by seizure itself.

**Method:** We retrospectively reviewed the medical records of children and adolescents with seizures attending the pediatric neurology department of Daejeon St. Mary’s Hospital during the period from April 2014 through August 2017.

**Results:** The study population consisted of 181 pediatric patients, aged between 3 months and 18 years. We found transient elevation of thyroid-stimulating hormone after seizures. Free thyroxine and triiodothyronine did not show significant variations. Abnormally elevated TSH was related with seizure duration.

**Discussion:** Neuronal excitability by seizures can affect to thyroid hormonal change and this probably reflects alternation of hypothalamic function.

**Disclosure:** No potential conflict stated.

## P08-21

**Clinical case of boy with Hypothalamic Hamartoma and seizures**

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**Introduction:** The hypothalamic hamartomas are rare congenital abnormalities that are presented with a classic triad of seizures, and especially gelastic seizure, precocious puberty and serious developmental delay. Also autonomic features such as flushing, tachycardia and altered respiration are widely present. Conscious may or not may be impaired. Gelastic seizures have been associated with hypothalamic hamartoma.

**Method:** Boy of 22 month old was referred to our hospital due to focal seizures in the left part of the face. Occasionally the episodes are generalized. Phenotypically healthy parents. From the age of 8 month old had presented characteristics of dimorphic features, precocious puberty, serious developmental delay and affected aggression. The neurological examination: broad base of steppage gait with broad base and slight bowed legs EEG: Diagram of sleep presented spike waves or spikes that are reported temporal-occipital with right lateralization and tension to generalize. BRAIN MRI: Svarsellar space occupying lesion that has the radiological characteristics of hamartoma of the tuber cinereum. Lab test: Abnormal levels of genital hormones, especially high levels of testosterone. Two months later after the presentation of focal seizures presented gelastic seizures refractory at the anticonvulsant therapy.

**Result:** Hypothalamic hamartomas must be taken in consideration in case of polymorphic seizure and endocrinological abnormalities.

**Conclusion:** The hypothalamic hamartoma must always be taken in consideration in case of endocrinological abnormalities and seizures. Currently the most effective treatment is surgical approach and new approaches such as endoscopy and radiosurgery.

**Disclosure:** No potential conflict stated.
POSTER PRESENTATIONS > POSTER SESSION 8
Epilepsy: miscellaneous, Neurorehabilitation

P08-22

A novel method to analyse and monitor walking capacity in children with Cerebral Palsy, to identify response after treatment

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Objective: Similar to healthy children, an age-driven development of the walking capacity is expected among children with cerebral palsy (CP). Our aim was to generate reference centiles for the six-minute walk test (6MWT) and the one-minute walk test (1MWT) in children with CP, GMFCS level 1 and 2, and to develop a method to quantify changes over a six-month period, considering also the expected progression under standard of care.

Methods: Retrospective analysis of data of children with CP who participated in a rehabilitation program between 2006 and 2017. The centiles were created using the lambda-mu-sigma (LMS) method. 6MWT and 1MWT were assessed at the beginning and end of the six-month training, as well as at a six-month follow-up.

Results: We created 6MWT and 1MWT age-related reference centiles using the data of 157 and 210 children with CP, GMFCS level 1 and 2 before a six-month rehabilitation treatment respectively (median age 6MWT 6.54 years, SD 2.54 and median age 1MWT 6.15 years, SD 2.51). A medium, clinically relevant 6MWT effect size of the treatment (Cohen’s d 0.69) was found among 78 patients (6.40 years, SD 2.16) whose data were available at the end of the treatment as well as at the follow-up. Similarly a small, clinically relevant 1MWT effect size (Cohen’s d 0.46) was found among 106 patients (6.02 years, SD 2.17).

Conclusions: With this novel method we can precisely quantify and monitor the response and effect of treatment on the walking capacity over a period of six months in children with CP, GMFCS level I and II, using the generated 6MWT and 1MWT reference centiles.

Disclosure: No potential conflict stated.

P08-23

Dyke-Davidoff-Masson Syndrome: a case report in a Filipino male adolescent

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Introduction: A 17-year-old Filipino male presented with recurrent left focal seizure with secondary generalization. Born of a non-consanguineous marriage, home-delivered, full term with no perinatal complications.

Method and Results: Had normal growth and developmental milestones until at 7-months-old when he had febrile encephalopathy. Since then he was left with residual left hemiplegia, dysarthria, cognitive delay and recurrent seizures occurring twice daily. He was able to go to school with minimal supervision, neither medical consult provided, nor medications given, thereafter, until he had repeated seizure at the age of 16. Refractory seizures, hemiparesis, facial asymmetry, and intellectual disabilities along with brain imaging evidence of cerebral hemi-atrophy with compensatory calvarial thickening and subsequent hyperpneumatization are consistent with Dyke-Davidoff-Masson Syndrome (DDMS).

Conclusion: A rare clinico-neuroradiologic condition occurring in fetal or early childhood period as a consequence of chronic brain insult. Diagnosis is established clinically with characteristic brain imaging findings. Multidisciplinary intervention is essential, primarily to optimize seizure control as well as provide quality of life.

Disclosure: No potential conflict stated.
**P08-24**

First report of ictal self-harm in a child with a Generalised Seizure Disorder with Absences and Eyelid Myoclonus

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Introduction: Ictal self-mutilating behaviours (SMB) are uncommon but well described in frontal/temporal lobe epilepsies. We describe a 9-year old child with drug-resistant idiopathic generalised epilepsy (IGE) with SMB.

Methods: A case review with home video-EEG-telemetry recording.

The birth & early developmental history were unremarkable. The child's seizure onset was in late infancy and consisted of staring blankly, eyelid flickering and with motor/hand automatisms. Her seizures occur daily and are drug-resistant. She has moderate learning disability.

Extensive testing (neurometabolic, gene panel including SLC2A1 and neuroimaging) was negative. Over the past year mother had complained of her 'picking' at parts of her body, usually her face (ears/gums/lips) and her nails & biting her fingers with her seizures, not at other times. In clinic scars could be seen in these areas.

A home video-EEG captured about 120 of her habitual seizures, activated by hyperventilation, photic stimulation and slow eye closure.

Results: The seizures were characterised by behavioural arrest with eyelid & forehead myoclonus, followed by bimanual complex automatisms. During these she at times put her hand in her mouth which her mother would promptly pull away and when banging her hands or trying to hit herself, her mother also interceded.

This supported mother’s description of the self-harm behaviours being related to her automatisms. The ictal EEG showed 3-4Hz generalized spike-and-wave discharges with a normal background, in keeping with absences. However the early age of onset, associated forehead and eyelid myoclonus and unusual automatisms were very peculiar, and not typical of Jeavons.

Conclusion: To our knowledge this is the first report of SMB in a child with an IGE and it queries our understanding of this phenomenon previously attributed to focal seizures exclusively.

Disclosure: No potential conflict stated.

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**P08-25**

Influence of cognitive and behavioural comorbidities on the level of Depression and Anxiety among children with Epilepsy

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Aim: To evaluate the impact of cognitive and behavioral comorbidities such as specific learning disorders or ADHD on the level of depression and anxiety among children with epilepsy.

Methods: 104 children with epilepsy aged 8-15 years with IQ>70 attending regular elementary schools were involved in the research. Participants completed Czech version of the Children’s Depression Inventory Scale and Freedom of Anxiety domain from the Piers-Harris self-concept questionnaire. Non-verbal intelligence was measured using Raven’s Progressive Matrices, cognitive and behavioral comorbidities were diagnosed using standard methods.

Results: Children suffering from epilepsy with specific learning disability and/or ADHD (n = 45) achieved significantly higher average scores compared to the children population’s norms (15.2 ± 9.5 vs. 8.7 ± 5.3; p = 0.006). However, values comparable to mean pediatric population (9.4 ± 9.9; p = 0.563) were recorded in children with epilepsy without these comorbidities (n = 59). The degree of freedom from anxiety in children with epilepsy and the comorbidities was not significantly different from in general population, or in children with epilepsy without the comorbidities. We demonstrated a significant negative effect of lower non-verbal intelligence on freedom from anxiety (r = 0.248, p = 0.011) and depression rate (r = 0.199, p = 0.043) and a significant correlation between the level of depression and freedom from anxiety (r = 0.673; p < 0.001).

Conclusion: Children with epilepsy and one of the comorbidities (ADHD, specific learning disability) are more likely to suffer from depression than the general population. On the contrary, prevalence of depression among children without this comorbidity is comparable to that in the regular population. Freedom from anxiety is equal in both groups, regardless of the presence of learning disability or ADHD.

Disclosure: No potential conflict stated.
A new guideline on the management of Spasticity in Hereditary Spastic Paraplegia

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Introduction: Hereditary spastic paraplegia is a group of clinically and genetically diverse disorders that result in progressive and generally severe lower extremity weakness and spasticity.

Method and Results: A guideline was prepared based on consultation with experts and regional specialist practice (Level D Evidence) supported by Level A-C evidence for individual treatment options. The guideline includes mode of action, dosage suggestions, side effect profile and cautions for the treatment modalities and summarises key management steps in a flow chart.

Management is based on identifying clear and realistic goals in three areas: improving mobility, increasing range of motion and relieving spasticity. These goals can be achieved through a combination of physiotherapy, medical agents and, occasionally, surgery.

As a first step, a trial of Dopamine should be considered if the diagnosis of HSP is in doubt. Furthermore some forms of HSP have shown response to Dopamine. Oral Baclofen is used as a first-line anti-spasticity drug followed by Gabapentin and Ti zanidine. Intrathecal Baclofen in selected patients has shown promising results; this should be considered early in eligible patients if oral medication is failing to achieve desired spasticity control or side effects limit oral dosing.

The evidence for the use of botulinum toxin in HSP is limited and unclear. Its benefits are greatest when combined with therapy and splinting. Diazepam can be used as an adjunct to other oral medications. Selective Dorsal Rhizotomy should only be considered for uncomplicated stable HSP when all other treatments have failed and quality of life is severely affected.

Conclusion: Managing spasticity well in patients with HSP can immensely improve their quality of life. We propose a standardised referral and management pathway that summarises the approach to treatment modalities for patients with HSP.

Disclosure: No potential conflict stated.
P08-28

Features of Autosomal Dominant Nocturnal Frontal Lobe Epilepsy in patients with mutations in the KCNT1 gene

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Introduction: Autosomal dominant nocturnal frontal lobe epilepsy (ADNFLE) is a family idiopathic focal epilepsy characterized by cluster seizures emanating from the frontal lobe of the cerebral cortex during slow sleep. The cause of the disease is some mutations in the genes: DEPDC5, CHRNA4, CHRN2, CHRNA2, KCNT1 and CRH. Mutations in the KCNT1 gene occur in less than 5%.

Objective: To analyze the course of ADNFLE in patients with some mutation in the KCNT1 gene.


Results: In all the cases, the mutations were de novo. The age of epilepsy onset was from 4 months to 2 years old. All the patients had nighttime hypermotor attacks with a cluster course from 2 to 7 attacks per night, from 5 to 33 seizures per month. Two patients had rare daily attacks in the form of focal seizures and tonic-clonic seizures. Interictal EEG revealed epileptiform activity in the fronto-temporal region in two cases; in one - there were no changes. Two patients had pharmacoresistant course: carbamazepine, oxcarbazepine, valproic acid, levitiracetam, topiramate, lamotrigine, and phenobarbital were not effective. One patient’s (c.2630C>T (p.A877V)) seizures were stopped by the combination of levitiracetam and valproic acid (but seizures became more frequent with carbamazepine intake). Psychiatric and behavioral problems were moderate in the patients with pharmacoresistant course and mild in the patient without seizures. Vagal nerve stimulation (VNS) therapy was used in one case. 7 months after implantation, the seizures became less frequent by 50-75%.

Conclusion: The most favorable course of epilepsy is observed in our patient with mutation c.2630C>T (p.A877V). VNS can be an effective treatment for pharmacoresistant ADNFLE.

Disclosure: No potential conflict stated.

P08-29

The first case of identification of KCNMA1 mutations in a child with a clinical diagnosis of juvenile Absence Epilepsy in Ukraine

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Introduction: Initially, the KCNMA1 mutations were illustrated in a large family with generalized epilepsy and paroxysmal nonkinesigenic dyskinesia [Du W, 2005]. Homozygous KCNMA1 mutation manifests with cerebellar ataxia, developmental delay, and seizures, but heterozygous KCNMA1 mutation with autosomal dominant inheritance will manifest only with absences and generalized tonic-clonic seizures.

Aim: To present the case of a correct etiological diagnosis of genetically determined epilepsy.

Method: A 17-year-old boy has been observed by a pediatric neurologist for 6 years with a diagnosis of Juvenile absence epilepsy. He receives valproate, he is free of seizures for 5 years. He feels well. Mother noticed the delay of the view-absence from 8 years, but did not consult doctors. The first and only generalized tonic-clonic seizure occurred after the sleep deprivation when the boy was 11 years old. During the month a clinical diagnosis was made: Juvenile absence epilepsy. It was confirmed by EEG and effective treatment was prescribed. At the age of 17, the boy’s parents agreed to a genetic testing using the gene panel (187) for epilepsy to identify genes in juvenile absence epilepsy (CLCN2).

Results: As a result, this gene mutation was not detected, but the mutation c.460G>T (p.Ala154Ser) was identified in KCNMA1. Heterozygous inheritance. Anamnesis of life has not been changed. The boy was born healthy from healthy parents whose relatives did not have epilepsy and other neurological diseases. So we have changed the diagnosis.

Conclusions: It is the first case in Ukraine. This case indicates the correct way to diagnose epilepsy from clinical to etiological with the obligatory use of genetic methods, but further collection of material is needed to determine the therapeutic tactics and duration of therapy.

Disclosure: No potential conflict stated.
Use of the Rehabilitation Complexity Scale to assess dependency and rehabilitation complexity in children receiving in-patient Neurorehabilitation at a Regional Neuroscience Centre (RNSC)

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Objective: To explore the feasibility of using the Rehabilitation Complexity Scale (RCS) to assess rehabilitation needs in children receiving in-patient neurorehabilitation in a RNSC.

Background: The RCS is established in adult rehabilitation for assessing complexity of care and therapy needs. Little data exist concerning its use in paediatric neurorehabilitation.

Methods: Children receiving specialist in-patient neurorehabilitation were scored on the RCS-Extended (RCS-E) by the multi-disciplinary team at weekly neurorehabilitation meetings over 15 months. Patients’ functional status was scored simultaneously by King’s Outcome Score for Childhood Head Injury (KOSCHI) and Modified Rankin Scale (MRS). Demographic details were recorded from the neurorehabilitation database. Statistical analyses were performed using IBM SPSS Statistics Version 21.

Results: 180 RCS-E, KOSCHI and MRS assessments were obtained in 34 patients, mean age=7.6 years (range 0.1-17). 43% were male, 57% female. 78% had ABI. There were significant differences between RCS-E scored on neurorehabilitation admission (mean=12.97, SD=2.48) and hospital discharge (mean=9.50, SD=3.70), the paired t test for total RCS-E (p<0.001), for care (p<0.001) and therapy subscales (p<0.001). Admission total RCS-E did not predict neurorehabilitation duration (r=0.26, p=0.10), but there was a relationship between rehabilitation duration and discharge total RCS-E (r=0.40, p=0.005). In ABI patients, correlations were seen between admission and discharge RCS-E and contemporaneous KOSCHI (admission, r=-0.60, p<0.001; discharge, r=-0.75, p<0.001) and MRS (admission, r=0.76, p<0.001; discharge r=0.74, p<0.001). However, total RCS-E on neurorehabilitation admission did not predict discharge functional status, assessed by KOSCHI (r=0.12, p=0.55) or MRS (r=0.09; p=0.65).

Conclusion: The RCS-E is easy to use in paediatric neurorehabilitation practice, although there are issues around the applicability of definitions of care need. The measure is sensitive to change over time and correlates with functional status.

Disclosure: No potential conflict stated.

Treatment Resistant Epilepsy and Spasticity in Infantile Ceroid Lipofuscinosis (INCL): a case report

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Introduction: INCL, or Santavuori-Haltia’s disease, is a progressive neurological disease caused by a mutation in palmityl–protein thioesterase-1 (PPT) on chromosome 1(p32). The incidence in Finland is high at 5/100,000 live births per year. Children appear to develop normally, but start regressing from 12 months and develop epilepsy by 2.5 years. Death occurs between 9-13 years.

Case report: This case report focuses on a 3-year-old boy, from a district general hospital in Finland, with a particularly aggressive disease. He had been under physiotherapy follow-up for motor delay and paucity of movements when he had his first seizure at 1.6 years of age. He soon developed myoclonic status epilepticus. The electroencephalography (EEG) taken during the seizure showed multiple bilateral spike slow wave discharges, with some focus in the parietal region. He was started on sodium valproate, with improving EEG results. MRI showed cerebral atrophy, thalamic abnormalities and white matter signal changes. The specific MRI changes were highly suspicious of INCL. Genetic diagnosis confirmed the most common PPT mutation in Finland; c.364A>T, p.Arg122Trp.

This patient’s epilepsy and spasticity has been challenging. He has required levetiracetam, topiramate, lamotrigine, clonazepam and baclofen pump in addition to sodium valproate. He was started on baclofen, tizanidine and levomepromazine for spasticity. Gastrocnemius Botox injections, fentanyl plasters and a baclofen pump were also trialled. Despite increasing doses of anti-epileptics, the seizures became more prolonged, requiring multiple phenobarbital courses.

Conclusion: This is an interesting case of INCL due to its particularly aggressive nature at an early age. Although the threshold for suspecting this disease is low in Finland, management of this life-limiting illness is difficult and requires a multidisciplinary approach.

Disclosure: No potential conflict stated.
**POSTER PRESENTATIONS > POSTER SESSION 8**  
Epilepsy: miscellaneous, Neurorehabilitation

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**P08-32**  
**Children’s adherence to antiepileptic medication: does socioeconomic status play a role? A systematic review**  
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**Introduction:** Low adherence to prescribed therapeutics remains an important cause of poor seizure control in paediatric epilepsy. This study aims to examine whether socioeconomic status (SES) can explain patterns of nonadherence to antiepileptics in the paediatric population.

**Methods:** A systematic search was performed independently by two authors using the PubMed database. Results were then corroborated. Search-term groups were summarised by the terms ‘paediatric’, ‘antiepileptic’ and ‘socioeconomic’. Peer-reviewed articles published between 1969 and 2019 were included, with no language or geographical restrictions. Studies reporting adherence following epilepsy surgery were excluded. Outcomes were compared between studies which used similar SES measurements. Study quality was assessed using a modified version of the ‘CEBM Level of Evidence tool’.

**Results:** The search identified 1089 studies, 10 of which met the inclusion criteria. Adherence was measured using either electronic medication caps (which measure regularity of medication use), drug levels on blood testing or by self-report. SES was determined based upon education, occupation and income. Seven studies demonstrated poor adherence among children with a lower SES. Three studies reported no relationship but were classified as being of low methodological quality or used less reliable markers of SES.

**Conclusion:** Children living at lower levels of SES show lower adherence to antiepileptic medication. They are consequently at higher risk of persistent seizures and associated deficits in cognitive function and development. This second point, however, has not been clearly demonstrated in the same literature. Intermediate factors, such as level of education, single-parent status and other family ill-health, are not consistently described. Targeting strategies and interventions to improve medication adherence of children from lower socioeconomic status families may be beneficial in long-term management of seizures.

**Disclosure:** No potential conflict stated.

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**P08-33**  
**Periodical Lateralized Epileptiform Discharges (PLEDs) with Hippocampal Atrophy in a child with past medical history of Benign Focal Epilepsy**  
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**Introduction:** PLEDs are EEG abnormalities consists of repetitive spike or sharp wave discharges, which are focal or lateralized over one hemisphere or bilaterally (BIPLEDs). PLEDs have been associated with cerebral infarctions, encephalitis, tumor or demyelination.

**Method:** We present a boy of nine years old who is referred to our clinic with somnolence, with brief episodes of disturbances of consciousness and sometimes focal epileptic seizures and focal and generalized episodes in the last month. He has a past medical history with focal seizures with good response to the antiepileptic treatment (oxcarbazepine). The lab tests were without abnormal findings. The sleep EEG consists of bilaterally (BIPLEDs) and sometimes focal (PLEDs) abnormalities. The CT and MRI brain were without abnormal findings. Various combinations of antiepileptic drugs were ineffective. The patient was submitted in pulses of methylprednisolone (MTP) for three days with clinical and EEG improvement. Brain Spectroscopy revealed atrophy of the right hippocampus.

**Result:** The patient was submitted in pulses of MTP for three days with clinical and EEG improvement. Brain Spectroscopy was held and revealed atrophy of right hippocampus.

**Conclusion:** PLEDs in a healthy child with former diagnosed benign focal epilepsy is a rare entity and always must be followed by an extended electrographic, clinical and radiological studying. The effectiveness of MTP arise the possibility of inflammatory process regarding the atrophy of hippocampus.

**Disclosure:** No potential conflict stated.
P08-34

Motor Dysfunction in Neurofibromatosis Type 1 with normal neurological examination: a muscular problem?

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Objective: Neurofibromatosis type 1 (NF1) is a multisystemic genetic disorder. Subclinical impairment of motor function and coordination may affect quality of life. We examined motor skills of children with NF1 and normal neurological examination in comparison with healthy control subjects (HC).

Method: Patients (n=41, 21 female, 20 male) and HC (n=32, 17 female, 15 male) 3-18 years were evaluated by an experienced and blinded physiotherapist using GMFM-88 scoring for gross motor function, Beighton scoring for hypermobility, 6-minute walking test for cardiorespiratory endurance, sit-to-reach test for flexibility. Strength was evaluated in 15 muscle groups by manual testing. Data were analyzed using SPSS(20.0).

Results: The NF1 group scored lower in the Walking, Running & Jumping section of GMFM-88. Hypermobility was found in 9/28 NF1 patients <11 years and 2/20 same age HCs (p>0.05). Six-minute-walking test results were mean 525.46±90.7 m in NF1 and 590.96±95.9 m in HC (p<0.05 before and after controlling for age and height). Sit-to-reach test showed more flexibility in NF1 <11 years than same age HCs. The NF1 group had lower strength scores considering age and sex: deltoid, iliopsoas, gluteus maximus, gluteus medius were weaker in females <11 years; iliopsoas in males >11 years, gluteus maximus, iliopsoas, in females >11 years.

Conclusion: The NF1 gene product, neurofibromin, has a role in muscle growth and metabolism. Therefore motor impairment may be expected independently of neurological abnormalities. The weakness in proximal muscles in NF1 (shoulder and hip belt) can result in lower scores in Walking, Running & Jumping in GMFM-88 and poorer performance in 6-minute walking test. Although hypermobility wasn't significantly different, a considerable number of <11 year-olds had increased mobility, suggesting compensation by age and usage. Age- and sex-related differences in affected muscle groups need to be investigated further in larger series.

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P08-35

Comprehensive approach to Paediatric Rehabilitation: creating a structured model of Neurorehab for social competence training in children

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Introduction: Social competence (SC) is a multidimensional concept reflecting the capacity to integrate behavioral, cognitive and affective skills to social contexts. It is critical to know the underlying neuropsychological mechanisms of SC to choose the most effective treatment options. The aim of this study was to create a theoretical model of the main components of SC to develop and adapt appropriate interventional devices for children with neurological disorders (ND).

Methods: The main components of SC: emotion perception, social attention and social anxiety, were evaluated using the Social domain in NEPSY-II assessment battery; Theory of Mind (ToM) skills were evaluated using ToM Stories test; executive functions using parents’ questionnaire BRIEF-P; social skills using two parents’ questionnaires: Social Cognition Questionnaire and Social Skills Rating System. To develop interventional devices 30 children with ND: epilepsy, traumatic brain injury, tics or stroke - and 10 healthy controls aged 8-13 years were included. Patients were trained using interactive computer-based applications on multitouch-multisensor tablet tops (MMT): Snowflake MultiTeach (MT) and Diamond Touch Table (DTT), plus virtual reality (VR) platform.

Results: We created a Structured SC Neurorehab model using modern technologies. At baseline, the patients demonstrated social incompetence compared to healthy controls. Trainings based on the structured intervention model showed improvements in patients in executive and cooperation skills, and coping with difficult social situations using Snowflake MT. Communication, language and metacognitive skills improved using DTT platform. Social anxiety decreased and emotion perception improved using VR techniques.

Conclusions: The Structured Model of Neurorehab for Social Competence helps to understand the theoretical connections between components of SC and suitable interactive platforms in the rehabilitation process. This will encourage more therapists to implement these modern interactive devices.

Disclosure: No potential conflict stated.
P08-36

**Drug Resistant Epilepsy in infant with GRIN2A, SPTAN1 and SCN2A mutations and probably Congenital Cytomegalovirus Infection**

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**Objective:** Presentation of the female twins, one with drug resistant epilepsy and GRIN2A, SPTAN1 and SCN2A mutations. Both girls also with probably congenital cytomegalovirus infection.

**Methods:** Genetic analysis was performed using NGS method and cytomegalovirus infection was confirmed by PCR methods and serological tests. Electroencephalography and neuroimagin examinations were conducted and repeated.

**Results:** Female twins were born at term by cesarian section, from the 1st IVF pregnancy. In epileptic infant polymorphic seizures started at the age of 3 month. She demonstrated different types of seizures (tonic, clonic, myoclonic, infantile spasms, gelastic). EEG at the onset was normal, but then hypersynchrony appeared. Repeated brain MRI examinations revealed normal results. GRIN2A, SPTAN1 and SCN2A mutations were found in epileptic girl, but her healthy sister has also SPTAN1 mutation. In mother GRIN2A, SPTAN1 and SCN2A mutations were absent. WES analysis in epileptic infant was negative. Epileptic seizures were resistant to many antiepileptic drugs, ACTH and ketogenic diet therapy. Drug resistant epilepsy will be treated with VNS. Infant with genetic epilepsy and intensive cytomegalovirus infection (neuroinfection was excluded) required also antiviral treatment with intravenous ganciclovir and oral valganciclovir especially during and after ACTH therapy. She has cerebral palsy with microcephaly. In her sister cytomegalovirus infection was confirmed at the same time (at the age of 2 month), but she was not treated antivirally. Now she is 2 years old and is healthy and with normal psychomotor development.

**Conclusion:** In epileptic infant SPTAN1 mutation was not pathogenic. Cytomegalovirus infection was probably congenital and may be acquired at the end of pregnancy.

**Disclosure:** No potential conflict stated.

P08-37

**DAT Questionnaire – Early detection of disorders associated with Dravet Syndrome (DS)**

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**Introduction:** Children with DS are known to be in risk for cognitive, behavioural, educational, psychosocial and psychiatric comorbidities. That represent a significant burden for the families.

**Aim:** We aimed to establish an approximate frequency of characteristics and comorbidities of DS beyond seizures, identify top concerns among caregivers, and provide direction for clinicians in care of DS patient and whole family.

**Methods:** Parents of 21 children with DS were interviewing using DAT questionnaire. The questionnaire was formed modelled on similar checklist concerning chronical neurological diseases. It cover 8 areas where difficulties may be expected and are important to detect timely: the course of early development, level of functionality in speech, self-care and mobility, the presence of various behavioural difficulties, specific psychiatric disorders, intellectual functioning level, learning and specific cognitive difficulties and family relationship functionality. For each area, information whether the subject had assessment and support was investigated.

**Results:** High frequency of development and intellectual disorders, speech/language delay, mobility impairment, sleeping and feeding difficulties, socioemotional and adapting behaviour problems comorbidities were confirmed. Importantly, our results clearly showed that an overall system support and help for children and parents, related to early detection and treatment of these specific disorders associated with DS, in our country is insufficient.

**Conclusion:** DAT questionnaire might provide an insight in specific but changeable “DAT profile” of individual with DS, both for verification of existing comorbidities and healthcare prioritization. We suggest that DAT questionnaire should be used in regular manner in every child with DS.

**Disclosure:** No potential conflict stated.
P08-38

Transition in Epilepsy – Croatian experience

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Introduction: Definition of transition according to American Society for Adolescent Medicine is targeted and planned follow-up of adolescents and young adults with chronic somatic and psychological diseases from pediatric health care to adult care. Despite all improvements in diagnostic and therapeutic care there is still a considerable number of pediatric patients with epilepsy and epileptic syndromes who have a permanent need for neurological care and treatment. The objective is to use current knowledge and gather new information in order to improve the process of transition in epilepsy.

Methods: Adolescents with epilepsy who became patients in adult care were given questionnaires specifically formed for them. Parents of these adolescents were also given a tailored questionnaire to gather information on their experience during or after transition. They were asked about their expectations, reality and suggestions for improvement in the process of transition of adolescents with epilepsy.

Results: Collected data indicated specific areas which could be improved, especially in preparation for the process. Adolescents included in this study had epilepsy for 15 years on average. 80% of adolescents considered pediatrics department to be the best place for their treatment, while 80% of parents questioned, didn’t know what transition was. Over 80% of parents considered appropriate to join their adolescents during neurologist visits. In 8% of adolescents, there was a change in diagnosis upon transferring to adult neurologist. Younger age was suggested for the onset of transition, as well as formation of specific transition clinics.

Conclusion: This survey enabled us to define areas that need improvement, and will guide us in formation of nationwide algorithm for transition of adolescents with epilepsy.

Disclosure: No potential conflict stated.

P09-01

SPG15 presenting as Early Onset Parkinsonism in a teenager: a case of Levodopa responsiveness

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Introduction: Hereditary spastic paraplegias (HSPs) are neurodegenerative and heterogeneous diseases that are clinically distinguished according to the presentation of signs and symptoms. Autosomal recessive hereditary spastic paraplegias with thin corpus callosum (AR HSP-TCC) are rare and complex disorders characterized by a genetic heterogeneity of which several genes (SPG11 and SPG15, SPG21, SPG47) have been identified. In SPG15, additional features have been described as mental retardation, motor neuropathy, dystarthisis and recently parkinsonism.

Methods: Clinical, genetic and neuroimaging retrospective data review.

Results: A 13-year-old male patient, born to non-consanguineous and healthy parents, was admitted because of a progressive gait disturbance and cognitive deterioration. He was healthy until 10 years old, when he noticed gait difficulties and dystarthisis, followed one year later by cognitive deterioration. These symptoms gradually progressed. Clinical examination demonstrated spastic paraplegia with bilateral extensor plantar reflexes and mild proximal motor deficit in the lower limbs, moderate bilateral akinesia, hypertonia, and hypomimia. Brain MRI showed thin corpus callosum with periventricular white matter changes. Molecular analysis of ZFYVE26/SPG15 gene detected a homozygous frameshift mutation c.918delA with both parents being heterozygous carriers. Patient was started on levodopa with improvement on gait, bradykinesia and facial hypomimia symptoms.

Discussion: Juvenile and young onset levodopa-responsive parkinsonism, which occurs before 20 and 40 years, respectively, may present as pure parkinsonian phenotype or may be more complex, including pyramidal signs. Among AR HSP-TCC, SPG11 was proposed as a cause of atypical juvenile parkinsonism, but SPG15 demonstrating parkinsonism has been previously reported in only two families. Our case strengthens evidence that levodopa-responsive parkinsonism may be an early feature of SPG15 and should be searched for in the case of juvenile levodopa-responsive parkinsonism in combination with spastic paraplegia.

Disclosure: No potential conflict stated.
P09-02

The applicability of the Scale for Assessment and Rating of Ataxia (SARA) in toddlers

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**Background:** In children, the Scale for Assessment and Rating of Ataxia (SARA) can quantify ataxia, but outcomes should be interpreted for age. In toddlers, age-related SARA control values are still lacking.

**Objective:** In healthy toddlers, we aimed to evaluate: 1. the feasibility of SARA performances and 2. the reliability of SARA sub-score tasks.

**Methods:** Six investigators assessed videotaped SARA performances in 42 healthy toddlers, respectively 2 (n=17), 3 (n=12) and 4 (n=13) years of age. We expressed SARA-feasibility as the % of children that were able to perform the SARA (sub)-score tasks. We expressed the reliability of scores by Intraclass Correlation Coefficients; ICC.

**Results:** At 2, 3 and 4 years of age, respectively 0%, 67% and 85% of the children were able to perform the complete set of SARA tasks. At 2, 3 and 4 years of age, incomplete SARA tasks were associated with insufficient attention span and with immaturity of the motor system (in 100%, 33%, 15% resp. and in 100%, 100% and 77%). Comparing SARA scores between children of 2 versus 4 years of age revealed significantly lower (better) scores in the last [mean SARA total: 21.0 vs. 7.0; p<.05 (Kruskall Wallis)]. ICC values were ‘fair’ in toddlers at 2, 3 and 4- years of age (Landis-Koch; ICC .322, .274 and .357 resp., ns). These outcomes could partly be influenced by a low variation in scores.

**Conclusion:** In toddlers, the feasibility of SARA subscore performances increases between 2 to 4 years of age. In the future, we aim to study the effect of a modified SARA scale in accordance with the physiological age-related cognitive and motor capacities of young children.

**Disclosure:** No potential conflict stated.

P09-03

Stabilisation of Progressive Dystonia with sequential STN DBS and ITB in a case of Pantothenate Kinase associated Neurodegeneration

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**Introduction:** We present the case of a 13 year old boy with early onset, severe and progressive dystonia parkinsonism due to pantothenate kinase associated degeneration (PKAN) who benefitted from sequential multimodality neuromodulation.

**Method and Results:** He was considered for compassionate Deep brain stimulation (DBS) for refractory dystonia at the age of 11 years with bilateral Globus pallidus interna and subthalamic nuclei (STN) implantation. Bilateral STN DBS led to sustained and objectively documented clinical, quality of life and occupational measure scores improvement. 1 year after DBS, there was stagnation of further clinical improvement with increasing periods of laryngeal and truncal dystonia for which intrathecal baclofen (ITB) pump therapy was instituted. The patient has had sustained symptom improvement for 1 year since ITB addition and this is reflected in parental reports, objective measures and sequential video recordings.

**Conclusion:** Our experience adds to a small number of cases with PKAN associated dystonia who have benefitted from STN DBS and provides evidence of clinical efficacy with concurrent ITB and DBS, which have individually been reported to be beneficial in some cases with PKAN.

**Disclosure:** No potential conflict stated.
A single centre experience of diagnostic yield in Ataxia in childhood

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Introduction: Childhood ataxias are a heterogeneous group of disorders, of which several remain undefined. Our objective was to report diagnostic yield of childhood ataxia in a quaternary clinic in the United Kingdom.

Methods: A retrospective case note analysis of 58 children/young people with ataxia from a quaternary clinic in the United Kingdom, between December 2010 and October 2018.

Results: A total of 33/58 (~57%) had an identifiable cause of ataxia. 12/58 (~21%) had Friedreich’s Ataxia; 5/58 (~9%) had Ataxia Telangiectasia; 2/58 had Spinocerebellar Ataxia 7 (SCA 7). 2/58 had ataxia following acquired traumatic brain injury (one following a cerebellar AVM bleed); 2/58 presented with acute ataxia with residual ataxia, in one case following rotavirus-associated cerebellitis. 17/58 (~29%) had cerebellar atrophy/hypoplasia of unknown aetiology, with MRI spectroscopy changes in 2 patients. 3/58 had a recurrent intermittent ataxia of uncertain aetiology, one of whom went on to receive a diagnosis of epilepsy. 3/58 had an ataxia of a dominant inheritance pattern (unidentified gene). 1/58 had an ataxia of uncertain aetiology associated with epilepsy and learning difficulties. 1/58 had each of the following: cerebellar AVM, hydrocephalus, inherited TTBK2 gene mutation, inherited mitochondrial DNA m.3243A>G mutation, chromosomal microdeletion including the FGF14 gene, congenital cerebellar malformation, progressive ataxia with a POLR3B mutation, P-O channelopathy, Episodic Ataxia type 1 (KCN1A mutation), Episodic Ataxia type 2, and Lhermitte-Duclos disease.

Conclusion: 33/58 (~57%) children/young people with ataxia in our cohort had a confirmed diagnosis. Diagnosis was made on clinical presentation, neuroimaging methods including MR spectroscopy, and serial brain MRI in case of cerebellar atrophy. We anticipate an increase in diagnostic yield with targeted genetic testing with ataxia gene panel.

Disclosure: No potential conflict stated.

Tone abnormalities and feeding difficulties in Allan-Herndon-Dudley Syndrome (AHDS): recognition of the natural history

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Objectives/Introduction: Allan-Herndon-Dudley syndrome, also known as monocarboxylate transporter 8 (MCT8) deficiency or tri-iodothyronine (T3) resistance, is an X-linked recessive hereditary condition caused by mutations in the SLC16A2 gene on the Xq13 chromosome.

Methods: A retrospective case analysis of three children genetically confirmed (SLC16A2 mutation) Allan-Herndon-Dudley syndrome for the natural history and clinical presentation.

Results:
1) A boy had early motor developmental impairment in infancy with variable tone and intermittent dystonia, strabismus, and white matter (WM) hypomyelination on MRI brain. By age 3 years, he had difficulty with dystonic spasms, feeding difficulties needing gastrostomy feeding and was non-ambulant.
2) A boy with a background early developmental impairment and severe intellectual disability had recurrent dystonic spasms presenting frequently in status dystonicus. He had gut dysmotility and feed-induced dystonia by 7 years of age. MRI brain revealed WM hypomyelination.
3) A boy with early developmental impairment, strabismus, feeding difficulties, a central motor disorder with central hypotonia and peripherally increased tone by 18 months of age. MRI brain revealed WM hypomyelination.

All 3 patients had evolving tone abnormalities, feeding difficulties, as well as thyroid function/free T3 level, and white matter myelination abnormalities. For the first two patients, dystonic spasms became progressively more problematic with age. Gut dystomotility was confirmed in patient 2, and feeding difficulties are present in patients 1 and 3.

Conclusion: AHDS should be considered as a differential diagnosis in a male with developmental impairment, an evolving cerebral palsy type picture with dystonia and evolving tone abnormalities, and white matter hypomyelination changes on MRI. Early diagnosis of tone abnormalities and feeding difficulties is important, to ensure more timely management.

Disclosure: No potential conflict stated.
P09-06

Functional parameter measurements in Ataxia Telangiectasia – A cross sectional study

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Aim: Ataxia telangiectasia (AT) is a neurodegenerative disorder of cerebellum, with multisystem involvement. Disease course is influenced by the progressive neurologic symptoms, and decreased abilities due to multisystem involvement, but longitudinal functional data is lacking. Our aim was to collect preliminary functional data which creates a frame for a disease specific scale.

Methods: Retrospective information of AT patients referred to the Assistive Technology Unit, was included in this study. Functional mobility scales and ADL parameters were recorded. We created a 51-point functional scale (ATFS) consisting of 3 ambulation items (home, school, outdoors), 5 ADL items and schooling.

Results: 27 participants, age 10.6±5.1, were enrolled and 168 measurement recorded. Patients walked at a mean age of 1.38±0.45 and lost ambulatory capacity at 8.65±2.1 years. Functional mobility scales (median GMFCS-4/FMS 5-2/FMS 50-1.5/FMS 500-1) correlated with age (Spearman correlations r=0.555, -0.617, -0.639, -0.662, p<0.01), but plateaued after 12 years of age. AT functional scale (ATFS) mean score was 37.46±7.88 (range 16-51), increased with age (Spearman correlation r=0.585, p<0.01), and showed progression also after wheelchair dependence.

Conclusion: In this study we show longitudinal functional data of ambulation and ADL skills in AT, and created a frame for a functional scale.

Disclosure: No potential conflict stated.

P09-07

Secondary Enuresis and urological manifestations in children with Ataxia Telangiectasia

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Objective: Ataxia telangiectasia (AT) is a neurodegenerative cerebellar disorder, caused by mutations in the ATM gene, involved in DNA repair. Radiosensitivity, progressive ataxia, immune deficiency and malignancies, are well known symptoms, but urological manifestations are scarcely described. Our aim was to characterize urologic manifestations in a large cohort of AT patients.

Methods: Retrospective cross-sectional chart study comprising 52 AT patients followed at a National AT Center.

Results: 25% of the cohort (13 patients/8 males) had urologic symptoms, which presented at 11±4.3 years. The most common symptom was secondary enuresis affecting 15% of the patients (8 children/4 males). Incontinence appeared at 8±6.2 years of age, and resolved spontaneously within 15±8.3 months in 6 patients. It preceded loss of ambulatory capacity by 1-2 years in 7 patients. Lumbosacral MRI were normal (4 children) and urine cultures (all) were negative. Urodynamic evaluation that was performed in only one patient revealed overactive bladder. Additional manifestations were macroscopic hematuria due to bladder telangiectasia in a 12-year-old, and renal cell carcinoma in a 22-year-old. Other manifestations unrelated to AT were nephro lithiasis, vesico-ureteral reflux and scrotal pain, each in 1 patient.

Conclusion: Transient secondary enuresis is a frequent finding in AT patients. Understanding this phenomenon might clarify the role of cerebellum in micturition.

Disclosure: No potential conflict stated.
Expanding the phenotypic spectrum of CACNA1 gene mutation

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**Introduction:** CACNA1 gene mutation is associated with familial hemiplegic migraine type 1, episodic ataxia type 2, and spinocerebellar ataxia type 6. Although ataxia is well known to be associated with this condition, other movement disorders like hyperekplexia, jitteriness and tremulousness are not well reported in CACNA1 disorders.

**Case study:** A baby boy born at 37 weeks gestation by vaginal delivery was admitted to Neonatal Unit at 2 hours of age for excessive jitteriness, exaggerated startle, sudden increased tone with stiffening or head nods on glabellar tap. He had two self resolving apnoeic episodes. Cerebral function monitoring and Electroencephalography were normal. He was diagnosed with hyperekplexia, commenced on Clonazepam. He responded well and was weaned off Clonazepam after 1 year. At 20 months, he presented with generalised tonic clonic seizures. He had 4 seizures during a 48 hour period. He was commenced on Sodium Valproate.

He has global developmental delay. At 3 years of age, he is able to stand with support and grasp objects. He is non-verbal. He is hypersensitive to loud noises and startles/gets upset with this. He has intermittent whole body tremors and jitteriness, predominantly when he is unwell or upset. Investigations including EEG, MRI brain and spine, metabolic tests, genetic tests including hyperekplexia screen did not yield any positive results. Further genetic analysis has shown a mutation in CACNA1 gene.

**Conclusion:** Myers et al,2016, reported 6 individuals with mutation in CACNA1 who had presented with epileptic encephalopathy, 2 of these children were also thought to have hyperekplexia. Our case describes a new condition with hyperekplexia, epilepsy, global developmental delay, tremors and jitteriness.

**Disclosure:** No potential conflict stated.

AADC Deficiency in Latin-America: improving diagnosis and awareness of a rare neurometabolic disease

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**Background:** Disorders of monoamine neurotransmitter metabolism have been increasingly recognized. These compounds have numerous roles including modulation of psychomotor function; hormone secretion; cardiovascular, respiratory, and gastrointestinal control; sleep mechanisms; body temperature; and pain. Aromatic L-amino acid decarboxylase (AADC) is central in the synthesis of biogenic monoamine neurotransmitters. AADC deficiency is a severe neurometabolic disorder, usually underrecognized, presenting early in life with hypotonia, hypokinesia, oculogyric crises, autonomic dysfunction, dysphoric mood, and sleep disturbance.

**Objectives:** To describe a cohort of patients with AADC deficiency

**Material and Methods:** Clinical, biochemical and radiological data retrospective analysis were reviewed, including the following items: demographic characteristics, genetic profile, and clinical manifestations.

**Results:** All patients showed normal body weights in the first few months of life. Their growth, however, began to slow down at the end of the first year, and their weight gain was minimal between 1 and 4 years of age, although all of them were treated with a combination of pyridoxine, dopamine agonists, and monoamine oxidase inhibitors. Neurological symptoms became evident in all patients during the first 6 months of life. Intellectual disability, truncal hypotonia, hypokinesia and hyperpomimia, dystonic movements and typical oculogyric crises in all patients. None of our patients had full head control, defined by the ability to hold their head upright in the sitting position, at their termination point in the study.

**Conclusions:** AADC deficiency is a neurotransmitter disorder with features presenting as early as in the first month of life. Hypotonia, hypokinesia, oculogyric crises and autonomic are clinical hallmarks of the disease and may lead to clinical suspicion. Clinical phenotype severity is variable, but the majority of patients show minimal motor development in the absence of treatment.

**Disclosure:** No potential conflict stated.
Systematic Movement Disorder evaluation including EMG assessment provides increased insight in children with Dyskinetic Cerebral Palsy

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Aim: Patients with dyskinetic cerebral palsy (CP) are often severely affected, difficult to treat and have fluctuating symptoms. With this study we aimed at developing a systematic approach with dystonia rating scales, imaging, aetiological search and electromyography (EMG) quantification of muscle tone for improved evaluation and follow-up.

Methods: Twenty-five children (age range 3.9-17.9, male/female ratio 17:8) with a diagnosis of dyskinetic CP prior to evaluation were included. All underwent an assessment of 1) Examination by a child neurologist and physiotherapist including functional level, joint mobility, reflexes and spasticity, 2) A video-based systematic evaluation and consensus-based non-blinded scoring of the movement disorder using the Burke-Fahn-Marsden Dystonia Rating Scale (BFM), Dyskinesia Impairment Scale (DIS) and Hypertonia Assessment Tool (HAT), 3) EMG recording, 4) Revision of MRI scans and search for genetic/metabolic aetiology.

Results: HAT assessment demonstrated dystonia in upper limb in 21 and in lower limb in 18. Mean total BFM score was 45.02 (range 0-85) and DIS level 38% for dystonia (range 0-72) and 13% for choreoathetosis (range 0-60). Sustained EMG activity was observed in 20/25 (16 in biceps brachii/4 in soleus). The diagnosis after evaluation was: dyskinetic CP (n=15), mixed dyskinetic/spastic CP (n=3), ataxic CP (n=1), unclassifiable CP (n=3) and Aicardi-Goutiere syndrome (n=3). Additional genetic testing with whole exome sequencing was performed in six patients, of whom one was normal, four are ongoing and one revealed a GRIN2A variant.

Conclusion: Variations in level of clinical measures of dystonia was found in dyskinetic CP, which correlated to the sustained muscle activity measured with EMG. Application of a systematic approach to classify dyskinetic CP by dystonia rating scales, imaging, aetiological search and quantification of muscle tone with EMG provided clinically useful information.

Disclosure: No potential conflict stated.
Conclusion: The detailed history, physical and neurological examinations of these cases and the correct definition of movement characteristics constitute the most important steps in the diagnosis. As in our patients, genetic diagnosis is useful for evaluating treatment options, predicting prognosis and genetic counseling.

Disclosure: No potential conflict stated.

P09-12

Spectrum of Alternating Hemiplegia of childhood – Experience of our clinic

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Introduction: Alternating hemiplegia of childhood (AHC) is a very rare neurodevelopmental disorder, caused by mutations in the ATP1A3 gene, characterized by recurrent episodes of temporary weakness or paralysis often affecting one side of the body. During some episodes the paralysis alternates from one side of the body to the other. Additional symptoms usually include intermittent abnormal eye movements, sudden triggered attacks of uncontrolled movements, dystonia or seizures.

Methods and results: 3 cases will be presented in detail, illustrating the clinical variability of AHC: a case with severe global development and pharmaco-resistant seizures, including severe status epilepticus, with onset in infancy, in whom the first unexplained hemiparesis occurred after age of 2, but also 2 other children with motor deficits attacks lasting for variable periods, with onset around the age of 2 years. If in the last 2 children the diagnostic was established based on clinical picture, in the first case the genetic testing helped to elucidate the etiology of the complex clinical picture.

Conclusion: The identification of a causative gene for AHC lead to a better understanding of the disorder and open new pathways for treatment. However, the disorder remains a challenge, in part, because of its rarity, complex and highly variable symptoms.

Disclosure: No potential conflict stated.
**P09-13**

**Intravenous Immunoglobulin therapy for childhood Fisher Syndrome**

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**Objective:** Fisher syndrome is an immune-mediated peripheral neuropathy, characterized by ophthalmoplegia, ataxia, and areflexia, mostly due to anti-GQ1b antibodies. Immuno-modulating treatments have been argued, but still not established. To know the efficacy of intravenous immunoglobulin treatment for childhood Fisher syndrome.

**Methods:** We retrospectively analyzed clinical recovery of childhood Fisher syndrome who had been treated with IV immunoglobulin (IVIg; n = 5), or no immune treatment (n = 5). We compared the disappeared times of ophthalmoplegia, ataxia, and areflexia, and clinical outcome between two groups. This study has been approved by Chiba University ethics committee.

**Results:** Total 10 children were enrolled in this study (male 6, female 4, average 8.6 years old). The IVIg treatment hastened the amelioration of ophthalmoplegia and ataxia, but disappearances of those symptoms at six months later were similar between two groups. Clinical outcome at one year later was favorable in both groups, leaving no neurological complications.

**Conclusion:** In adult Fisher syndrome, it is already reported that IVIg slightly hastened the amelioration of ophthalmoplegia and ataxia, but the times of the disappearances of those symptoms were similar among three groups. Our study also confirmed similar results even in childhood Fisher syndrome. In childhood Fisher syndrome, IVIg treatment seemed not to have influenced patients’ outcomes, presumably because of good natural recovery as well as adult one.

**Disclosure:** No potential conflict stated.

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**P09-14**

**Cognition and emotion regulation in Early Onset Ataxia**

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**Objective:** We aimed to evaluate cognition and emotion regulation of patients with early onset ataxia (EOA). EOA is a movement disorder caused by a dysfunction of the cerebellum or its networks, developing before the age of 25. Recent research has emphasized the cerebellum’s role in cognition and emotion regulation. Deficits concerning executive functioning, language, working memory, and spatial perception have been reported, but systematic evaluation and an investigation of the relation with emotion regulation is lacking.

**Method:** In 24 EOA patients (19 male, MAge=19 yrs, SD=8.38, MIQ=78.75, SD=17.95) we performed a neuropsychological assessment covering intelligence (subtests from the WISC or WAIS), memory (RAVLT, Doors, Digit span), attention and processing speed (LDST, TMT), executive functions (BADS-C zoo map), social cognition (FEEST-36, ToM Nepsy-II) and language (Fluency). Patients’ proxies filled in the CBCL or ABCL to assess anxiety and withdrawn behavior. Test data were compared to an age- and gender matched healthy control group (n=24, 17 male, MAge=19 yrs, SD=7.88, MIQ=102.75, SD=11.71).

**Results:** After controlling for verbal IQ, verbal learning (p=.032) was significantly lower in the EOA patients. Other tests did not differ between the two groups. Anxiety was negatively correlated with emotion recognition (p=.02). Withdrawn behavior was negatively correlated with ToM (p<.041) and emotion recognition (p=.033).

**Conclusion:** Apart from deficits in verbal learning, our patients showed intact cognitive functions. Deficits in verbal learning have not been reported earlier in EOA. This finding can have implications for treatment as studies on other patient groups have shown that deficits in verbal learning can hinder treatment compliance. In addition, we found an association of social cognition and emotion regulation in EOA patients. Future research needs to find out more about consequences of this relation.

**Disclosure:** No potential conflict stated.
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Aim: To investigate: 1. the accuracy of phenotypic early onset ataxia (EOA) recognition among developmental conditions including developmental coordination disorder (DCD) and hypotonia/hypoactive muscle activation (HHM), and 2. the effect of proven “EOA-instructions” on phenotypic consensus.

Methods: We included 32 children (4-17 years), diagnosed with EOA (n=11), DCD (n=10) and HHM (n=11). Three pediatric neurologists independently assessed videotaped motor behavior both phenotypically and quantitatively by the Scale for Assessment and Rating of Ataxia (SARA). We determined: 1. phenotypic - interobserver agreement and - homogeneity (% phenotypes with full consensus by 3/3 observers), 2. SARA (sub)score-profiles per phenotype, 3. the effect of three proven “EOA-instructions” on the phenotypic consensus, including “machine-learning” data with inertial sensors.

Results: Phenotypic EOA inter-observer agreement was substantial (Gwets-AC1:.80; p<.001). Phenotypic discrimination was homogeneous in 100% (EOA vs HHM) and 76% (EOA vs DCD). Despite overlapping SARA-scores between phenotypic mismatches (EOA vs DCD), SARA subcore-scores were different. After phenotypic re-assessment with EOA-instructions, homogeneous discrimination of EOA versus DCD increased to 86%.

Conclusion: Phenotypic discrimination between EOA and developmental conditions (DCD, HHM) is reliable, but the separation between EOA and DCD lacks full consensus. The re-assessment data with EOA-instructions may implicate that machine-learning techniques could support the phenotypic consensus on EOA-recognition.

Disclosure: No potential conflict stated.

Can we phenotypically distinguish Early Onset Ataxia from Developmental Coordination Disorders?

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Introduction: Non-lesional cerebellar Early Onset Ataxia (EOA) concerns a heterogeneous group of progressive disorders with limited therapeutic options. Recent EOA studies have shown that exergame (video-game) training may improve motor coordination, but the underlying mechanism is unclear. If cerebellar motor learning is involved, we hypothesized that exergame training would improve cerebellar parameters, independent of muscle force alterations. In ambulant EOA children, we aimed to study the effect of a medically designed “ice-skating exergame” on balance, posture and muscle force parameters.

Methods: We included 5 ambulant age-matched EOA children and controls (age range: 4-9 years). Each child completed home-based exergame training sessions (duration: 30 minutes, frequency: 3x/week, period: 6 weeks). We determined the training effect on: 1. Scale for Assessment and Rating of Ataxia (SARA, -total and –posture) scores, 2. Pediatric Balance Scale (PBS) scores, 3. muscle force alterations (i.e. altered muscle force ± SD) and 4. personal goal attainment scores (GAS).

Results: Included children revealed “improved” calculated median points of: SARA-total and -posture: -1 (0 to -1) and -1 (-3 to -1) versus 0 (2 to 0) and 0 (2 to 0); PBS 3 (-3 to 1) versus 0 (1 to 0) and GAS: 2 (0 to 2) versus n.a. [median (range); EOA versus controls, respectively]. Muscle force did not change.

Conclusions: In EOA children, ice-skating exergame data revealed a potentially beneficial effect on balance and posture, independent of muscle force. Since the motor learning effect seems stronger in children with cerebellar pathology than in controls, it is tempting to speculate that other mechanisms (such as prefrontal visual-motor compensation) could be involved. Hopefully, our future data will elucidate this.

Disclosure: No potential conflict stated.
Usefulness of MRI Classification System (MRICS) to determine the aetiology of Cerebral Palsy

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Introduction: Cerebral palsy (CP) is the permanent disorder of movement/posture/motor function originating from the non-progressive injury/abnormality of the developing brain. Brain MRI is an important step in the diagnostic work-up to reveal the aetiology. Our aim was to determine the role of cranial MRI to clarify the aetiology of CP. MRICS defined by the European network of CP (SCPE) was used.

Methods: 402 children with CP were enrolled from the area covered by our University Hospital, 257/402 (64%) had at least one MRI scan. Data on perinatal history, CP subtype, motor (GMFCS and BFMF scores) and cognitive functions and presence of epilepsy were collected.

Results: Spastic CP was the most common with 86% (60% bilateral, 26% unilateral), the rate of dyskinetic and ataxic CP was 3 and 11 %, respectively. Focal neurological signs seemed to be the most alarming symptoms for the paediatricians to perform MRI. 80% of patients with unilateral spastic CP had MRI. Brain maldevelopments and grey matter injuries (GMI) were found in 18.7% and 19.8% of our patients, respectively. The rate of white matter injuries was the highest (35%); 69% of these patients were born before 37 weeks of gestation. 83.7% of patients with maldevelopments and 80% of children with GMI were born at term. MRI revealed no abnormality in 14% of children with CP. The best values on gross motor, fine motor and cognitive function tests were reached by children with normal MRI and with GMI. The prevalence of epilepsy was above 60% in every group with abnormal MRI.

Conclusions: In 86% of children with CP MRI helped to clear aetiology. It is highly encouraged to perform cranial MRI in every patient with CP.

Disclosure: No potential conflict stated.

Application of next-generation sequencing in the identification of genes associated with paediatric Movement Disorders

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Introduction: The identification of genetic causes of movement disorders has a significant impact on the definition of different phenotypes. The introduction of NGS has led to an exponential increase in the rate of diagnosis in both previously unknown rare genetic diseases and in common but heterogeneous genetic disorders.

Methods: We conducted a retrospective cohort study analysing all the data of the NGS panel of MD of the paediatric movement disorder clinic of the Ospedale Bambino Gesù. The panel includes 103 genes and has been used since 2015.

Results: Overall 212 patients have been analysed. We gathered the patients according the prominent MD into seven main phenotypic groups: chorea (n=20), dystonia (n=85), paroxysmal movement disorder (n=48), myoclonus (n=2), NBIA (n=12), neurotransmitters (n=7) and tremor (n=3). Pathogenic variants were detected in 44 out of 170 patients leading to an overall diagnostic yield of 26%, similar to the ratio of previously published papers on exome sequencing cohorts of MD. The dystonia and paroxysmal movement disorders groups had the higher ratio of mutation detected (29%), followed by chorea (28%) and NBIA (25%). Isolated and combined dystonia had a similar diagnostic rate (27.8% versus 29.2%). No mutation were detected in myoclonus, tremor and neurotransmitters. This could be explained for by the smaller number of patients referring to our clinic for these conditions and for, tremor, for the lack of specific genes targeting these phenotypes. Our cohort is mainly paediatric with very few early adulthood exceptions. This could explain the lack of parkinsonian syndromes in our cohort compared with others.

Conclusion: We have demonstrated that our NGS panel helps in the diagnosis of different movement disorders and it identifies new variants increasing our knowledge on genetic causes of MD.

Disclosure: No potential conflict stated.
Audit of a tertiary centre experience with symptoms (Tics, Tourettes, OCD) within the PANDAS spectrum

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Background: There is ongoing controversy over the use of antibiotics in tic disorders.

Methods: Patients were identified via the electronic clinic letters system, if they were seen in Child Health between April 2010–April 2013 and had any of ‘Tourettes’, ‘OCD’, ‘Tics’ or ‘PANDAS’ mentioned. Demographics, symptoms, other diagnoses, duration of symptoms, investigations, treatment (penicillin, other antibiotic, or other), and investigations (ASOT, anti-DNAse, throat swabs) were noted. Inclusion Criteria: acute symptoms, <18 yrs. Exclusion criteria: chronic symptoms, <18 yrs. Other cause/association

Results: 50 children were identified (31 male, 19 female). Age range at presentation was 2–18 yr, with 3 <5 yrs, 28 5–10 yr, 16 11–15 yr and 3 16–18 yr. In terms of investigations, 28/50 (56%) patients had a positive result. 41 had ASOT, of which 21 were positive (>200). 32 had AntiDNAse B titres, of which 20 were positive (>300). 4 had throat swabs, of which 3 were negative, 1 with +ve ASOT, 1 with +ve AntiDNAseB, and 1 with no other investigations done. One had a positive throat swap also had a raised ASOT.

Twenty-eight patients were treated with Penicillin V (PenV). With positive results were treated: 2 lost to follow up, 2 suggested course PenV – unknown if given, 1 admission for rehabilitation, 1 PenV allergic. 3 with negative results were treated (1 for 6 months–outcome unknown, 1 is on ongoing prophylaxis, and 1 had asplenia and is on long term PenV). Three not investigated were treated. 19 (68%) had an improvement of some kind. In 6/19 the tics recurred; 3 had further Penicillin and resolved, while 2 continue on long term Penicillin.

Discussion: There is a case for an antibiotic course at the onset of acute tics.

Disclosure: No potential conflict stated.

Genetic causes of Congenital Mirror Movements associated with brain malformations

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Introduction: Mirror movements (MM) are involuntary movements of a side of the body that mirror intentional movements on the opposite side. MM that appear in infancy or early childhood and persist beyond the age of 10 years represent congenital MM (CMM). CMM have been reported in association with mutations in DCC, RAD51 and NTN1, and DNAL4. These patients usually demonstrate a normal brain MRI, although partial or complete agenesis of the corpus callosum (CC) is described in patients with heterozygous DCC mutations. A combination of CMM and brain malformations has been described in association with AHII related Joubert syndrome and alpha-dystroglycanopathy due to a novel POMK mutation.

Method: Whole exome sequencing was performed on members of two families manifesting a combination of CMM and brain malformations.

Family 1
A mother, her 4-year-old son, her 6-month-old daughter, and her fetus were evaluated due to similar brain malformations. The son and the otherwise healthy mother showed CMM. The neuroimaging findings in all four affected members included frontal dysgria, the CC and vermis hypoplasia, and asymmetric ventriculomegaly.

Patient 2
A 22–month-old patient was evaluated because of global developmental delay. On neurological examination she demonstrated CMM. Brain MRI showed bilateral frontal dysgria, the CC and vermis hypoplasia, and asymmetric ventriculomegaly.

Results: WES in family 1 revealed a novel heterozygous p. Thr312Met, c.935C>T mutation in the TUBB3 gene. Sanger sequencing on the 4-year-old son confirmed the mutation. WES on patient 2 revealed a homozygous mutation c.935C>T in the POMGNT1 gene. The patient’s parents harbor the same heterozygous mutation.

Conclusion: TUBB3 and POMGNT1 cause abnormal axon guidance via different mechanisms resulting in CMM associated with brain malformations.

Disclosure: No potential conflict stated.
Coexistence of mutations in FBXO7 and DLD causes a Complex Neurodegenerative Disorder with clinical and neuro-radiological overlapping with NBIA

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Background: Complex neurodegenerative disorders are difficult to characterize due to overlapping signs implying several neurologic pathways. The uncommon coexistence of mutations in different genes in consanguineous families makes the definitive genetic diagnosis challenging. The aim of this study was to define the genetic bases underlying disease in a patient who suffered from a complex neurodegenerative course with iron brain deposition in neuroimaging.

Methods: A gene-panel and a CGH-array was applied and additional studies in fibroblasts were performed including protein expression analysis and localization study in order to establish if the detected variants could be causative mutations.

Results: The patient is a 22-year-old girl born to consanguineous parents who was first assessed at age 2 because of acute ataxia and mild developmental delay. She progressively developed chronic ataxia, seizures, recurrent encephalopathy, parkinsonian-pyramidal syndrome with dopa-induced dyskinesias, bulbar dysfunction, upgaze limitation and cognitive decline. Brain MRI at 15 years disclosed substantia nigra and pallidal hypointensities on T2, FLAIR and GRE sequences. Dat-Scan showed normal nigrostriatal uptake. The proband harbors two homozygous mutations: c.368C>G (p.Ser123*) in FBXO7, implicated in parkinsonian-pyramidal syndrome, and c.100A>G (pThr34Ala) in DLD, involved in dihydrolipoamide dehydrogenase deficiency. Further analyses in patient’s fibroblasts have demonstrated that there is no expression of FBXO7 protein and that DLD is mislocated and hence, cannot exert its mitochondrial function properly.

Conclusions: We describe a complex progressive motor and neuropsychiatric disorder due to a FBXO7 defect and DLD mislocation. Radiological investigations suggested that parkinsonian-pyramidal syndrome in this patient shares similar mechanisms of neurodegeneration to NBIA disorders. Next generation sequencing and cell studies provided a definitive molecular diagnosis and insights into cellular mechanisms linked to neurodegeneration.

Disclosure: No potential conflict stated.
Neurodegeneration with Ataxia, Dystonia, and Gaze Palsy, childhood-onset; NADGP: a case report

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Introduction: Childhood-onset neurodegeneration with ataxia, dystonia, and gaze palsy (NADGP) is an autosomal recessive progressive disorder. NADGP is caused by homozygous mutation in the SQSTM1 gene on chromosome 5q35. NADGP is characterized by onset of gait ataxia, cognitive decline, and gaze palsy in the first or second decades. In this case report, a 12-year-old male patient diagnosed with ataxia and diagnosed with NADGP was presented.

Case Report: A 13-year-old male presented with complaints of gait disturbance. From the story, it was learned that the complaint of gait disorder started when the patient was 6 years old. The patient was diagnosed with Familial Mediterranean Fever at the age of 8 and was using colchicine treatment. The patient during follow up, it was learned the movements slowing down and the tremor started in his hands. It was learned the patient’s complaints increased over time and slowed down in all movements. Physical examination of the patient revealed ataxic gait, bradykinesia, tremor and cerebellar test abnormalities. The patient’s eye fundus was normal. In the test of intelligence, intelligence age was found to be 7 years old. Brain magnetic resonance imaging was normal. Whole-exome sequencing is performed with a pre-diagnosis of hereditary ataxia. C749Dup(p.Leu251SerFs*4;)(GRChr37):g.179252221dup. homozygous variant was detected in the SQSTM1 gene. Patients were diagnosed with NADGP. Genetic counseling was given to the family and the patient was followed up.

Conclusion: NADGP begins with atactic walking and congestive stagnation. It is a disease characterized by the presence of gaze paralysis in the first or second decade, additionally the presence of dysarthria, dystonia and athetoid movements. It is important for early diagnosis to consider this disease in the differential diagnosis of patients with ataxia.

Disclosure: No potential conflict stated.

ADCY5-related Dyskinesia: report of 2 patients

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Background: Mutations in the ADCYS gene cause choreiform, myoclonic, and dystonic paroxysmal movements affecting the extremities, neck, and face. Hypotonia and delayed motor milestones may be present in more severely affected infants.

Methods: Retrospective case notes review.

Results: Case 1. A 3-year-old girl presented with global development delay at 13 months of age. On the physical examination she showed frequent buccolingual dyskinesias, axial hypotonia and choreodystonia. Metabolic, neurophysiological and brain MRI were normal. Partial exome sequencing revealed a pathogenic mutation in the ADCYS gene (c.1252C>T/p.Arg418Trp). L-dopa trial was suspended due to adverse effects.

Case 2. A 19-year-old woman presented with learning difficulties and obsessive-compulsive disorder, clumsiness, choreodystonia and facial myokimias. Metabolic studies were normal and brain MRI showed decrease in the size of the basal ganglia. A movement disorder gene panel detected a mutation in the ADCYS gene (c.1253G>A/p.Arg418Gln). She has been treated with propranolol, primidone, escitalopram and bromazepam with partial improvement.

Conclusion: ADCYS-dyskinesia causes a phenotype of coreo-dystonia with developmental delay. Clinical features and disease course vary among patients. Treatment options are limited due to adverse effects. No effective treatment has been established. Response to medication is difficult to evaluate because some patients have long periods of remission.

Disclosure: No potential conflict stated.
Response of Movement Disorder to Deep Brain Stimulation in patients with variants in GNAO1

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Introduction: Mutations in the GNAO1 gene are manifested as: 1) Neurodevelopmental disorder with involuntary movements (OMIM 617493) and 2) Epileptic encephalopathy, early infantile, 17 (OMIM 615473). Both phenotypes associate with moderate to severe psychomotor retardation, epileptic seizures and crises of hyperkinetic movement/status dystonicus.

Methods: Retrospective case notes review.

Results: Patient 1. An 8-year-old girl presented severe hypotonia, intellectual disability (GMFCS V, CFCS III, MACS III), epilepsy treated with Levetiracetam, dystonic tetraparesis and dyskinetic crisis (BFMDRS motor 64/120, disability 30/30). Genetic testing detected a de novo mutation in the GNAO1 gene (c.545C>T, p.Thr182Ile). Prior to Gpi DBS surgery she presented one episode of status dystonicus. After the Gpi DBS surgery she presented an improvement of dystonia with less frequent generalized hyperkinetic crisis. At 6-month follow-up, she still showed some episodes of dystonia/dyskinesia, including jaw-opening dystonia. Episodes of jaw-opening dystonia improve with baclofen treatment. Current Gpi DBS stimulation is Gpi Left C (+) 0 (-) 1 (-), 1.8V, 130 Hz, 450 µs and Gpi Der C (+) 9 (-) 1.8 V, 130 Hz, 450 µs. Patient 2. A 7-year-old boy with moderate intellectual disability (GMFCS IV, CFCS III, MACS III) and generalized dystonia (BFMDRS motor 64/120, disability 19/30) underwent to Gpi DBS (Gpi Left C (+) 2 (-) 3V, 130Hz, 90µs and Gpi Der C (+) 10 (-) 3V, 130Hz 90µs). Genetic testing detected a de novo mutation in the GNAO1 gene (c.625C>T, p.Arg209Cys). A decreased in dystonia was observed in the first month after surgery.

Conclusions: Gpi DBS is an effective treatment option in patients with GNAO1 mutations and should be considered early. Baclofen can be useful to decrease jaw-opening dystonia.

Disclosure: No potential conflict stated.

Clinical description of Ataxia in Ataxia-Telangiectasia (Louis-Bar Syndrome)

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Objective: Ataxia telangiectasia (A-T) is a genetic early-onset autosomal recessive ataxia. We intended to observe the course of A-T according to gender, age, immunological state and to evaluate balance, speech and swallowing functions systematically.

Methods: Patients (n=27,13girls,14boys) with A-T from 20families (parental consanguinity in 15/20) were given the structured and unstructured Clinical Global Impression(CGI) scales specific for A-T. Balance was evaluated by physiotherapists using the Pediatric Berg Balance Scale(PBBS), Trunk Control Measurement Scale and WII balance board. Families completed a questionnaire describing swallowing behavior.

Results: Mean age at onset of symptoms was 23.8months (7mo–7y) and at diagnosis, 59.8months (12mo–11.5y). The most common first symptom, beginning at 6–8months old, was truncal ataxia. In sitting position this appeared as the child leaning backwards and realigning to midline, or in standing position, taking a few steps back and then forward to the previous site. This finding is described by all parents when they are asked specifically. All patients had motor delay, various degrees of articulation problems and/or language delay before the onset of apparent ataxia. None had severe or recurrent infections. One patient who developed Hodgkin lymphoma at 8years is currently in remission. Three families had a history of malignancy. We compared the CGI sore with balance tests in 10patients(4-15 y) and found the PBBS had the best correlation with CGI score.

Conclusion: There is significant delay between the symptoms and the diagnosis in A-T. We draw attention to the typical presenting symptom we practically name as “leaning and realigning”. Speech therapy should be considered early to support adaptive functions in these children who are cognitively normal. CGI and PBBS are reliable tools for objective evaluation of ataxia. Physiotherapists should be involved in the follow-up of A-T patients.

Disclosure: No potential conflict stated.
Variant Ataxia-Telangiectasia in a child presenting with Laryngeal Dystonia

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Disclosure: No potential conflict stated.

Introduction: Dystonia is a common hyperkinetic movement disorders in children however making an early and definitive diagnosis of dystonia can sometimes be challenging for clinicians. Herein, we report a case of a 16 years-old girl presented with laryngeal dystonia due to compound heterozygocity of a known pathogenic and a novel variant in ATM gene.

Case report: A 16 years-old female patient admitted with complaints of fatigability and dysarthria. Neurologic examination was normal, except for dysarthria and facial weakness. Myasthenia was suspected and further investigations were performed. Electromyography with repetitive nerve stimulation was normal. Acetylcholine receptor antibodies and MuSK antibodies were negative. For further genetic investigation of possible neurometabolic disease, TruSight Inherited Disease Sequencing Panel (Illumina Inc.) was used. She was found compound heterozygous for ATM variant. The variant c.8147T>C (p.Val2716Ala) has been described [5], whereas non sense variant c.7424T>G (p.Leu2475Ter) has not been described so far but is predicted in silico to be pathogenic. The unaffected parents were heterozygous for the variants. Serum alpha-fetoprotein level was 65.32 ng/ml. At the age of eighteen, she developed facial and cervical dystonia. Subsequently, treatment with L-DOPA was started at 4 mg/kg/day for a week and then the dose was increased to 8 mg/kg/day. There was dramatic improvement in her symptoms by levodopa therapy.

Discussion: Clinicians should be aware of variant A-T when investigating dystonia with unknown etiology. Elevated serum alpha-fetoprotein level can be a low-cost useful screening tool. It is important to recognize variant form of A-T, as patients can avoid radiation exposures unnecessarily, as well as symptoms can improve with treatment. Therefore, A-T should be considered in a case of laryngeal dystonia, even without ataxia or telangiectasia.

Disclosure: No potential conflict stated.

A case of Spastic Paraplegia-15 with a novel pathogenic variant in ZFYVE26 Gene

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Introduction: Hereditary spastic paraplegia (HSP) is a group of rare neurodegenerative disorder with genetic and clinical heterogeneity. It has autosomal dominant (AD), autosomal recessive (AR), and X-linked forms. HSPs are clinically classified into “pure” and “complicated” (complex) forms. SPG11 (KIAA1840) and SPG15 (ZFYVE26) are the most common AR-HSPs with thin corpus callosum (TCC). They typically present with early cognitive impairment in childhood followed by gait impairment and spasticity in the second and third decades of life.

Case report: Here, we present a patient girl, born to a couple who were first cousins, was admitted to the pediatric neurology outpatient clinic at 14 years of age because of walking with help, dysarthria and forgetfulness. Her examination revealed a motor mental retardation, bilateral leg spasticity, increased deep tendon reflexes in lower limbs, bitareal pigmentary retinopathy; TCC and white matter hyperintensities on brain MRI, sensorimotor axonal polyneuropathy findings in lower limbs on electromyography. Based on the clinical features and the imaging studies, the diagnosis of hereditary spastic paraplegia was suspected.

Targeted next generation sequencing (NGS) was performed using Inherited NGS Panel that consists of 579 gene associated with mendelian disorders. Analysis of the patient revealed a c.6398_6401delGGGA (p.Arg2133Asnfs*15)(Ekzon35) homozygous novel change in ZFYVE26 gene. We evaluated this variant as ‘likely pathogenic’ according to the ACMG Standards and Guidelines recommendations.

Discussion: Genotype-phenotype correlation of HSP is complicated due to heterogeneity. The clinical similarity of HSP types increases the importance of genetic diagnosis. There are few reports about pathogenic variants in ZFYVE26 gene in the literature. This case report is one of the few studies that revealed a novel pathogenic variant in ZFYVE26 gene using NGS.
Focal Cervical Dystonia in Stickler Syndrome – Supporting the role of visuospatial processing contributing to dysfunction of the head neural generator

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Objective: We describe a child with cervical dystonia and review hypothesised mechanisms for neural coordination of head position.

Method: Case report with video footage of a two-year-old boy with cervical dystonia. The child presented with severe myopia, abnormal neck movements and daily vomiting. The child demonstrated a “straight-ahead preference” with frequent movements of his head to extreme flexion in one of all different directions. Between changes in position, he was able to interact normally, maintain fixing, following and balance. He had otherwise normal neurological examination and development. There was a strong family history of severe myopia.

Results: MRI brain, dystonia gene panel, and cervical spine X-rays and CT were unremarkable. Genetic analysis showed a heterozygous pathogenic variant in COL2A1 in the patient and his mother, consistent with Type 1 Stickler Syndrome. He had left chronic retinal detachment involving the macula, and a left cataract. He underwent left eye cataract surgery and retinal detachment repair. He has only light perception in his right eye (acuity 0.475logMAR). His dystonia resolved transiently when his eyes were covered post surgery.

Conclusions: The role of a neural integration system in cervical dystonia combining visual information, neck proprioception and input from the cerebellum has been widely discussed. This child’s unusual presentation of focal cervical dystonia presents a unique model of cervical dystonia with abnormal visuospatial processing, supporting a causal role for visuospatial processing in some if not all cases of cervical dystonia.

Disclosure: No potential conflict stated.

High doses of Intrathecal Baclofen in the treatment of Severe Generalized Dystonia in a patient with Pantothenate Kinase-associated Neurodegeneration

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Introduction: Generalized dystonia is one of the clinical manifestations in pantothenate kinase-associated neurodegeneration (PKAN).

Objectives: To describe our own experience in using high doses of intrathecal baclofen in the treatment of severe generalized dystonia in a patient with PKAN.

Object: A boy, 8 years old, with the homozygous mutation p.Gly411Arg/p.Gly411Arg in the 6th exon of the gene PANK2. Clinical manifestations of the disease included: psychoverbal regression, strabismus, dysphagia, progressive generalized dystonia, pigmentary retinopathy and the « tiger’s eye » on MRI. Due to dystonia, the patient lost the skills to move, there were severe violations of breathing and swallowing, hyperthermia and arterial hypertension.

Results: In the treatment of generalized dystonia, we used the combinations of trihexyphenidyl, botulinum toxin, clonazepam, baclofen, levodopa in the highest possible dosages. Due to the lack of effect, titration of sodium thiopental was used. Deep brain stimulation of the globus pallidus internus was the next step. Decrease in the severity of dystonia was noted in the first week after implantation, with subsequent ineffectiveness. After a positive test with bolus intrathecal injection of baclofen, the baclofen pump was implanted with the catheter location at the level of the third ventricle. The dose of baclofen was gradually increased to be effective with the control of side effects. 2200 mcg of baclofen a day helped to reduce significantly the manifestations of generalized dystonia without side effects. The period of observation of the patient is 2 years and 8 months with a good persisting effect.

Conclusion: High doses of intrathecal baclofen with an intracranial location of a catheter can be effective for generalized dystonia in patients with PKAN.

Disclosure: No potential conflict stated.
Introduction: MPAN (Mitochondrial membrane Protein Associated Neurodegeneration) belongs to a family of rare and lethal neurodegenerative diseases named NBIA (Neurodegeneration with Brain Iron Accumulation), due to the recurrent observation of iron deposits in the brain. Characterized by parkinsonism, general dystonia and optic atrophy, MPAN is defined by pathogenic variants in the gene C19orf12, which encodes for a protein localizing to mitochondria, ER and MAM. So far, C19orf12 has been suggested to be involved in autophagy initiation by promoting the formation of autophagosomes.

Methods and Results: To better understand the molecular mechanisms underlying the pathology of MPAN and to develop new treatment strategies for the disorder, we investigated the role of C19orf12 in the cell and performed a drug screening in a Drosophila model of MPAN. The involvement of C19orf12 in autophagy was assessed by immunocytochemistry. Results showed that compared to control cells, fibroblasts isolated from MPAN patients lacking C19orf12 generate fewer autophagosomes and are unable to remove depolarized mitochondria, thus confirming the predicted role of C19orf12 in the initial steps of autophagy and suggesting an involvement of C19orf12 in mitophagy. Having established a link between the absence of C19orf12 and the impairment of autophagy, we screened 153 regulators of autophagy in an unpublished Drosophila model of MPAN. The model, generated by downregulating the two orthologues of C19orf12, shows a lethal phenotype as flies are unable to eclose from pupae. 14 of the screened compounds were able to rescue the phenotype. Their therapeutic efficacy will be further evaluated in a published Drosophila model of MPAN, showing clear signs of neurodegeneration, and in neurons differentiated from patient-derived iPSCs, currently being established in our lab.

Conclusion: The most promising drug will be selected for a clinical trial.

Disclosure: No potential conflict stated.
POSTER PRESENTATIONS > POSTER SESSION 9
Movement Disorders

P09-32

Early-Onset Parkinsonism

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Introduction: Parkinsonism corresponds to an entity widely described in adults, but little recognized in the child population. It is defined by the presence of 2 or more cardinal signs: rest tremor, bradykinesia, rigidity or loss of postural reflexes. Primary and secondary causes are described, the latter being the most common in pediatric patients. The aim of this study is to characterize child population with early-onset parkinsonism.

Methods: Retrospective descriptive study, analysis of clinical records and revision of videos of pediatric patients with parkinsonism. Patients with drugs induced parkinsonism were excluded.


Conclusions: In our serie, early-onset parkinsonism manifests mainly with bradykinesia/akinesia and rigidity. Rest tremor is rare. The most common associated symptom was dystonia. Childhood parkinsonism can be a manifestation of different pathologies, its most frequent causes are secondary.

Disclosure: No potential conflict stated.

P09-33

Classic Ataxia Telangiectasia beyond the age of 30 years

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Introduction: Patients with classic ataxia telangiectasia (A-T) generally die in the second or third decade of life due to malignancies or respiratory deficiency. Clinical descriptions of A-T tend to focus on the signs and symptoms at presentation. However, during the course of the disease, new problems emerge. We felt that patients with classic A-T who survive beyond the third decade of life suffer from a complex multisystem disorder with a largely unknown extent and severity. Therefore, we studied the full clinical picture of classic A-T in long survivors.

Methods: Clinical data from Dutch patients were retrospectively collected from their medical records and our A-T database. In addition, we searched the literature for clinical descriptions of classic A-T patients who survived beyond the age of 30 years.

Results: In the Dutch cohort seven classic A-T patients survived the age of 30 years. Twelve additional patients were retrieved by the literature search. Common problems in older patients with classic A-T were inseparably linked to ageing. Most patients had pulmonary, endocrine, cardiovascular, and gastrointestinal problems. In addition, almost all patients had a severe tetraparesis with dysarthria and contractures. This led to immobilization and frequent and long admissions to the hospital, and eventually, a poor quality of life. Most patients expressed the wish to no longer undergo intensive medical treatments, and waived follow-up programs.

Conclusion: Paucity of descriptions in the literature, and withdrawal from medical care complicate the obtainment of follow-up data. Nevertheless, it is clear that long survivors with classic A-T have to deal with many physical and psychosocial issues. Decisions about life-prolonging treatments and chances of recovery should be well considered.

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Electroencephalographic changes in children with Speech Disorder after late prematurity in neonatal period

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Background: According to international statistics, the amount of speech disorder among children increased significantly, it shown this problem global character. Late premature newborns, especially 34-36 gestational age, have the biggest percentage of speech disorder among children population. The main goal of our research is to find prognostic markers in neonatal period for detection speech disorders in late preterm children.

Method: Clinical, genetic, electroencephalographic, tomography (MRI, CT) and survival data with assessment speech disorders on Clinical Evaluation of Language Fundamentals were gathered.

Results: Our database include 3 years old 90 children with different speech impairment who was born late preterm. Their bioelectric brain activity were analyzed in neonatal period and then during 3 years follow-ups. In our research strong correlation between electroencephalographic changes in late premature children brain and speech disorder were demonstrated. In 38% of children with speech sound disorders was a decrease in the amplitude of the dominant rhythm in the temporal leads. Moreover, in their subgroup - phonemic disorders -31% was the flashes of high-amplitude slow waves in the delta range in the central leads, which was significantly different from children were born in term. In the frontal leads, the amplitude indices were lower in children with stuttering (28%) . In 9% children with dysarthria have discharges of epileptic activity, including isolated epileptic discharges in 5% and in 4% generalized epileptic discharges.

Conclusion: Thus, this study explains the need for EEG screening in children with speech disorders. The revealed disorganization of cortical rhythmic in children with different types speech impairments can be considered as a mechanism of neuronal breakdown associated with instability and disruption of the relationship between parts of the brain.

Disclosure: No potential conflict stated.

Neurodevelopmental consequences of Traumatic Brain Injury in children

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Introduction: Traumatic brain injury (TBI) is one of the most common causes of childhood disability around the world and can make children vulnerable to pervasive cognitive deficits, deficits in adaptive behavior, reduce socio-personal functions, and leads to significant morbidity. In this study, the various dimensions of traumatic brain injury and its neurodevelopmental consequences were examined and discussed using suitable researches.

Methods: This narrative review article was conducted by searching related keywords in PubMed/Medline using medical subject heading (MeSh), Scopus, Embase using Embase subject heading (Emtree), ScienceDirect, and Google Scholar databases. In addition to using keywords for finding the papers, the related article capability was used to find more papers. From the found papers, published papers from 2005 to 2018 were chosen to enter the paper pool for further review. Ultimately, 100 articles were used in this paper to conduct a comprehensive review of the neurodevelopmental consequences of traumatic brain injury in children.

Results: As a consequence, TBI results in a substantial financial burden. The associated costs should be considered in two aspects of direct medical cost such as emergency department services, imaging, and rehabilitation; and also indirect cost in loss of wages to patients and families; which is estimated to account for US$60 billion per year in US healthcare spending.

Conclusion: Considering the various side effects of this injury, it is self-evident that the importance of examining its various aspects (such as epidemiology, at-risk groups, causes, preventive measures, mitigating measures for complications and etc) is needed. This article attempts to address the various aspects of the disease in detail.

Disclosure: No potential conflict stated.
Targeted study of the executive functions in Paediatric Stroke finalized at telematics cognitive training

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Objective: Pediatric arterial ischemic stroke (AIS) is one of the ten causes of death in pediatric age and a major cause of disability.

Several studies investigated the cognitive functioning of children after stroke, finding IQ significantly lower in children with AIS compared to controls, although within the average range. Only a few studies focused on attention and executive functions (EF) using miscellaneous neuropsychological measures, often not fully adequate.

We aimed to assess cognitive outcomes following pediatric AIS in a subset of clinically and neuroradiologically completely characterized patients.

Methods: We selected scholar patients with a diagnosis of AIS and we studied them with a general and neurologic examination, MRI, EEG, PSOM and a neuropsychological battery of tests assessing attention, inhibition, working memory and cognitive flexibility. Moreover, parent-rated questionnaires were administered to obtain a description of children's emotional and behavioral functioning.

Results: 15 children (11 males) were observed (age 7-14 years; M±=12.2, SD±=20.9). Two were perinatal and the others were pediatric AIS. Five patients showed a normal profile on executive functions, five had a mild impairment and five had a severe impairment. Interestingly, 75% of females showed a normal profile compared to 18% of males. Additionally, the more severe the EF impairment was, the more impaired the emotional and behavioral functioning was too, although the relationship wasn’t statistically significant. No correlation was found between lateralization and EF impairment.

Conclusion: We performed a targeted neuropsychological study in a group of school-age patients, with pediatric and perinatal stroke, finding a significant variability in the executive functions profiles. These tests allowed us to identify the subgroup of patients who needed cognitive-rehabilitative treatment, eventually with an innovative telematics cognitive training recently started at our center.

Disclosure: No potential conflict stated.

Indole Tryptophan Metabolism and Cytokine S100B in children with ADHD: daily fluctuations, response to methylphenidate and interrelationship with depressive symptomatology

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Introduction: Indole tryptophan metabolites (ITM) have been involved in several neuropsychiatric diseases, such as attention deficit and/or hyperactivity disorder (ADHD). Our aim is to investigate the participation of ITM and the serum cytokine S100B (glial integrity marker) in ADHD physiopathology, by measuring their levels and daily fluctuations before and after administrating methylphenidate (MPH) to a sample of ADHD children.

Methods: 107 ADHD patients (ADHD) and 41 controls (CG, n=41), aged 5-14 years, were recruited. Blood samples were obtained at 09:00 and at 20:00, and only in the ADHD 4.63 ± 2.3 months after starting MPH. A factorial analysis was conducted with Groups, Hour of Day and Depressive Symptoms (DS) as factors (STATA 12.0).

Results: Tryptamine (TA) and indoleacetic acid (IAA) showed no differences between both groups. TA reached higher nocturnal values in all cases (p<0.0001), without changes in relation to MPH or DS factors. At baseline, ADHD patients with DS+ showed IAA significantly higher levels in the morning (p<0.0001), that were reduced by 50% after MPH (p<0.002). Indolepropionic acid (IPA) levels in the morning were slightly lower in the CG (p<0.1) and significantly higher in the ADHD-DS+ (p<0.03). MPH induced a decrease of IPA concentrations and restored the daily profile (p<0.007). S100B exhibited higher concentrations in the morning (p<0.002) and a non-significant trend to higher values in ADHD-DS+ patients after MPH.

Conclusions: Changes in the IMT and S100B values induced by MPH basically differed by hour of day and DS factors until reaching values and a day/night profile that were similar to the CG. These variations may influence the clinical response to treatment.

Disclosure: No potential conflict stated.
P10-05

A rare case of Global Developmental Delay – Gillespie Syndrome

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Introduction: The approach of a child presenting global developmental delay is often difficult because of the complex etiology this condition has. Pathogenic variants in the ITPR1 gene cause Gillespie syndrome, an autosomal dominant disorder characterized by motor delay, congenital hypotonia, iris hypoplasia, nystagmus, mild to moderate visual impairment, progressive cerebellar hypoplasia, ataxia, as well as mild to severe mental retardation.

Material and Methods: We are presenting the case of a 1 1/2 years old boy, with a family history of multiple sclerosis (mother), presenting with global developmental delay, central hypotonia, facial dysmorphism, nystagmus, visual impairment, stereotype movements and also gastroesophageal reflux and recurrent vomiting with an age of onset of 2 months. He was extensively investigated: normal cerebral MRI at 5 months, normal aCGH, normal metabolic screening, normal nerve conduction studies.

Results: Genetic testing, whole exome sequencing (WES), was performed in order to establish the etiology of the severe global developmental delay and it revealed a pathogenic variant in the ITPR1 gene and a variant of uncertain significance in the NEXMIF gene. The clinical picture was considered compatible with Gillespie syndrome, underlining in the presentation each of the clinical features characterizing this rare disorder, within the published data. A mutation in the NEXMIF gene may explain some additional features, such as the gastroesophageal reflux.

Conclusions: Genetic investigation of global developmental delay with no apparent cause is a key investigation, mandatory for an early diagnosis; further studies are needed to explain the complex etiology of global developmental delay.

Disclosure: No potential conflict stated.

P10-06

Paroxysmal Tonic Upgaze – A multifactorial disorder responsive to Carboanhydrase inhibition

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Introduction: Paroxysmal tonic upgaze (PTU), defined as an involuntary upward movement of the eyes, has been considered a benign phenomenon but can also be associated with ataxia and persistent neurodevelopmental problems. Four different causes of PTU are discussed: immaturity of the brainstem, depletion of neurotransmitters, immunological mechanisms, and genetic disorders including mutations in the CACNA1A, GRID2 and SEPSEC genes. No effective treatment has been reported so far.

Methods: We report on clinical and genetic data of eight children with PTU (age at onset: 5 months to four years; five male, three female); six of them also exhibiting symptoms of ataxia and / or developmental delay. PTU was persistent in five and transient in three patients.

Results: Brain MRI (n=6) showed no abnormalities in the brainstem and CSF studies (n=2) did not comply with metabolic diseases. Genetic work-up (whole exome n=6; CGH-array n=4) did not reveal any abnormal findings explaining PTU. Irrespective of the clinical background, therapeutic acetazolamide (n=3) or sultiame (n=2) treatment was effective in all five children who received this therapy.

Conclusion: Carboanhydrase inhibition should be considered in patients with persisting forms of PTU. None of our patients had any mutations in genes associated with PTU. As brain MRI and CSF analyses failed to reveal further causes, we presume PTU to be of multifactorial etiology.

Disclosure: No potential conflict stated.
P10-07

Sleep quality in children with Attention Deficit Hyperactivity Disorder (ADHD) and Sensory Modulation Difficulties (SMD)

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Introduction: Sleep disorders have been reported in up to 85% of children with ADHD. 40%-60% of children with ADHD exhibit sensory modulation difficulties (SMD) in addition to the core symptoms of ADHD. Children with ADHD who exhibit sensory symptoms have been reported to experience more significant functional difficulties.

Aims: We aimed to evaluate whether SMD affect sleep characteristics of children with ADHD. Method: 25 children with ADHD and SMD, 13 children with ADHD without SMD and 38 controls (ages 8-11) were recruited and assessed, using the Conner’s Parent Rating Scale–Revised: Short Form, the Short Sensory Profile (SSP) and The Children’s Sleep Habits Questionnaire (CSHQ).

Results: In the ADHD and SMD group, 66% of children had lower quality of sleep, compared to 14% of children in the ADHD without SMD and 21% in the control group (χ2=28.1, p<0.001). A multivariable model revealed that children with ADHD and SMD had sleep scores that were lower than controls, whereas children with ADHD and no SMD were indistinguishable from controls. Use of stimulants, gender, mother’s education and age had no significant contribution.

Conclusion: In this pilot study, we found that difficulties in modulation of sensory input may correlate with lower quality of sleep in children diagnosed with ADHD.

Disclosure: No potential conflict stated.

P10-08

Magnetic Resonance Imaging findings in children with Developmental Delay from resource limited areas

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Introduction: MRI is the gold standard imaging technique in evaluating developmental delay in paediatric patients. It precisely depicts the structural abnormalities of the brain parenchyma and ventricular structures which helps in both diagnosing the etiologies of developmental delay and formulating its preventive strategies. Ischemic changes, Malformations, Metabolic, Genetic and white matter diseases are among the widely prevalent findings shown by MRI from studies all over the world. There is wide variation of pattern of such abnormalities throughout the world. We aimed to find out the pattern of such abnormalities in a resource limited country.

Methods: It is a prospective observational study of MRI brain of 508 patients between age group five months and seventeen years, who were referred for evaluation of developmental delay. Siemens 1.5T machine was used to perform MRI on all subjects and data were analysed based on different etiological groups. All the patients were categorically divided into either presenting with only developmental delay or developmental delay with other neurological features such as seizures, neuroregression and behavioural changes.

Results: MRI was abnormal in 87 % (443/508) patients. Neurovascular/Ischemic changes were most prevalent and was seen in 67.2 %(298/443) subjects. Leucodystrophies and structural malformations were seen in 9.48 %(42/443) and 10.8 %(48/443) cases respectively. Hydrocephalus not explained by ischemic aetiology, and bilirubin related changes were seen in 4.5 % (20/443) and 7.9% (35/443) patients respectively.

Conclusions: In developing country ischemic changes are still the most common finding in DD, which relates to limitation in resources availability at neonatal setups. The second striking finding of this study is the very high percentages of bilirubin related changes that emphasizes the lack of proper and timely interventions to prevent and manage neonatal jaundice.

Disclosure: No potential conflict stated.
Neonatal Hypoxic Ischemic Encephalopathy, seizures and neurological outcome: insight from the EEG spectral analysis

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Objective: It is known that occurrence of seizures increases by 2-5 times the risk of neurological sequelae in neonatal hypoxic ischemic encephalopathy but, it has not yet been clarified whether they damage the brain per se or if they occur in patients with more severe brain dysfunction. The aim of this study was to analyse the EEG spectral bands in patients with and without seizures in relation to the outcome.

Methods: Thirty-six neonates undergoing hypothermia for moderate to severe hypoxic ischemic encephalopathy underwent multichannel interictal EEG recordings at the 13th mean hour of life (range 8-24). All spectral EEG frequencies from 0 to 30 Hz in steps of 0.5 Hz in all channels were analyzed using Fast Fourier Transformation. The Relative Power Percent (RPP) of each spectral band was calculated. The outcome was measured using the Griffiths Scales of Mental Development; outcome was defined abnormal when the quotient was less than 70 in at least one subscale.

Results: 6/36 patients had seizures (17%); 12/36 (33%) had abnormal outcome. We found a significant difference between spectral frequencies of patients with and without seizures: Patients with seizures had an increased RPP compared to patients without seizures (p<0.001). No significant differences were seen between spectral frequencies of patients with normal and abnormal outcome, when we excluded patients with neonatal seizures.

Conclusion: This study provides preliminary data suggesting that spectral EEG changes characterizing the interictal EEG of patients with seizures and neonatal hypoxic ischemic encephalopathy may be associated with abnormal outcome.

Disclosure: No potential conflict stated.

Motor outcome after Therapeutic Hypothermia in infants with Hypoxic-Ischaemic Encephalopathy

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Introduction: In term infants, therapeutic hypothermia for hypoxic-ischaemic encephalopathy (TH-HIE treatment) can prevent and ameliorate dyskinetic cerebral palsy (CP). Dyskinetic CP can be assessed by the phenotype and also by the Dyskinesia Impairment Scale (DIS; i.e. the summed score for dystonia (DIS-D) and choreoathetosis (DIS-C))1, which is interpretable against age-related values in healthy children. In a cohort of (pre)school children, that has previously been treated with TH-HIE, the association between phenotypic and quantitative assessment is still unknown.

Methods: From an eligible group of previously treated TH-HIE children (UMCG; 2009-2012), we included all (pre)school children that consented to participate (n=21). Three paediatric neurologists and seven independent investigators provided phenotypic and quantitative (DIS) assessment, respectively. We associated the motor phenotype with quantitative DIS scores and also with parental reports about the child’s global cognitive functioning.

Results: Phenotypic motor outcomes were: normal (n=18), mildly abnormal (n=2, i.e. discretely ataxic) and abnormal (n=1; cerebral palsy [CP] with spasticity and dystonia). The normal and mildly abnormal phenotypic subgroups revealed similar DIS scores, which were lower than dyskinetic CP scores (mean difference: 65 points; p<0.05)1 and higher than in healthy, age-matched control children (mean difference: 19 points; p<0.05).1 The only child with CP revealed pathological DIS scores and impaired cognitive functioning.

Conclusion: In previously treated TH-HIE (pre)school children, the motor outcome parameters are favourable with non-pathologic DIS scores, that exceed age-matched control values. Follow-up studies may elucidate whether these sub-optimal DIS scores should be interpreted from developmental or from pathological perspective.

Disclosure: No potential conflict stated.
Cognitive Visual Dysfunctions in children with Autism Spectrum Disorders and other developmental disabilities

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Objective: Attention orienting is a cognitive process that facilitates the movement of attention focus from one location to another: this may be impaired in autism spectrum disorders (ASD) and other developmental delays. Dorsal and ventral attention networks comprise the process of attention orienting. In this study, we aimed to evaluate whether children with ASD and other developmental delays have a specific visual processing deficit.

Methods: We retrospectively reviewed the medical records of pediatric patients with ASD and other developmental delays who had Modified Checklist for Autism in Toddlers (M-CHAT) and cognitive visual assessment questionnaire performed at Uijeongbu St. Mary’s Hospital from January 2017 to March 2018.

Results: A total of 45 pediatric patients (32 males, 13 females) were identified. The mean age at M-CHAT performed was 29.7 months (range, 17 – 48). They were diagnosed as ASD (n = 13), global developmental delay (n = 13), and language delay (n = 19), respectively. Children were divided into 2 groups by M-CHAT results as follows; 1) Patients who screened positive on the M-CHAT (n = 38); 2) Patients who screened negative on the M-CHAT (n = 7). Children who screened positive on the M-CHAT show a particular deficit on tasks that require processing predominantly attributed to the dorsal stream (p < 0.05). When we compared the gender and diagnostic differences in dorsal and ventral function deficits, no statistically significant differences were observed.

Conclusion: ASD have common features with other developmental disorders, reflecting a greater vulnerability of the dorsal stream. On this aspect, cognitive visual assessment may serve as an alternative screening tool for children with ASD and other developmental delays.

Disclosure: No potential conflict stated.

Correlation between weak clinical signs of Epilepsy and the findings of the first EEG record in a population of patients with diagnoses of Epilepsy and ASD

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Objective: To describe the findings of the first EEG performed on a consecutive group of patients with ASD, selected for presenting subtle epilepsy criteria.

Methods: Prevalence retrospective study of the findings of the first EEG, performed on 28 ASD patients (24 boys and 4 girls) (Age = 9.4 ± 3.8 years) out of 86(18%) who were diagnosed for ASD (304) and Epilepsy (478) in our department. They were included because showed a weak suggestive anamnesis of epilepsy (recurrence of paroxysmal behavioural disorders (BD), sleep (SD), abnormal movements (AM), headaches (HA) and observed seizures (OS)). The results of the EEG are divided into three groups: Normal (N); Abnormal (AN); Pathological (P).

Results: The EEG indication criteria frequencies were: BD=13(50%), SD=11(42.3%), MD=11(42.3%), HA=5(19.2%), OS=4(15.3%) (3 absences and a subtle partial motor seizures). The results of the EEGs were: AN=6(22.2%) and PAT=22(77.7%) (Interobserver agreement=96.3%). They were focal in 22(81.4%), generalized 11(40.7%), secondarily generalized 9(33.3%) and exclusively generalized 2(7.4%). No clinical characteristics showed statistical association with any specific EEG pattern.

Conclusions: The indication of EEG in patients with ASD who present recurrent subtle symptoms of epilepsy, either alone or in combination, provide a diagnostic yield superior to that of the EEG indicated by epidemiological risk in the general ASD population.

Disclosure: No potential conflict stated.
Prevalence of non-benign and probably non-benign CGH-Array CNV among a referral population of ASD children

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Objectives: To describe the frequency of non-benign or probably non-benign copy number variants (nBpnB-CNV) in an ASD population studied by means of CGH-array.

Methods: Retrospective prevalence study of nBpnB-CNV in a closed referral population of 32909 children under 15 years-old, based on a public health department of a European Region. The patients with suspected ASD were sent to our multidisciplinary team for the diagnosis and treatment of ASD. In 2018, 125 ASD patients were confirmed. A group of 119 accepted to be tested for CGH-array (Cytoarray Plus 180K) designed for CNV related to DNA regions involved in mental retardation, developmental delay, ASD, and malformative syndromes. Gender, clinical comorbidities (Epilepsy, Complex-ASD) and history of epilepsy, induced significant differences in its association with nBpnB-CNV.

Results: 34 (28.6%) out of 119 ASD patients showed some nBpnB-CNV (Boys=89; Girls=30). The more frequent affected regions were 15q11.2 (3 deletions, 1 duplication) and 22q11.22 (4 duplication). Complex-ASD patients were 2.5 times more likely to present nBpnB-CNV than Simple-ASD patients (OR=2.55) (Cl: 1.13-5.8). Neither gender, type of CVN or history of epilepsy, induced significant differences in its association with nBpnB-CNV.

Conclusions: 1) The CGH-array resolves approximately one third of the aetiologic diagnosis of the ASD patients. 2) The nBpnB-CNV could discriminate between complex and simple ASD phenotypes.

Disclosure: No potential conflict stated.
P10-15

Study of the efficacy of behavioural parent training in the treatment of Egyptian school-aged children with Attention Deficit Hyperactivity Disorder

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Introduction: Attention Deficit Hyperactivity Disorder (ADHD) is the most common neurodevelopmental disorder in childhood, characterized by hyperactivity, impulsivity and/or inattention. Treatment of ADHD consists of a variety of approaches including parenting support, educational accommodations, behavioral and cognitive therapy, and/or medication. Our aim was to study the efficacy of structured group-based behavioral parent training program (BPT) in the alleviation of the core symptoms of ADHD and its co-morbid conduct problem among school-aged children with ADHD.

Method: Multi-group design prospective study with pre and post assessment with an Arabic form of Conners’ Parent Rating Scale short form (CPRS-48). Participants were 45 school-aged children (age range from 6-10 years) with a diagnosis of ADHD according to DSM-5 diagnostic criteria. Children were recruited from the Pediatric Neurodevelopmental outpatient clinic of Alexandria University Children’s Hospital. Different interventional modalities were implemented including; medication (MED-only; Atomoxetine, n=15) either alone or in combination with the parent training program (BPT and MED, n=15) or Neurofeedback training (NFT and MED, n=15).

Results: Behavioral parent training program showed significant reduction of CPRS’s scores of conduct problem (P <0.001), inattention (P=0.040), and peer relationship (P<0.001) in comparison to the other studied interventions. Although Combined (BPT and MED) showed a significant decrease in learning problem scores (P<0.001) and hyperactivity/impulsivity (p<0.001), no statistically significant difference was found with the other studied groups. Conclusion: combined structured group-based behavioral parent training program and medication showed superior efficacy than the other studied interventions; (NFT and MED) or (MED-only). Implementation of BPT in the management of children with ADHD is very essential, especially in low-income countries where expensive interventions may not be widely affordable.

Disclosure: No potential conflict stated.

P10-16

Visual perception processing in children with reading disabilities and who are born with very low birth weight

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Introduction: In this study, we comparatively examined characteristics of reading disabilities of “very low birth weight infants” (VLBWIs) against those displaying general reading disability in visual perception processing.

Research Subjects: This study had a total of 111 children: 28 first to third grade children born as VLBWIs at Osaka Medical University Hospital and Saiseikai Suita Hospital between April 2007 and March 2010 and who and 83 first to third grade children who visited LD center at Osaka Medical University with the primary complaint of learning difficulty in the past three years. All participants had an FSIQ score of 80 or higher per WISC-IV.

Methods: A Japanese guideline examination for the diagnosis of dyslexia and the WAVES test for examining visual perception and eye-hand coordination were conducted on the children. They were divided into two groups according to the presence or absence of reading disability: Dys group and N-Dys group. They were also classified according to the birth weight: those born with < 1500g (VLBW group) and those with ≥ 1500g (LBW/NBW group). Further, a two-way ANOVA analysis was performed to compare WAVES results between the groups: VLBW and LBW/NBW and Dys and N-Dys.

Results: The WAVES results showed that there was an interaction between the groups in “shape distinguishing” abilities, i.e., being able to distinguish minor differences by precisely observing the shapes (p < 0.05) and “shape copying,” i.e., the ability to configure shapes (p < 0.05).

Discussion: The results showed that in the reading disability of VLBWIs, visual perception processing and shape composition abilities are particularly lower. Therefore, it is necessary to consider supporting reading disability of VLBWIs by focusing on these differences.

Disclosure: No potential conflict stated.
Study on cognitive profiles of patients with 22q11.2 Deletion Syndrome: comparison with the findings of Williams Syndrome

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Objective: Patients with 22q11.2 deletion syndrome (22q-) are known for relatively higher verbal IQ than performance IQ. More precise knowledge of their cognitive abilities is needed to improve their quality of life and our understanding of human brain functions.

Methods: Two females in their high teens with 22q- (full IQ, performance IQ, verbal IQ: 74,75,79 and 67,64,80, respectively) participated in the following investigations.
1). Benton facial recognition test for facial recognition, one of the functions of the ventral stream of the visual system.
2). Benton three-dimensional block construction test for visuo-spatial construction ability (VSC), one of the functions of the dorsal stream of the visual system.
3). Neurophysiological investigation to determine the presence or absence of face inversion effect (FIE: latencies for processing inverted faces compared to upright faces are delayed in healthy adults).

The results were compared with the data of patients with Williams syndrome (WS) in a previous study.

Results:
1. The results of the facial recognition test of participants with 22q- were lower than the standard data of adults >16 years old.
2. In three-dimensional block construction test, one of the participants with 22q- performed as well as normal adults, indicating good VSC. The other did worse.
3. The participant with good VSC showed FIE despite her poor facial recognition ability. The other participant with 22q- did not.

A WS patient with better VSC showed FIE, although patients with poorer VCSs showed no FIEs in spite of their better facial recognition abilities.

Conclusion:
Facial recognition abilities are poor in patients with 22q-, but a patient with good VCS showed FIE as in normal adults. With the data of WS patients, FIE may be related more to visuo-spatial function than facial recognition.

Disclosure: No potential conflict stated.

Economic burden of care and treatment options for patients with Rett Syndrome: two systematic literature reviews

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Introduction: Rett syndrome, a rare disorder caused by mutations in the X-linked MECP2 gene, occurs almost exclusively in girls and leads to severe developmental impairment.

Methods: Two systematic literature reviews related to Rett syndrome were performed on 25/6/2018. A search of economic burden in Medline, Embase, Cochrane Library, and Database of Abstracts of Reviews of Effects (DARE) yielded 133 articles; type and costs of interventions were extracted from 9 articles (4 studies). A search of clinical trials in Medline, Embase, ClinicalTrials.gov, and Cochrane Library yielded 652 articles; efficacy and safety were extracted from 28 articles (19 studies).

Results: In the economic burden studies, enteral feeding and assisted walking increased the risk of respiratory-related hospital admissions, while length-of-stay was lower in younger patients. Mean recovery-stay after scoliosis-correcting surgery was 18.2 and 12.3 days in each of two studies. Care integration improved outcomes and reduced costs. Of 19 clinical studies identified (14 randomized controlled trials, 5 single-arm; N=8–73; follow-up 1–26 months), 18 focused on pharmacological symptom treatment; none targeted the underlying cause. The most common primary endpoints were Rett syndrome Gross Motor Scale, Clinical Severity Score, Motor and Behavioral Assessment, and the Anxiety Depression and Mood Scale. Significant clinical benefits were demonstrated for naltrexone, trofinetide, and mecasermin vs placebo, but most treatments showed no significant improvement. Recent clinical practice guidelines and treatment patterns data were limited.

Conclusions: There are little data on costs of Rett syndrome management. There is also a lack of effective therapies; those available only manage symptoms. There is great demand for safe and effective treatments targeting the underlying cause, such as gene therapy, which could improve quality of life and prognosis of patients with Rett syndrome.

Disclosure: OD, BEM, TAM, and RA are employed by AveXis, Inc. OD is employed by AveXis, Inc. and holds stock in AveXis, Inc./Novartis. BM is an employee of SSI Strategy, a company contracted to support AveXis, Inc. VT, EA, MB, JC, KB, and VG are employed by Creativ-CEutical, a consultancy company working for various pharmaceutical industries, including AveXis, Inc.
P10-19

Understanding early relationship between Autism Spectrum Disorder, Developmental Delay and Epilepsy in infants with Tuberous Sclerosis Complex: preliminary results from the EPISTOP Project

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Background/aim:
Tuberous sclerosis complex (TSC) is associated with a high risk of early seizures and a wide range of neuropsychiatric disorders, including developmental delay (DD) and autism spectrum disorders (ASD). The relationship between ASD, epilepsy, and cognition is still poorly understood. The EPISTOP project is a multi-center prospective study focused on identification of biomarkers of epileptogenesis. In this study, we aimed at comparing neurodevelopmental outcome with epilepsy variables and timing of antiepileptic treatment.

Methods:
Infants were prospectively followed from 6 to 24 months of age through neuropsychological assessments; neuropsychological outcome was correlated with history and type of seizures, age at seizure onset/first abnormal EEG, standard versus preventive treatment given before seizure onset, and response to treatment.

Results:
Data were available for 82 patients. A cognitive developmental quotient >80 at 6 months of age predicted a normal developmental trajectory without DD nor ASD symptoms at 2 years of age (p=0.025). ASD was significantly associated with a history of epilepsy (p=0.017; RR:6.0), particularly if seizure onset was in the first year of life (p=0.025; RR:2.7). Seizure onset in the first year of life was also associated with a high risk for DD (p=0.001; RR:4.6). Sixty-five percent of children who received preventive treatment had normal development, compared to 47% of those who received standard treatment. ASD rate was similar in the two groups (standard 33%, preventive 30%).

Conclusions:
ASD presence in TSC was inextricably linked with cognitive level and refractory, early onset epilepsy. A rigorous, prospective clinical follow-up including EEG and formal developmental assessment is warranted to identify infants at risk for DD or ASD, to ensure early intensive behavioral intervention to potentially minimize the impact of these comorbidities on daily life functioning.

Disclosure: No potential conflict stated.
P10-20

Novel gene mutation of Molybdenum Cofactor Deficiency

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Introduction: Molybdenum cofactor deficiency is a rare metabolic condition characterized by brain dysfunction (encephalopathy) that worsens over time. Molybdenum cofactor deficiency is caused by mutations in the MOSC1, MOSC2, or GPHN gene. There are three forms of the disorder, named types A, B, and C. The forms have the same signs and symptoms but are distinguished by their genetic cause: MOSC1 gene mutations cause type A, MOSC2 gene mutations cause type B, and GPHN gene mutations cause type C.

Methods and Results: Herein we are reporting a 2 months old child who presented to our hospitals with seizure disorders, post cardiac arrest. After clinical evaluation, and thorough investigations, uric acid was undetectable. MRI brain showed periventricular leukomalacia- HIE picture, with bilateral frontal lobe white matter loss with extensive cystic formation and thinning of corpus callosum. Molecular genetic testing showed pathogenic deletion c.604_624del p.(Gly202_glu208del) in exon 4 of MOCS1 gene in homozygous state.

Conclusion: To best of our knowledge this variant was not yet reported in any literature yet.

Disclosure: No potential conflict stated.

P10-21

Missense variant in the ASXL2 gene in a teenage girl with Developmental Delay, Hypotonia and Bilateral Ptosis: variant of Sashi Pena Syndrome?

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Background: In 2016 six patients with de novo heterozygous truncating variants in ASXL2 were described with a specific phenotype consisting of macrocephaly, neonatal feeding difficulties, hypotonia, developmental disabilities and distinct facial dysmorphisms. This disease was named the Sashi Pena syndrome. So far it has only been described in truncating variants in the ASXL2 gene.

Case presentation: We present a 13 year-old girl with a heterozygous missense variant in a conserved region of exon 13/13 of the ASXL2 gene (whole exome sequencing) who displays developmental delay, behavioural issues, cognitive regression, hypotonia, bilateral eyelid ptosis, tongue fasciculations and areflexia. This genetic variant was not found in the mother. As the father is deceased, we cannot confirm that this is a de novo mutation. Regression of behaviour and neurological signs were first reported at the age of 10. MRI brain, EMG and ultrastructural analysis of the skin were normal. There was no organic aciduria, plasma carnitines were normal and there was a general elevation of amino acids. GABA was slightly increased in cerebrospinal fluid. Though still a possible diagnosis, succinate semialdehyde dehydrogenase deficiency seems less likely because there was no 4-OH-butyric aciduria. Possibly, this is a first case of a patient with Sashi Pena syndrome caused by a missense variant in ASXL2.

Conclusions: This case report describes a patient with a missense mutation in the ASXL2 gene who displays symptoms similar to those of patients with the Sashi Pena syndrome, so far only described in patients with truncating variants in ASXL2. Possibly, missense mutations in this gene can lead to a (variant of) the Sashi Pena syndrome. Additional cases with missense mutations in ASXL2 are needed to confirm or deny this hypothesis.

Disclosure: No potential conflict stated.
P10-22

The Role of the arcuate fasciculus depending on hemisphere in children with Developmental Delay: a preliminary study

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Introduction: In adults, language is lateralized to the left hemisphere of the cerebrum. However, the role of each cerebral hemisphere in language development of toddlers is not clear yet.

Objective: To investigate the role of arcuate fasciculus in clinical development aspect, especially on language development of children, we assessed the relationship between the absence of AF and development status depending on hemisphere.

Method: A retrospective chart review was done in 139 patients who underwent MR imaging of the brain performed at 3T, including 30 direction diffusion tensor imaging (DTI) after visiting PM&R Department outpatient clinic with delayed development. Among them, 12 patients showed the absence of arcuate fasciculus. Patients were divided into 3 groups based on the direction of absent AF; Right hemisphere, Left hemisphere and bilateral. A Kruskal wallis test was done to determine statistical differences of Developmental Quotient (DQ), Receptive Language Quotient (RLQ) and Expressive Language Quotient (ELQ) between three groups.

Results: The mean age of 12 patients was 30.4 ± 20.26 months. Five showed the absence of bilateral AF and the right AF was not identified in five. The left arcuate was absent in 2 patients. There was no statistically significant difference between the three groups on DQ in all domains. The DQ on language domain was 58.8 in right AF(-) group, 61.0 in left AF(-) group and 63.4 in bilateral AF(-) group.

Conclusion: Unlike adults, it seems that the unilateral hemisphere of children does not dominate in language function. Further cumulative and prospective data are needed to understand the role and correlation between language development and arcuate fasciculus at DTT. And serial DTT can provide important information to anticipate the prognosis of the pediatric patients with delayed development.

Disclosure: No potential conflict stated.

P10-23

DiGeorge Syndrome presenting with seizures

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Introduction: DiGeorge syndrome was described for the first time in 1968 as a defect affecting structures derived from the third and fourth embryonic pharyngeal arches along with absent parathyroid glands. According to the low incidence of this disease as well as a wide spectrum of symptoms, it is essential to report cases with less prevalent features.

Methods and Results: In this case report, a child was introduced with a diagnosis of DiGeorge syndrome presenting with seizures. The patient was a 27-day-old baby girl due to seizures admitted to Hospital Imam Reza (AS), Mashhad, Iran. Hypocalcemia was observed in early clinical trials requested. The patient underwent echocardiography according to holosystolic murmur grade 3/6 auscultation, which showed a patent ductus arteriosus (PDA), tetralogy of Fallot (TOF), ventricular septal defect (VSD), atrial septal defect (ASD), and pulmonary atresia (PA). No thymus was found on chest X-ray, and evidence of previous conflicts was observed in the heart. Finally, fluorescent in situ hybridization (FISH) was performed to check out Tuple gene deletion on chromosome 22q11.2, and the diagnosis was confirmed for DiGeorge syndrome.

Conclusion: Although the incidences of neurological symptoms associated with hypocalcemia suggest a wide range of diseases as a differential diagnosis, pediatrics should consider the heart disorders for DiGeorge syndrome through clinical examinations and imaging, if necessary.

Disclosure: No potential conflict stated.
Epidemiology of Intellectual Disability (ID) in a population-based cohort of patients with Cerebral Palsy (CP)

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Objective: We aimed to describe the epidemiology of ID (defined as IQ<70) in a cohort of patients from a population-derived CP registry, in the Athens Metropolitan area (SCPE member C31).

Methods: Data on intellectual ability (derived through psychometric testing or school placement by educational authority) of 1016 patients born between 1999-2010 were recorded. Statistical processing and correlation analysis for clinical parameters [Gestational Age (GA), CP type and severity, epilepsy, vision, hearing, associated non CNS anomalies] and neuroimaging patterns according to the SCPE MRI Classification System was performed.

Results: Data on cognitive status were acceptable in 801 children (61,55% of<37wks GA;41,20% were non ambulant / GMFCS: IV-V); 525/801 children (65,54%) were recorded as having ID. Absence of ID was mainly recorded in preterms (pr=0.000). The prevalence of ID was not significantly different in the subgroups of preterms born at<28wks, 28-32wks, 32-34wks and 34-37wks (pr=0,912). ID was associated with non ambulation[GMFCS IV-V status (p<0.001)], poor manual abilities[BMFM IV-V (p<0.001)], epilepsy (p<0.001), hearing disability (p<0.003) and non CNS congenital anomalies (p<0.038).

Full term children with ID had significantly different MRI lesions (maldevelopments and miscellaneous findings) from children without ID (white and grey matter lesions) (p<0.001); no significant difference of normal MRIs in the groups with- and without- ID.

Conclusions: CP severity and non-ambulatory status are significantly correlated with ID. Absence of ID was more frequent-ly recorded in preterm-born children. In full-term born CP patients ID was significantly correlated with maldevelopments and miscellaneous MRI findings. Further study of the clinical profile and neuroimaging correlations of patients with or without ID is warranted.

Disclosure: No potential conflict stated.
**P10-25**

Preschool screening of children aged 5 years to evaluate Neurodevelopmental Disorders in a rural city of Japan

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**Objective:** In Japan, a medical examination is legally mandatory at infancy, 1.5 years, and at 3 years; however, children are not examined after that until entering elementary school. Lately, screening neurodevelopmental disorders at 5 years through preschool evaluation has gained momentum. We aimed to conduct preschool screening of children aged 5 years to evaluate neurodevelopmental disorders.

**Methods:** A retrospective, observational study was conducted; we enrolled 546 children (age, 5 years) and conducted individual operability, verbal, and exercise tasks. Doctors interviewed and examined all the children between April 1, 2016 and March 31, 2018. Neurodevelopmental disorder was clinically diagnosed based on The Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition. Most intelligence tests were evaluated using the Wechsler's index.

**Results:** Of the total, 86 children (15.7%) were introduced to the hospital. Of these, 51 children (9.3%) were diagnosed with neurodevelopmental disorders, 35 (6.4%) were diagnosed with dysarthria, 8 were diagnosed with no disorders, and 7 children did not visit the hospital. The disorders were classified as follows: autism spectrum disorder (28; 5.1%), attention deficit/hyperactivity disorder (25; 4.6%), intellectual disorder (5; 0.9%), and developmental coordination disorder (8; 1.5%). Diagnosis was sometimes duplicated for a single child. Moreover, 71 of 79 children who visited the hospital received individual rehabilitation therapy, and 62 (78.5%) were counseled by doctors at follow up.

**Conclusions:** Children aged 5 years were effectively evaluated for neurodevelopmental disorders. This screening identified neurodevelopmental disorders that could not be identified during previous medical examinations, thereby facilitating consultation and support at primary school entrance to target children.

**Disclosure:** No potential conflict stated.

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**P10-26**

Pilot study to investigate the microstructural brain changes after taking Methylphenidate in children with Attention-Deficit/Hyperactivity Disorder (ADHD)

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**Aim:** ADHD is one of the most common neurodevelopmental disorders that affects up to 5-9% of school-aged children. We aim to study whether there are distinctive microstructural brain changes as shown by diffusion kurtosis (DK-MR) imaging after taking Methylphenidate in school-aged children with ADHD.

**Method:** 2 children age 6 & 8 years old with confirmed diagnosis of ADHD were recruited. Severity of ADHD was assessed by the Strengths and Weaknesses of ADHD Symptoms and Normal Behavior Rating Scales (SWAN) questionnaire. Both cases were treated with Methylphenidate with dosing according to treatment response. Case subjects had plain MRI Brain (including T1 & T2 weighted images) and DK-MR imaging. Both subjects had neuroimaging study at diagnosis prior to treatment with Methylphenidate (T0) and neuroimaging study again after being on Methylphenidate for 3 months’ duration (T3).

**Results:** Both cases have improved SWAN scores after taking Methylphenidate. After taking Methylphenidate for 3 months’ duration, the largest changes in DKI metrics were found in the mid temporal lobe with 1-2% increase in the fractional anisotropy (FA), mean diffusivity (MD) and the mean kurtosis (MK). Our results are in contrary to previous findings where individuals with ADHD showed no significant age-related increase in MK.

**Conclusion:** Our pilot cases provide preliminary evidence of microstructural changes suggestive of improved structural integrity in the mid-temporal lobe of the brain after taking Methylphenidate.

**Disclosure:** No potential conflict stated.
Cerebellar disruption at term equivalent age and motor impairment at 3 years of age in preterm infants with mild intraventricular haemorrhage: quantitative assessment using Diffusion Tensor Imaging

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Purpose: Effects of mild intraventricular haemorrhage (mIVH) on neurodevelopment in preterm infants are controversial. We investigated relationships between white matter impairment assessed using diffusion tensor imaging (DTI) at term equivalent age (TEA) and neurodevelopment at 3 years of age between mIVH and no-IVH groups.

Subjects and Methods: Nineteen infants (mIVH, n=10; no-IVH, n=9) born at postmenstrual age (PMA)<28 weeks and 20 infants (mIVH, n=3; no-IVH, n=17) born at 28≤PMA<30 weeks were included. Fractional anisotropy (FA) and apparent diffusion coefficient (ADC) in the corticospinal tract (CST), superior cerebellar peduncle (SCP), and middle cerebellar peduncle (MCP) were measured using tractography, alongside cerebellar volume at TEA. These values and the developmental quotient (DQ) at 3 years of age were compared between the groups and relationships between the values and the DQ were analysed.

Results: In the SCP, FA values in the mIVH group born at PMA<28 weeks were significantly lower than those in the no-IVH group (p=0.0024). The CST and MCP were not significantly different. The mIVH group born at PMA<28 weeks had a lower posture-motor (P-M) DQ at 3 years than the no-IVH group (p=0.03). Cerebellar volume was significantly less in the mIVH group born at PMA<28 weeks than in the no-IVH group (p=0.03). In the mIVH group, the SCP FA and P-M DQ were not correlated. Cerebellar volume and any DQ values were not correlated.

Conclusion: This study showed that mIVH in extremely preterm infants affected the SCP, cerebellar volume at TEA, and motor development at 3 years of age. Further studies are needed to clarify the neurodevelopmental outcome in infants with mIVH.

Disclosure: No potential conflict stated.

The role of Topiramate in the management of childhood Tourette’s Syndrome: a case series

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Introduction: Tourette’s syndrome is a childhood neurodevelopmental disorder, characterised by persistent motor and vocal tics. Anti-dopaminergic drugs have commonly been used despite their side-effect profile, including sedation and arrhythmias. Limited evidence supports the use of topiramate, an antiepileptic, in older children, however further evidence investigating its potential safety and efficacy in younger children is needed.

Methods: This retrospective case series analysed the clinical letters of children attending outpatient clinics at a tertiary hospital. Inclusion criteria determined that study patients had to have a confirmed diagnosis of Tourette’s syndrome, be prescribed topiramate with evidence of a dosing regime, and had at least one follow-up appointment. Multivariate logistic regression using clinico-demographic information was performed.

Results: Fourteen patients, with a mean age at onset of 7.8 (3; 13), met inclusion criteria. Three-quarters of patients reported reduced tic severity (11/14). No significant difference in clinico-demographic variables was noted between responders and non-responders, with a comparable dosing regimen (25-300mg; 50-150mg). Six patients (42.9%) experienced adverse effects, commonly including behaviour or mood disturbance. The majority of these patients (5/6) required discontinuation, of whom two-thirds noted improvement on discontinuation and one-third experienced tic recurrence. Multivariate analysis found that individuals with a first-degree family member with tic disorder were nearly four-times as likely to have adverse effects (p=0.053), with females also at increased odds (p=0.097).

Conclusion: This study adds to the growing evidence-base supporting the efficacy of topiramate in the treatment of Tourette’s syndrome. However, a notable side-effect profile was found, and thus further research is required to identify a safe dosing regimen.

Disclosure: No potential conflict stated.
**P10-29**

**Biallelic Neurofascin variants affect paranodal axoglial junctions causing neurodevelopmental impairment and central and peripheral demyelination**

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**Introduction:** Axon pathfinding and synapse formation are essential processes for nervous system development and function. The assembly of myelinated fibres and node of Ranvier is mediated by a number of cell adhesion molecules including the Neurofascin (NFASC) alternative isoforms Nfasc186 and Nfasc140, located in the axonal membrane at the node of Ranvier, and Nfasc155, a glial component of the paranodal axoglial junction.

**Methods:** We identified 8 individuals from 5 unrelated families, exhibiting a neurodevelopmental disorder characterized by a spectrum of central (intellectual disability, developmental delay) and peripheral (early onset demyelinating neuropathy) involvement, found by exome or genome sequencing to carry one frameshift and four different homozygous non synonymous variants in NFASC.

**Results:** Expression studies using immunostaining identified absent expression of the Nfasc155 isoform because of the frameshift variant and a significant reduction of expression was also observed in association with two non synonymous variants affecting the fibronectin type III domain. Cell aggregation studies revealed a severely impaired Nfasc155 CNTN1/CASPR1 complex interaction as a result of the identified variants. Immunofluorescence staining of myelinated fibres showed a severe loss of myelinated fibres and abnormalities in the paranodal junction morphology.

**Conclusion:** Our findings establish that recessive variants affecting the Nfasc155 isoform can affect the formation of paranodal axoglial junctions at the nodes of Ranvier. The genetic disease caused by biallelic NFASC variants includes neurodevelopmental impairment and a spectrum of central and peripheral demyelination as part of its core clinical phenotype. Our findings support possible overlapping molecular mechanisms of paranodal damage at peripheral nerves in both the immunemediated and the genetic disease, but the observation of prominent central neurological involvement in NFASC biallelic variant carriers highlights the importance of this gene in human brain development and function.

**Disclosure:** No potential conflict stated.

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**P10-30**

**Novel compound heterozygous STN1 variants can cause Coats Plus Syndrome**

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**Aim:** Coats plus syndrome (CP) is a rare autosomal recessive disorder, characterised by retinal telangiectasia / exudates (Coats disease), a distinctive pattern of leukodystrophy, intracranial calcification and cysts, as well as extra-neurological features including gastro-intestinal bleeding and portal hypertension, and osteopenia with a tendency to fractures. CP is most commonly due to loss-of-function mutations in CTC1. CTC1 constitutes part of the CST (CTC1-STN1-TEN1) complex, and two patients have been described with CP due to biallelic mutations in STN1. Together with the observation of homozgyosity for a specific loss-of-function mutation in POT1 in a sibling pair, these observations highlight a defect in the maintenance of telomere integrity as the cause of CP, although the precise mechanism leading to the microvasculopathy seen at a pathological level remains unclear. Here, we present the molecular investigation of a child with features of CP.

**Methods:** We assessed the phenotype to be CP and undertook targeted sequencing.

**Results:** Whilst sequencing of CTC1 and POT1 was normal, we identified novel compound heterozygous variants in STN1: one loss-of-function – c.894dup, p.(Asp299Argfs*58); and one missense – c.707T>C, p.(Leu236Pro).

**Conclusion:** Given the clinical phenotype and evaluation of the variants that we observed using American College of Medical Genetics (ACMG) guidelines, we suggest that this is only the third patient identified to date with CP due to mutations in STN1.

**Disclosure:** No potential conflict stated.
Evaluation of the malnutrition risk and the factors affecting it by applying the STRONGkids Scale in Pediatric Neurology service using the STRONGkids Scale

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Aim: Malnutrition is a common and important problem for hospitalized patients. It is possible to determine high-risk patients for malnutrition with the answers given to the questions in a short time without the need for anthropometric measurement with STRONGkids. In this study, it was aimed to evaluate the risk of malnutrition and the factors affecting it by applying the STRONGkids scale to inpatients.

Materials and methods: Our study was performed on 200 patients between 5 months-18 years of age hospitalized in Pediatric Neurology service. Age, gender, anthropometric measurements, length of stay, presence of underlying diseases, hospitalization diagnoses, measurements of the scale and responses were recorded. The characteristics of the groups with low, medium and high risk were investigated statistically.

Results: Of our patients 44% were girls and 55.5% were boys. The mean age of the patients was 5.2 ± 4.7 years (median age was 4.0 years). The most common diagnosis was epilepsy (44.5%). This was followed by neurometabolic diseases (11.0%). In our study, malnutrition was observed in 21% of the patients, 6% of them chronic and 15% of them acute. In our study, the yes response to the questions in those with high risk among the malnutrition risk groups was significantly higher (p <0.001). Malnutrition risk and need for intervention were found to be higher in patients with underlying disease at admission (p <0.001).

Conclusion: To our knowledge, a study evaluating the nutritional status of patients hospitalized in the Pediatric Neurology Service using the STRONGkids scale has not been performed before. Our findings support the use of STRONGkids as a screening tool to identify patients with a high risk of malnutrition and to increase healthcare providers awareness of nutritional assessment.

Disclosure: No potential conflict stated.

Nuchal cord prevalence and relation with neurodevelopmental outcome at the age of one years through the five years

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The aim: To determine the prevalence of tight-nuchal cord (t-NC) and loose nuchal cord (l-NC) in newborns and their association with a neurodevelopmental outcome in children at the age of one year.

Methods and subjects of research: The research was retrospectively-prospectively out in two cantonal hospitals at USK in a five-year period. The study included 160 examined and 115 children in the control group. The examined group was made up of newborns with t-NC and l-NC. Apgar score and the mode of delivery is noticed, neurodevelopmental monitoring is continuous, and the assessment of neurodevelopment was made at the end of the first year of life according to the Munich functional scale.

Results: The APGAR score was statistically significantly decreased in the group of children with NC (p <0.001), and in the case of t-NC values of APGAR scores were statistically significantly lower compared to the loose NC. (p <0.001). The mode of vaginal delivery in the control group is statistically significant. (p <0.001) The neurodevelopmental delay at the end of the first year were significantly associated with t-NC and low APGAR scores. (p <0.001)

Conclusion: Nuchal cord prevalence coincides with the nuchal cord prevalence in other countries. Delay in neurodevelopment was in children with low APGAR scor and t-NC. (p<0.001). Early diagnosis of t-NC and early intervention on delivery are important factors for a better neurodevelopment of a child.

Disclosure: No potential conflict stated.
P11-01

Long term analysis of the rate of respiratory function decline in patients with Duchenne Muscular Dystrophy (DMD) in a real-world setting: the SYROS Study

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Introduction: In the Phase III DELOS study, idebenone reduced respiratory function decline rate over 52 weeks; however, data beyond one year is limited. Here, we characterized respiratory function evolution during long-term idebenone treatment compared to untreated periods.

Methods: SYROS is a real-world study in former DELOS patients who transitioned to idebenone under Expanded Access Programs following a variable untreated period. Patients were managed according to routine clinical practice. Annualized forced vital capacity and peak expiratory flow decline rates, expressed as percent predicted (FVC%p, PEF%p), were estimated using random coefficient regression models and a prospectively planned analysis was conducted. Comparisons were made between treated and untreated periods. In addition, treatment periods were also compared to a matched (based on baseline FVC%p) external cohort from the CINRG-Natural History Study. Data on bronchopulmonary adverse events (BAEs) and hospitalizations were collected.

Results: Data from 18/64 former DELOS patients were available. At baseline, mean (SD) age, FVC%p and PEF%p were 14.9 (3.3) years, 47.0% (19.8%) and 43.8% (15.6%); all patients were glucocorticoid non-users and 83.3% were non-ambulatory. Patients were treated for an average (min-max) of 4.2 (2.4–6.1) years, versus an average untreated period of 2.1 (1.0–5.5) years. The annual decline rate was approximately halved with idebenone treatment (FVC%p 4.1% vs 7.5%, PEF%p 6.4 vs 2.3). During idebenone treatment, decline remained low during each treatment year (up to 6 years) compared to matched external controls. The risk of BAEs was reduced by 68% during long-term treatment versus untreated periods, leading to fewer hospitalizations due to respiratory causes (0.06 vs 0.15 events per year).

Conclusion: The previously observed effect of idebenone in reducing the rate of respiratory function decline was consistently maintained for up to 6 years.

Disclosure: All authors are paid consultants for Santhera Pharmaceuticals and are investigators in prior/current studies with idebenone in DMD. G. Buyse is co-inventor of relevant patent applications.
Consistent long-term effect of Idebenone on the rate of respiratory function decline in advanced patients with Duchenne Muscular Dystrophy (DMD)

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Introduction: Two 52-week, placebo-controlled trials (Phase II DELPHI, Phase III DELOS) showed that idebenone consistently reduced respiratory function decline rate in patients with advanced DMD. We now present data on long-term idebenone treatment, from the DELPHI-Extension study, and SYROS – a long-term follow-up of DELOS patients who transitioned to idebenone after an untreated period. The aim was to assess the consistency of the long-term effect of idebenone on respiratory function and compare to expected decline rates in untreated patients from the CINRG Duchenne Natural History Study (DNHS).

Methods: 15 DELPHI-E and 18 SYROS patients with abnormal (<80%) forced vital capacity (as percent predicted, FVC%) were treated with idebenone for an average of 2 and 4.2 years, respectively. Annualized FVC%p decline rates were compared between the two studies. Rates were also compared to untreated matched controls (based on baseline FVC%p) from CINRG-DNHS and to untreated periods in SYROS.

Results: In DELPHI-E and SYROS, mean (SD) baseline age was 15.7 (2.5) and 14.9 (3.3) years, and FVC% was 53.7% (20.2%) and 47% (19.8%), respectively. Most patients (86.7% and 83.3%) were non-ambulatory. For a 2-year period, data were available for both studies and for untreated patients. The average annual decline rate was comparable in treated patients (4.5% and 4.8% in DELPHI-E and SYROS) and lower than in untreated patients (6.5% and 8.3% in CINRG-DNHS and while untreated in SYROS, respectively). During years 3–6, the annual decline rate ranged from 1.8%–4.3% in treated patients (SYROS) and 6.4%–6.6% in untreated patients (CINRG-DNHS). A comparable treatment effect was seen for peak expiratory flow (PEF%p).

Conclusion: The treatment benefit of idebenone, slowing respiratory function decline rate, was maintained for up to 6 years during open-label treatment.

Disclosure: All authors are paid consultants for Santhera Pharmaceuticals and are investigators in prior/current studies with idebenone in DMD.G. Buyse is co-inventor of relevant patent applications.
Cardiac Troponin T (cTnT) as a highly sensitive parameter for Spinal Muscular Atrophy (SMA) in a floppy infant

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Introduction: Studies with new therapeutics for SMA patients showed the best outcome when treatment was started pre-symptomatic. Thus, early detection, e.g. via genetic newborn screenings, is required. Pilot projects have already been implemented in a few countries. High costs and lack of availability of genetic testing in certain regions are challenging early access to treatment and require other screening methods. Studies in adults with neuromuscular diseases have shown elevated cTnT levels without cardiomyopathy. We evaluated whether increased cTnT is detectable in SMA patients and if it correlates with disease severity.

Methods and Results: Since 03/2016 we followed 24 patients with SMA. Serum samples were obtained as part of the routine work-up before initiation of treatment. The high sensitivity cTnT-Test by Roche Cobas was used. Cardiac disease was excluded clinically, by echocardiography and by measuring Troponin I (cTnI). Disease severity was determined by SMA type and in SMA1 patients by the need for ventilation within two months after treatment initiation. All cTnI levels were normal. cTnT was 3-10-fold above the upper limit of normal (14ng/L) in infants with SMA1 (80±39). Values of non-ventilated patients were lower than in ventilated patients (p=0.06). cTnT was significantly higher in SMA1 than in SMA2/3 patients (p=0.0002).

Conclusion: Our data show that cTnT is elevated in all patients with SMA1 and might be useful as a highly sensitive parameter for SMA in floppy infants. Due to lack of a control group and a group of patients with other differential diagnosis of a hypotonic infant, specificity can’t be predicted. Further studies with an increased number of patients evaluating the course of cTnT in other SMA types from birth on are required to determine, if milder affected patients could also be detected earlier.

Disclosure: No potential conflict stated.
Compensation strategies used to move a filled glass to the mouth in Duchenne Muscular Dystrophy

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Objective: Knowledge of upper extremity (UE) compensation strategies in Duchenne muscular dystrophy (DMD) could aid in management of UE functioning and development of clinically important outcome measures for clinical trials. This study aims to describe and quantify compensation and factors influencing the ability to move a filled glass to the mouth (GTM; weight: 200g).

Methods: 16 DMD patients and 12 healthy controls (HCs) were asked to perform 10 GTMs in front of Microsoft’s Kinect®. Presence of compensation was determined visually: neck flexion, shoulder abduction/endorotation, trunk movement, and elbow support. UE body points were derived from kinect® depth data to analyse compensation at each movement cycle; data from DMD patients were compared to the HCs normal range. In addition, forearm weight, elbow flexion and shoulder abduction strength (N) were assessed.

Results: 12 patients were able to perform GTM. Three patients used no compensation. Compensation strategies included: shoulder (1x), trunk (1x), shoulder+trunk (1x), shoulder+trunk+neck (1x), elbow+neck (1x), elbow+trunk (1x), elbow+trunk+neck (3x). Using Kinect®, neck flexion and trunk movement could be objectified in all patients who used this compensation strategy, whereas shoulder abduction could be objectified in one (33%) and elbow support in none of the patients. All patients with elbow flexion strength >1.5x the combined weight of forearm and filled glass were able to perform GTM. Two patients with elbow flexion strength <1.0x the combined weight were able to perform GTM; they had shoulder abduction strength >2.5x the combined weight.

Conclusion: DMD patients use various compensation strategies, of which neck flexion and trunk movement could be objectified and quantified using Kinect®. Combined with knowledge of influencing factors, this could aid in management of UE functioning and development of clinically important outcome measures.

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Recurrent Hypokalemic Periodic Paralysis due to CACNA1S mutation

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Introduction: Hypokalemic periodic paralysis (HPP) is an autosomal dominant ion channelopathy. HPP has an autosomal dominant inheritance due to missense mutation in the skeletal muscle ion channel genes (CACNA1S/SCN4A).

Case presentation: A 13-year old man presented to the emergency department with generalized weakness in the middle of the night. When exploring the patient presented a flaccid quadriplegia, the blood sample analysis showed decreased levels of potassium (2.3 mmol/l) and hypoglycaemia 44 mg/dl, prior that night he consumed a carbohydrate-heavy meal after and intense exercise. Other causes of hypokalemia were ruled out. He was admitted into our pediatric ward and potassium replacement was initiated with a total recovery of the symptomatology within a day. EMG showed a characteristic decrease of Compound Muscle Action Potential (CMAP) below 40% after 5 minutes exercise, genetic testing showed a pathogenic mutation in CACNA1S p.(Arg1239His) confirming diagnosis.

Four other episodes occurred while being inpatient until a low-carbohydrate diet was established, keeping him free of episodes.

Her sister presented at 19 months of age with generalized seizures, LEV was initiated maintaining her free of seizures.

Conclusions: HPP is a rare condition which should be considered in young males presenting with episodes of sudden onset of muscle weakness. HPP can easily be excluded by checking serum potassium levels during acute episode and genetic testing must be done to provide appropriate genetic counseling. There is no specific treatment except for potassium replacement during acute episodes and some authors suggest implementation of low carbohydrate diets which was necessary in our case. This condition has an incomplete penetrance in females and an association with epilepsy hasn’t been found.

Disclosure: No potential conflict stated.
P11-09

Expanding the phenotype of Mitochondrial Thymidine Kinase 2 mutations

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Objective: Mitochondrial thymidine kinase (TK2) is the catalytic enzyme for the phosphorylation reaction of pyrimidine deoxyribonucleosides, the first step in the conversion of deoxyribonucleosides into deoxyribonucleotide triphosphates. TK2-mutations are responsible for disorders of mtDNA nucleotides supply encompassing a broad phenotypic spectrum, with myopathy and progressive external ophthalmoplegia being prominent clinical characteristics. On this case report we describe a 14-months boy with a mitochondrial DNA depletion syndrome (MDDS) harboring a TK2 gene pathogenic mutation, described for the first time, at a homozygous state.

Methods: A 14-months old boy presented with persistently high creatine phosphokinase serum levels and mild transamini- nasemia. Clinical examination, including muscle strength, muscle tone, tendon reflexes, cranial nerves and coordination, was normal, but even if the infant could sit and stand unsupported, he had not yet achieved independent walking. The patient underwent an open biceps brachii in the framework of an under- lying myopathy.

Results: Muscle biopsy revealed myopathic changes with ab- normal variation of muscle fiber diameter and multiple cytochromoxidase-negative muscle fibers with few ragged red (trichrome Gomori staining) and/or ragged blue (succinate dehydrogenase staining), confirming the diagnosis of mito- chondrial myopathy. Genetic testing on muscle revealed an already known pathogenic c.416C>T, p.Ala139Val mutation in homozygosity, in the TK2 gene.

Conclusion: We present a paediatric patient with MDDS due to an homozygous pathogenic mutation in TK2 gene, previously described only in heterozygous state, in two severely affected twins expanding the clinical and mutational spectrum of the TK2-related MDSS. More cases are needed to investigate ge- notypic correlations and potential modifiable factors contrib- uting to phenotypic variations and differing outcomes in pa- tients with the c.416C>T, p.Ala139Val mutation in the TK2 gene.

Disclosure: No potential conflict stated.

P11-10

Evaluation of knowledge level of NUSİNERSEN treatment in SMA families followed by a tertiary Paediatric Neurology clinic

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Introduction: Spinal muscular atrophy (SMA) is a neuromuscular disease characterized by progressive muscle loss. With the approval of Nusinersen as a disease modifying genetic treatment, the disease has been followed with great interest all over the world. This study has been designed to evaluate the awareness and expectations of caregivers of SMA patients about treatment and to measure the effect of education.

Method: The parents of 32 SMA Type 1 patients under Nusin- ersen treatment and 22 SMA Type 2 and 3 patients who were candidates for treatment were invited to an educational con- ference. They were asked to fill the questionnaires before the meeting and to refill the forms after the education.

Results: 37 parents (15 type 1, 14 Type 2 and 5 Type 3) were en- rolled in the study. Mean age of parents was 40.09±8.47 years and 54%(n=20) were female. 17 parents (5 type 1, 5 type 2, 1 type 3)(46%) refilled the forms. Educational level of the parents was 24.3% primary school and 10.8% secondary school, 21.6% high school and 21.6% university. 31% of the answers were wrong in the first questionnaire, whereas 32.9% of the answers were wrong after the meeting. The difference was insignificant (p>0.05). The most common worry was about the access to medicine. Type I parents ex- pected improvement in pulmonary functions, whereas Type 2 and 3 patients to gain ability to walk. None of the parents were aware of the vaccination recommendations for SMA. None of the patients were worried about treatment related complica- tions.

Conclusion: Spinraza treatment is a challenge with big expec- tations for both clinicians and the families. We recommend to develop an effective educational program to increase aware- ness and compliance to treatment.

Disclosure: No potential conflict stated.
VIPN (Vincristine Induced Peripheral Neuropathy) – Neurological complications of Oncology treatment

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Introduction: In the past few decades there is an increase in survival among children with malignancies thanks to the new oncological protocols and newer chemotherapeutics. Despite this, we are still facing with complications of those treatments, and one of those complications are peripheral neuropathies which are linked to chemotherapeutics like vincas, taxanes and platins. One of the most commonly used chemotherapeutic agent in children is vincristine. Vincristine induced polyneuropathy (VIPN) is dose dependent and occurs with an incidence of 30% -80% of which severe forms occur in 1.6% to 7%. The symptoms of the disorder can be classified into three major categories: sensory, motor and autonomic.

Methods: The aim is to point out the need to monitor development of neurological complications in oncology patients like VIPN, ability to use EMNG in monitoring those children and timely modification of oncological treatment to prevent evolution of severe forms. In the past 2,5 years in Children’s Hospital Zagreb nerve conduction studies were done in sixteen children treated with VCR. The reason for EMNG was the development of clinical symptoms of polyneuropathy, high cumulative dose of VCR or neurological symptoms that may indicate leukemic infiltration of the CNS.

Results: Eight of sixteen had NCS signs of motor VIPN, two developed severe motor polyneuropathy and VCR was replaced by another chemotherapeutic. Three of sixteen children developed sensory-motor VIPN and two sensory VIPN.

Conclusion: VIPN is a significant clinical problem in children treated with VCR and can result in chronic pain, limited mobility, loss of proprioception and balance. VIPN is particularly demanding for detection and monitoring in pediatric patients and it is important to use multidisciplinary approach because modification of therapy can help improve long-term quality of life.

Disclosure: No potential conflict stated.

A paediatric case of anti-MuSK Antibody-Positive Ocular Myasthenia Gravis

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Introduction: Myasthenia gravis (MG) is characterized by muscle weakness with diurnal fluctuation. Usually, MG is caused by autoimmune mechanism and most of them have acetylcholine receptor (AChR) antibody. Recently other autoantibodies, such as muscle-specific receptor tyrosine kinase (MuSK) antibody and lipoprotein receptor-related protein 4 (LRP4) antibody, have been found in MG. The case with anti-MuSK antibody usually reported to occur in young female adults or female infants or toddlers, and to have prominent oculobulbar symptoms.

Case: A 13-year-old girl was referred to the department of pediatric neurology due to recently developed bilateral ptosis. The symptom gradually worsened over time and accompanied with diplopia and dysarthria. On neurologic examination, muscle tone and deep tendon reflexes were intact, but extraocular movement was limited, especially in lateral gaze. Magnetic resonance imaging of the brain showed no abnormality. Neostigmine test showed positive response, and repetitive nerve stimulation test revealed a decrement of compound muscle action potential. Serum creatine kinase was normal, and anti-AChR antibody was negative. However, anti-MuSK antibody was positive (65.1nmol/L, reference value ≤0.02). Initially, pyridostigmine was prescribed, and steroid was added at day 8, and then azathioprine at day 20. She showed complete recovery at day 28 on medication.

Conclusion: We report a case of anti-MusK antibody-positive ocular MG in a 13-year-old-girl who showed complete improvement with immunosuppressants.

Disclosure: No potential conflict stated.
Clinical, genetic and neuropathological heterogeneity in a paediatric cohort with Nemaline Myopathy

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Introduction: Nemaline myopathy (NM) is a clinically and genetically heterogeneous muscle disease, thought to be one of the most common congenital myopathies. The diagnostic hallmark is the presence of distinct rod-like inclusions.

Methods: A pediatric cohort observed (between 2002-2019) in a tertiary center from the north of Portugal was reassessed.

Results: Nine patients (5 males, 4 females) with ages between 1 and 20 years were diagnosed with NM. Two patients were cousins and other two had family history of miopathy. Seven had a neonatal presentation: 4 presented with severe congenital phenotype, with tetraparesis, distal arthrogryposis, and severe axial and bulbar involvement, requiring invasive ventilatory support and tube feeding; 3 presented with classic congenital phenotype. One died aged 2 years. Two patients presented infantile phenotype. All nine patients eventually needed ventilation support and one performed scoliosis surgery. Five were able to walk between 18 and 72m (34m average). No one had cardiac involvement. Muscle biopsy was performed in five: all presented rods, mainly peripherally dispersed, variable proportion of affected fibers and with no clear relation with clinical severity. The most frequent defective gene in this cohort was nebulin (NEB) affecting six patients. ACTA2 gene mutations were identified in two patients and a novel heterozygous missense variant in KLHL41 gene was identified in one patient.

Conclusion: Considering the variability presented and the cohort size no genotype-phenotype correlations were drawn. Nevertheless, the absence of cardiac involvement in this cohort is concordant with previous reports.

Disclosure: No potential conflict stated.

Nusinersen: A tertiary centre experience in Type 1 Spinal Muscular Atrophy

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Background: Nusinersen, an antisense oligonucleotide designed to treat 5q- Spinal Muscular Atrophy (SMA), is currently available in Portugal for SMA patients. In clinical trials, treated SMA type 1 patients achieved a substantial motor milestone response. Our aim is to report the clinical results of nusinersen in a tertiary centre in Portugal.

Methods: We performed a retrospective study of type 1 SMA patients treated with nusinersen. Demographic, clinical (including motor scores – CHOP-INTEND), ventilation and feeding parameters were obtained from clinical records.

Results: We are currently treating 5 SMA type 1 patients – current mean age 16,4 months (range 8–25 months), four with 2 copies of SMN2 and one with 3 copies of SMN2. Mean time from first symptoms to diagnosis confirmation was 3,1 months (range 0,3-10,0) and from genetic confirmation to beginning of treatment was 1,1 months (range 0,5-1,7). Only 3 patients had ≥ 6 months of treatment (5,6 and 9 administrations of nusinersen), and they all improved at least 4 points in CHOP-INTEND score (mean change 10.0 points). The eldest patient (25 months-old) began treatment at 2,3 months and has achieved independent sitting. Prior to treatment, 2 patients required continued non-invasive ventilation (NIV) and one 14 hours per day. After 6 months of treatment they all reduced time of NIV up to 8 hours per day. Gastrostomy was performed in 2 patients during treatment and one required tube feeding. No side effects of treatment were noticed.

Conclusion: We observed an improvement in motor function and ventilatory support in SMA type 1 patients with ≥ 6 months of treatment. Despite our small sample, our findings are promising and contribute to the increasing evidence that early diagnosis and treatment are paramount.

Disclosure: No potential conflict stated.
Genetic testing for Indonesian Duchenne and Becker Muscular Dystrophy patients: the era of personalized medicine

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Introduction: Duchenne/Becker muscular dystrophy (DMD/BMD) is the most common genetic neuromuscular disease in children, resulting from a defect in the dystrophin gene located on Xp21. Mutation profiles of the DMD gene in Indonesian patients are not available. Precise mutation analysis is needed to apply mutation-specific therapies currently developed. This study was conducted to reveal the mutation spectrum of DMD gene in Indonesian population, and analyzed the potential amenability by exon skipping therapy.

Methods: We recruited 43 unrelated Indonesian DMD/BMD patients in Dr. Sardjito Hospital and UGM Academic Hospital. DNA was analyzed using multiplex polymerase chain reaction (mPCR) and multiplex ligation-dependent probe amplification (MLPA) to detect deletion or duplication in the DMD gene. The carrier status of mother and sister were also determined.

Results: All patients had very high serum CK levels. 53.5% patients underwent muscle biopsy and showed the absence or partially expressed dystrophin staining. MPCR study was performed 34 cases and revealed deletions in 44.1% cases. Out of 43 subjects, MLPA study showed deletions accounted for 69.7%, while duplications were the remaining 11.6%. Eight patients (18.6%) with DMD phenotype showed no deletion nor duplication. Out of 27 available samples from mothers, carrier status was confirmed on 14 cases, meanwhile only 1 sister carried mutated DMD gene. Furthermore, 46.5% patients are potentially amenable to exon skipping therapy.

Conclusion: MLPA is found to be an easy and quick technique to identify deletion and/or duplication in DMD patients and detect the carrier status, while mPCR study can be performed in limited resources to screen deletions. Further study is needed to elucidate point mutation and to serve information needed for the amenability to mutation-specific therapy.

Disclosure: No potential conflict stated.

A newly defined Fukutin gene mutation in a child with Fukuyama-Type Congenital Muscular Dystrophy

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Introduction: Congenital muscular dystrophy is a clinically and genetically heterogenous group of disorders which are inherited autosomally recessively that present with early-onset progressive muscle weakness. Fukuyama-type Congenital Muscular Dystrophy (FCMD) is a rare, inherited, autosomal recessive, congenital muscular dystrophy. A defect in the fukutin (FKTN) gene on chromosome 9q31-33 is responsible for the clinical manifestations. Very few cases of FCMD were reported outside of Japan, herein, we present a Turkish child with a new gene mutation with FKMD.

Case report: A 2-year-old boy hospitalized to our pediatric intensive care unit due to lower respiratory tract infection. He had generalized hypotonia, muscle weakness, developmental delay, neuromotor retardation since birth. He is the first child of 2nd degree relative parents. Physical examination revealed as generalized hypotonia, prominent atrophy in extremity muscles, hypoactive deep tendon reflexes and no eye involvement. Laboratory testing revealed elevated transaminases and creatin kinase levels. Cranial magnetic resonance imaging showed global cerebral atrophy, gliotic changes in the right ventricle and widened subarachnoid space. Histopathological examination of muscle biopsy samples showed myopathic/dystrophic findings in addition to no staining for alpha-dystroglycan. Whole exome analysis for alpha-dystroglycanopathy showed previously undescribed heterozygote mutation in the FKTN gene: c.358T>C (p.Trp120Arg). The diagnosis of FCMD is based by clinical findings (hypotonia since birth, neuromotor retardation), elevated serum creatine kinase levels, neuroimaging findings, muscle biopsy findings and molecular genetic analysis of FKTN gene. Genetic consultation was given to the family.

Conclusion: To the best of our literature knowledge, we described new heterozygote de-novo mutation in FKTN gene in a child with FCMD.

Disclosure: No potential conflict stated.
One year of Nusinersen treatment in Spinal Muscular Atrophy (SMA) in Hungary

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Introduction: Nusinersen is an antisens oligonucleotide enhancing the production of the SMN protein. Its effectiveness was shown in several types of SMA by clinical trials, thus it received EMA approval. In Hungary, nusinersen treatment was started in April, 2018. Our aim is to summarize our experience with safety, tolerability and efficacy.

Methods and Results: By 1st March, 2019, 36 patients have started the therapy in one of the two Hungarian centres. Mean age of patients at the start of the treatment was 6.5 years (0.4-17 y). 8 patients were type I. (5-125 months), 15 patients were type II. (1.3-12 y), 13 patients were type III. (4.5-17 y). Ultrasound guided lumbar puncture was performed in cases of difficult spine with a success rate of 100%. We performed approximately 150 injections. The most frequent side effects were headache (10%), backache (12%) and vomiting (12%). There were no treatment termination because of any side effects.

By now, 8 children have received the first six treatments. Motor function has improved in all children. In type II-III. patients, 1-11 point improvement was shown by the Hammersmith Functional Motor Scale Expanded version and 3-14 point increase was shown by the Hammersmith Function tests. In type I. patients, the change in the CHOP-INTED score and walk test results also increased by 22-26 meters in type III. patients. In type II. patients, the change in the CHOP-INTED score was between 16 and 21 points.

Conclusion: Outside of clinical trials, nusinersen seems to have the same safety and tolerability profile. We found similar efficacy of nusinersen in the everyday clinical practice, in heterogeneous patient population, in all three types of SMA.

Disclosure: No potential conflict stated.

The RESTORE Registry: a resource for measuring and improving Spinal Muscular Atrophy (SMA) outcomes

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Introduction: Dramatic changes in the SMA treatment landscape have altered the outlook of this disease. The RESTORE Registry was created to assess outcomes of patients receiving SMA treatment, provide information on the effectiveness and long-term safety of new/emerging treatments, document patient survival, and collect information on healthcare resource utilization, caregiver burden, patient functional status, and quality of life.

Methods: The RESTORE Registry is a prospective, multicenter, multinational, observational study governed by a steering committee of SMA experts committed to ensuring data quality and publishing findings. Participating centers include those involved in existing and evolving SMA registries (e.g., iSMAC, TreatNMDD, NeuroNEXT, Cure SMA) and SMA treatment centers recruited de novo. Data from existing patients enrolled in partnering registries are transferred to the RESTORE Registry database. Data for newly diagnosed patients are added as they enroll. Follow-up is 15 years from enrolment or until death, whichever is earlier. Assessments include SMA history and treatment, pulmonary, nutritional, and motor milestones, healthcare resource utilization, work productivity and activity impairment, adverse events, quality of life, and survival.

Results: The RESTORE Registry has been established and the first patients have been enrolled in the US. Medical centers in Europe have been activated and patients enrolled according to treatment availability and data reporting needs.
Conclusions: The RESTORE Registry has begun recruiting SMA patients, allowing short- and long-term patient outcomes assessment and extended evaluation of emerging SMA treatments, including gene therapy.

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Burden of illness of Spinal Muscular Atrophy Type 1 (SMA1)

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Introduction: SMA1 is a rare, rapidly progressing, debilitating, genetic neuromuscular disease. Data on cost burden are limited and must be updated as the treatment landscape evolves. The first SMA treatment, nusinersen, was recently approved in the US (23/12/2016) and EU (30/05/2017). We undertook two retrospective claims analyses of real-world healthcare resource utilization (HRU) and costs among SMA1 patients.

Methods: SMA1 patients ≤1-year old were identified and matched (1:1) with a random sample of infants in the QuintilesIMS PharMetrics Plus Health Plan Claims Database (US; 02/2011–11/2016). SMA1 patients were identified in Symphony Health’s Integrated Dataverse® (US; 09/2016–08/2018). HRU and costs were described.

Results: Significantly more SMA1 patients in PharMetrics (n=119) had ≥1 all-cause HRU claims vs. matched patients (98.3% vs. 54.6%, P<0.0001). Mean all-cause HRU and costs were higher for SMA1 infants; extrapolated all-cause total annual costs, based on month 1 post-diagnosis, were $324,751 (SMA1) vs. $3,294 (matched). SMA1 patients in Symphony (n=349, median follow-up of 7.9 months) had an average 59.4 days with medical visits/year (inpatient, 14.1; related to respiratory failure, 13.4). In nusinersen-treated patients (n=45), those values were 56.6, 4.6, and 11.4 days following treatment initiation. Excluding nusinersen-related costs, mean healthcare costs per-patient-per-year were $137,627 (median: $144,487) for the first 3 months (loading phase), $36,882/month (median: $16,132) thereafter. EU data (pooled and country-specific) available at the time of the congress will be presented.

Conclusions: The economic burden of SMA1 is substantial, even among patients treated with nusinersen.

Disclosure: JS has received personal compensation from SSI Strategy; MG-L and ML are employees of Analysis Group, Inc. which has received consultancy fees from AveXis, Inc. to the conduct of this study; MD, OD, RA, and DMS are employed by AveXis, Inc. OD and DMS hold stock or stock options with AveXis, Inc./Novartis
**P11-20**

**Paediatric Anti-3-Hydroxy-3-Methylglutaryl-Coenzyme A Reductase antibody associated Immune Necrotizing Myopathy (anti-HMGCR INM) may mimicking Limb Girdle Muscular Dystrophy in presentation**

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**Objective:** We report clinical, radiological and pathological features of two patients with anti-HMGCR antibody associated necrotizing myopathy (INM), mimicking slowly progressive limb girdle muscular dystrophy (LGMD). The treatable nature of these disorders calls for early recognition and treatment but there was significant delay in diagnosis in both cases.

**Methods:** Both patients were referred to a tertiary paediatric neuromuscular centre. We summarise their clinical presentation, investigations, muscle pathology, imaging findings, the diagnostic and treatment challenges. Data was retrieved retrospectively from medical records.

**Results:** Case 1 is 18 year-old girl with onset of progressive axial and proximal weakness and rash at age 9 years. Case 2 is a 14-year old girl with severe lower limb myalgia and cramps, but little weakness from age of 9 years. CK was 14000 U/L and 13000 U/L, respectively. Lower limb muscle MRI in both showed increased STIR signal in gluteal and thigh muscles but limited fatty infiltration. Muscle pathology was in keeping with necrotising myopathy in both, with prominent sarcolemmal complement C5b9 labelling of non-necrotic fibres, no significant MHC-I upregulation and normal immuno-panel for dystrophy-associated proteins. Case 1 was treated with steroids, methotrexate, infliximab, mycophenolate mofetil, cyclophosphamide with limited response. She responded best to regular IVIG. Case 2 has been recently diagnosed and treatment is planned. Case 1 also carries a heterozygous LMNA gene variant of unclear significance, further confounding the diagnostic process.

**Conclusion:** These cases highlight diagnostic challenges of anti-HMGCR INM, as the chronic symptoms may mimic LGMD, with partial response to immunomodulation. Lower limb muscle MRI and biopsy can be useful discriminatory tools but overlapping features can be challenging to interpret. Anti-HMGCR antibody testing should be considered in all cases of undiagnosed LGMD.

**Disclosure:** No potential conflict stated.

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**P11-21**

**Phenotypic variability in two maternal cousins with Calpainopathy**

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**Introduction:** Calpainopathy is a muscular dystrophy characterized by symmetric and progressive weakness of proximal limb–girdle muscles. It is caused by mutations of CAPN3 gene, which codes for calpain-3, a muscle-specific proteolytic enzyme. The phenotype shows intrafamilial and interfamilial variability ranging from severe to mild.

**Methods:** We studied the clinical cases of two maternal cousins (a 12 years old boy and a 15 years old girl) with elevated creatine kinase levels and clinical findings suggestive of Calpainopathy. In one of the cousins the diagnosis was confirmed by muscle biopsy. Information was collected by chart review.

**Results:** The boy experienced the first symptoms at 4 years old (2010) versus 9 and a half years old (2012) in the case of the girl. The pelvic girdle was the first affected in both cases. At 9 years old (2015), the shoulder girdle started also to be affected in the boy while the girl, at 15 years old, still has no shoulder girdle impairment at all. At the present moment, the boy has severe impairment of the pelvic girdle being only able to walk with support and moderate impairment of the shoulder girdle with an Egen Klassifikation Scale Version 2 score of 13 out of 51 points while the girl has only mild pelvic girdle impairment with a North Star Ambulatory Assessment test result of 29 out of 34.

**Conclusion:** In conclusion, these cases illustrate and reinforce the fact that disease onset age and the clinical course of Calpainopathy can show important intrafamilial variability. One important lesson is that the disease should not be excluded in relatives only because they lack symptoms and creatine kinase could be used for screening.

**Disclosure:** No potential conflict stated.
P11-22

Limb-Girdle Muscular Dystrophy Type 2O as a clinical manifestation of POMGNT1 gene mutation

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Introduction: The limb-girdle muscular dystrophies (LGMDs) are a heterogeneous group of genetic disorders generally characterized by weakness of the shoulder and the pelvic girdle muscles. LGMD type 2O (LGMD2O) belongs to a group of rare muscular dystrophies named dystroglycanopathies, which are characterized molecularly by hypoglycosylation of α-dystroglycan (α-DG). LGMD2O usually present in late childhood as congenital muscular dystrophies with multiple organs involved (muscle, eye, brain). Variable rates of progression, proximal muscle weakness, mild pseudohypertrophy, microcephaly, and mild mental retardation is usually noted. Serum creatine kinase (CK) level is elevated. Muscle histology shows fiber size variability and reduced α-DG.

Methods and Results: Here we report a patient with POMGNT1 1p34.1 c550C>T and c461C>A variations. A 3 years old boy presented to medical attention with clumsiness and frequent falls. Cognitive milestones were acquired at the expected ages, although his initial motor development was slightly delayed. He developed proximal limb muscle weakness at the age of 4 with difficulty rising from a sitting position and climbing stairs. His Gower sign was positive. There was hypertrophy of the calves and quadriceps and wasting of the hamstring and deltoid muscles. Laboratory evaluation showed an elevation of serum CK (10913 IU/l and 24646 IU/l at 3 and 4 years of age, respectively; the normal range 172 IU/l). Dystrophin and ANOS; DYSF, GAA, SCGB, SCGD, CAPN3, FKRP, SGCA, SGCD, TCAP gene evaluation performed for Duchenne muscular dystrophy (DMD) and LGMD and produced negative results. Clinical exome sequencing showed POMGNT1 gene mutation 1p34.1 c550C>T and c461C>A variations. This mutation is related to retinitis pigmentosa, muscular dystrophy-dystroglycanopathies type A,3, type B,3 and C,3.

Conclusion: Clinical findings and genetic evaluation lead us to LGMD2O.

Disclosure: No potential conflict stated.

P11-23

Electrophysiological diagnostic of neuromuscular diseases in new-borns, infants and toddlers

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Introduction: Recognizing neuromuscular disease in newborns, infants and toddlers is even for the experienced neuro-paediatrician a challenging task. Many neuromuscular diseases present in the beginning only with very minor symptoms, other cases are quite severe with i.e. generalized muscular hypotonia requiring mechanical ventilation and making a proper clinical assessment difficult. However, early treatment of neuromuscular conditions can alter the prognosis significantly. The children’s hospital of Eastern Switzerland has become a major centre for neurophysiological diagnostic in children.

Methods and Results: We have established a workup to precisely assess the neuromuscular system in newborns and toddlers. Our assessment protocol starts with the basic study of sensory and motor nerves and typically a EMG of the M. tibialis anterior. Depending on the results of the basic study the examination is extended based on the clinical picture. In the case of a Floppy infant with a suspicion of a myasthenia a single fibre EMG is conducted typically at one of the muscles innervated by the cranial nerves. If an asymmetrical weakness is present the examination focuses on the affected muscle and its contralateral counterpart.

Based on this assessment protocol we can diagnose a significant number of neuromuscular disease. In this presentation we will show examples how spinal muscular atrophy can be diagnosed early by recording pathological discharges during wake and sleep, how a congenital myasthenic syndrome can be diagnosed by single fibre EMG techniques and how especially in clinical apparent myotonia an examination of the mother can show myotonic discharges and lead to the diagnosis of myotonic dystrophy in the child.

Conclusion: We conclude our presentation with an outlook of the current developments in pediatric electro-neuromyography.

Disclosure: No potential conflict stated.
P11-24

Spinal rigidity, scoliosis and progressive respiratory impairment: clues to SEPN1 related Myopathy

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Introduction: Mutations in SEPN1 gene coding for selenoprotein N1 result in a spectrum of neuromuscular disorders with distinct histopathological features, referred as SEPN-related myopathies, which share a similar clinical phenotype characterized by early-onset axial and neck weakness, progressive scoliosis and spinal rigidity as well as severe respiratory insufficiency.

Methods: We describe two cases of SEPN1 related myopathy placing emphasis on the diagnostic clues and the clinical progression.

Patients: A 2-years-old girl presented with significant neck extensor weakness and mild axial and limb girdle weakness. On examination she demonstrated absence of deep tendon reflexes, positive Gower’s sign and a mild scoliosis. Serum CK was normal and muscle biopsy findings were consistent with mild myopathic changes with fatty tissue infiltration. DNA analysis of the SEPN1 gene revealed a homozygous mutation c.713dupA previously described as disease causing for multiminicore myopathy. The second case is that of 5-years-old boy with a history of hypotonia, progressive proximal muscle weakness and swallowing difficulties from the first year of life. On examination he presented with prominent spinal rigidity, kyphoscoliosis and a positive Gower’s sign. Serum CK was mildly elevated. DNA analysis identified compound heterozygous variants c.872G>A/c.1397G>A in the SEPN1 gene. Both children are ambulant at the age of 6 and 9.5 years, respectively. The young boy has undergone orthopedic surgery 4 months ago currently being on non-invasive ventilation.

Conclusions: SEPN-related myopathies can remain unrecognized because of the relatively benign course of the disease. Prominent head lag with preserved mobility and moderate CK elevation, scoliosis and spinal rigidity should prompt genetic testing for mutations in the selenoprotein N1 gene. Accurate diagnosis will help identify early the need for intervention with non-invasive ventilation.

Disclosure: No potential conflict stated.

P11-25

Muscle ultrasound comparison between early, intermediate and late onset Friedreich’s Ataxia

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Introduction: Friedreich’s Ataxia (FA) can be subdivided into pediatric (p-FA), intermediate (i-FA) and very late (VLOFA)–onset (starting <18, 18-40 and >40 years of age, resp). P-FA, is often characterized by sensory neuropathy, (cardio)myopathy and motor neuropathy (during the later disease course), VLOFA with combined symptoms including spasticity, whereas the symptomatology of i-FA is still unclear. In the present study, we aimed to elucidate discriminative muscle ultrasound features between these FA subgroups.

Methods: We compared quantitative muscle ultrasound parameters between n=12 p-FA [9 (range: 4-17)* and 25 (range 12-53) ** years], n=9 i-FA [20 (range 18-23)* and 42 (34-53) ** years], and n=3 VLOFA [40 (range 40-, 69)* and 73 (55- 79) ** years], (median age of onset* and assessment**, resp.) and age-matched healthy controls. FA-phenotypes were compared regarding MUD of proximal (biceps and quadriceps) and distal (tibialis-anterior) muscles and the distal-to-proximal MUD-ratio (for differentiation between neuropathy and myopathy) of the leg muscles (calculated as: MUDtibialis-anterior / MUDquadriceps).

Results: MUD outcomes of all investigated muscles were higher in p-FA, i-FA and VLOFA than healthy controls (all p<.001). MUD data of the total FA group showed a positive correlation between FA and healthy controls but not between different FA subtypes. From myopathic perspective, these data may imply that p-FA, i-FA and VLOFA may still concern the same disease spectrum, despite different phenotypic appearances.

Conclusion: In FA, quantitative MUD parameters are associated with age. Quantitative MUD parameters can distinguish between FA and healthy controls but not between different FA subtypes. From myopathic perspective, these data may imply that p-FA, i-FA and VLOFA may still concern the same disease spectrum, despite different phenotypic appearances.

Disclosure: No potential conflict stated.
Guillain–Barré Syndrome: analysis of Acute Inflammatory Neuropathies from a tertiary centre

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Introduction: Guillain–Barré syndrome (GBS) is the most frequent cause of acute flaccid paralysis in the occidental world. The diagnosis of SGB is clinical and supported by complementary exams which in the early phase of the disorder may be normal. We aim to characterize clinical and demographically a cohort of patients admitted with GBS.

Methods: Retrospective, observational study from 2003 to 2018. Consultation of clinical processes and complementary exams available. GBS was subclassified into variants acute demyelinating inflammatory (AIDP), axonal motor sensory (AMSAN), axonal motor (AMAN) neuropathies, amongst others.

Results: A total of 24 patients (males/female=56.3%/43.8%, mean age=6.5days, SD=4.3) were included. The most frequent phenotypic variant was AIDP (n=13), followed by AMAN (n=3), Miller-Fisher syndrome (n=3) and paraparesis (n=2). AMSAN (n=1), Pharyngeal-cervical-brachial (n=1) and pure ataxia (n=1) were comparatively less frequent. There were two patients with simultaneous AIDP and acute disseminated encephalomyelitis. In 46% (n=11) of cases, there was preceding infection. Ten patients presented initially severe neuropathic pain, leading to incorrect initial osteoarticular diagnosis in 12.5%. Severe dysautonomia (n=2) and respiratory failure with invasive ventilatory support (n=1) were rare complications. CSF albuminocytologic dissociation was present in 46% (n=11) and conduction nerve study alterations occurred in all patients. Identification of infectious included Mycoplasma pneumoniae, Campylobacter and EBV primo-infection. All patients were treated with 2-5 days cycle of human immunoglobulin. No patients had atypical subacute or evolution to chronic inflammatory evolution. 92% patients had a good evolution with full recovery at 12 months follow-up. Only 2 patients had minimal neurologic sequels.

Conclusions: GBS at pediatric age may be challenging, especially regarding less frequent clinical variants. In our cohort, the presence of severe neuropathic pain was particularly prevalent, requiring a higher level of suspicion.

Disclosure: No potential conflict stated.

Reservoir with a thoracic spinal catheter used for intrathecal delivery of Nusinersen in a patient with Type 2 Spinal Muscular Atrophy

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Objectives: Nusinersen is an antisense oligonucleotide approved for all types of Spinal Muscular Atrophy (SMA). Patients with SMA develop neuromuscular scoliosis. Drug delivery via lumbar puncture is often difficult to perform, therefore, we administered Nusinersen using a subcutaneous intrathecal catheter (SIC) system by connecting a titanium port with a bacteriologic filter for safe drug administration to the spinal cord.

Design/methods: A 15-year-old male type 2 SMA (with neuromuscular scoliosis, spinal fusion and two posterior spinal rods extending from upper thoracic to lower lumbar spine) was prescribed with Nusinersen therapy. The first loading dose was successfully administered, nevertheless, it was not possible to perform the second one due to the complex spinal anatomy. We decided, working with Neurosurgery department, to perform a thoracic laminectomy. A soft intrathecal catheter was introduced into the subarachnoid space via a durotomy within the spinal fusion segments. An implantable reservoir was placed subcutaneously into the abdominal wall and then it was connected to an intrathecal catheter. Device implantation took 2 hours and it was well tolerated. The second loading dose of Nusinersen could be injected in the same intervention. At this moment, the patient has already completed all four loading doses with no complications related to the reservoir (the 3rd and 4th ones did not required local or systemic analgesia, respiratory precautions or sedation). Cerebrospinal fluid was withdrawn from the reservoir and blood test results were normal. The patient has not experienced any adverse events related to the Nusinersen therapy.

Conclusions: Preliminary observations reveal that the use of a reservoir with intrathecal catheter connected to the thoracic spinal canal, is a viable and safe option to deliver intrathecal Nusinersen in patients who have extensive spinal fusion and instrumentation.

Disclosure: No potential conflict stated.
**P11-28**

**Neuromuscular Diseases in paediatric palliative care: a clinical challenge**

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**Objectives and Methods:** The objective was to describe epidemiologically patients with neuromuscular diseases and their approach by the PPC team and compare the support and assistance received by them with those suffering from other neurological diseases.

**Methods:** Retrospective descriptive study of patients with neuromuscular diseases derived to PPC between 2013-2018.

**Results:** 170 patients were attended, 82/170 (48%) presented neurological pathology and, 23/82 neuromuscular disease:12 metabolic diseases (8 mitochondrial encephalomyopathies,1 Pompe disease,1 Niemann-Pick disease,1 non-ketoic hyperglycemia), 5 AME type i, 3 myotonic dystrophy of Steinert and 2 nemaline myopathies. No significant difference was found in the follow-up time, with a median of 55 days (IQR 28.5-127.5) in neuromuscular patients versus 154 days (IQR 60-123) in the rest of the neurological patients.

The differences in frequency between respiratory and nutritional support neuromuscular disease/others neurological patients: respiratory support:nasal cannula: 34%/23%; NIV: 17%/3.4%; MV 8%/1.6%. Nutritional support: nasogastric song 56%/27%; gastrostomy 26%/29%.

The assistance to patients with neurological diseases is similar to that of other neurological pathologies, with a median of 16 phone calls (IQR 5.5-40) and median consultations of 7 (IQR 2.25-15.75) and home visits of 1 (IQR 0 -5).


**Conclusions:** The establishment of PPC as an specific area of pediatrics has led to a significant improvement in the quality of life of patients with neuromuscular diseases. Patients with neuromuscular diseases require greater respiratory and nutritional support than other neurological diseases. Neuromuscular diseases represent a care challenge in CPP due to its variability and prognostic uncertainty, requiring comprehensive and multidisciplinary care.

**Disclosure:** No potential conflict stated.

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**P11-29**

**Mortality and sedation at the end of the life in neurological patients in a paediatric palliative care unit**

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**Introduction and objectives:** The death of a child is usually difficult for the family and those close to them to understand and accept. In Spain, pediatric palliative care units (PPCU) are becoming facilities that are increasingly specialized in meeting all the needs of the child and their family. The objective of this study is to characterize patients with neurological disease who died in a PPCU and analyze the underlying diseases, the causes and the environment in which the deaths occur.

**Results:** During 2012-2017, 55 deaths occurred, of which 23 patients (41%) had a neurological disease. 9 patients (39,1%) required sedation at the end of life (EOL). Midazolam was used in all cases and also 7 patients received morphine. Administration via subcutaneous 6/9 and peripheral 3/9. Patients who died of diseases related to the underlying disease 4/25 required sedation less frequently (p< 0.01) unlike the rest of patients who required sedation at the EOL. Patients who required sedation in EOL died with greater frequency at the hospital 7/9 than those who didn’t. All the families were monitored during the bereavement process.

**Conclusions:** Patients who die while under the care of a PPCU mostly belong to two main groups of patients, namely cancer and neurological patients. We found relationship between sedation in EOL and causes of death. Most patients with neurological diseases die from complications related to their underlying disease, usually respiratory. The need for sedation at the end of life is shown to condition the place of death. Sedation at the end of life is shown to condition the place of death. It is important to promote the creation of PPCUs to care for these patients and their families.

**Disclosure:** No potential conflict stated.
Intrathecal administration of Onasemnogene Abeparvovec gene-replacement therapy for Spinal Muscular Atrophy Type 2 (STRONG)


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Introduction: Onasemnogene abeparvovec (AVXS-101), a survival motor neuron (SMN) gene-replacement therapy, treats the SMA genetic root cause. In a phase 1/2a study, intravenous AVXS-101 improved outcomes of SMA type 1 patients. STRONG (multicenter, phase 1/2a study [NCT03381729]) assesses intrathecal AVXS-101 for SMA type 2.

Methods: SMA type 2 patients (biallelic SMN1 loss, 3xSMN2) who could sit but not stand/walk aged ≥6–<60 months receive a one-time intrathecal AVXS-101 infusion in a dose-escalation study (dose A: 6.0x10^{11}; dose B: 1.2x10^{11}; dose C: 2.4x10^{11} vg). After demonstrating acceptable safety of dose A and B, the remaining planned dose B patients were dosed. The first 3 dose C patients were approved in Dec 2018. For dose B and C, 12 patients ≥6–<24 months and 12 patients ≥24–<60 months are planned for each dose. Primary endpoints are safety/tolerability, optimal dose, unsupported standing ≥3 seconds (≥6–<24 months), and Hammersmith Functional Motor Scale-Expanded (HFMS-E) score change from baseline (≥24–<60 months) at 12 months post-dose.

Results: As of Feb 19, 2019, 30 patients were enrolled at 11 sites. Enrollment is complete for dose A (N=3, ≥6–<24 months) and B (N=25; n=13, ≥6–<24 months; n=12, ≥24–<60 months), and ongoing for dose C (2 doses). As of Sep 27, 2018, no safety/tolerability concerns have been identified; 1 patient experienced 2 serious adverse events (elevated alkaline phosphatase, respiratory failure). 4/10 patients (≥24 months) with 1-month post-dose data had ≥3-point HFMS-E score increase from baseline. 3 patients achieved 4 additional milestones. An update will be presented.

Conclusions: Results from STRONG show intrathecal AVXS-101 delivery is feasible and well tolerated, with no safety concerns to date, and may be a promising SMA type 2 treatment.

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**P11-31**

**Dynein Heavy Chain Mutation: a case series**

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**Introduction:** Dynein Heavy Chain (DYNCH) mutations have been well described with various neurological conditions including hydrocephalus, peripheral neuropathy, abnormal cortical development and distal spinal muscular atrophy.

**Case series:** We present our case series of three children with DYNC1H1 mutations presenting with a spectrum of neurological conditions including arthrogryposis, epilepsy, cortical malformation and distal spinal muscular atrophy with a motor peripheral neuropathy.

**Discussion:** Recently dominant DYNC1H1 mutations were reported with a clinical phenotype of cortical malformation and distal spinal muscular atrophy.

**Conclusion:** It is important to recognise this phenotypical spectrum for accurate diagnosis and further management of this condition.

**Disclosure:** No potential conflict stated.

**P11-32**

**Charcot-Marie-Tooth Disease associated with elevated creatine kinase and proteinuria due to Inverted Formin 2 (INF2) gene mutation**

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**Introduction:** Inverted formin 2 (INF2) protein is a member of the diaphanous-related formin which accelerates both actin polymerization and depolymerization. INF2 also regulates actin-dependent mitochondrial fission. Recently, mutations in INF2 gene identified in patients with the Charcot-Marie-Tooth neuropathy (CMT) with focal segmental glomerular sclerosis (FSGS).

**Methods:** Here, we represent an eight-year-old Turkish boy, who diagnosed as CMT, elevated creatine kinase and mild proteinuria related with INF2 mutation.

**Result:** An eight-year-old boy presented with gait disturbance since the age of 3. He had muscle weakness, reduced deep tendon reflexes, and foot deformities. The electrophysiological studies showed demyelinating and axonal sensorimotor neuropathy. His creatine kinase (CK) level was 588 U/L. Since the presence of neuropathy together with mildly elevated CK, our preliminary diagnosis was mitochondrial disorder. However, metabolic screening, brain and spinal MRI were normal. mitofusin 2 mutation was not detected. Muscle biopsy was normal. Nerve biopsy was adipose tissue. After INF2 gene mutation was detected by whole exome sequencing, proteinuria was also detected.

**Conclusion:** To the best of our knowledge, this report is the first of a Turkish patient with CMT and proteinuria due to INF2 gene mutation. This is also the first case in the literature who had CK elevation in INF2 gene mutation. Since, it is known that INF2 affects mitochondrial length and endoplasmic reticulum-mitochondrial interaction in an actin-dependent manner. Elevation of CK may be due to mitochondrial dysfunction. However understanding of pathogenesis is possible with further molecular studies.

**Disclosure:** No potential conflict stated.
P11-33

Early-onset Distal Myopathy related to a novel homozygous mutation in the MYH7 gene in a 17-year-old girl

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Introduction: Myosin is essential for muscle contraction by ATP hydrolysis and formation of muscle filaments. The MYH7 gene encodes for a subunit of the heavy b-chain subunit which is found in slow type 1 muscle fibers and in the heart ventricles. Mutations in the MYH7 Gene are well-characterized as a common cause of genetic cardiomyopathies. Moreover, MYH7 mutations cause different myopathy phenotypes like early-onset distal myopathy and myosin storage myopathy. We report an early-onset distal phenotype in a girl due to a novel MYH7 mutation.

Patient: A 17-year-old Syrian girl was admitted to our outpatient clinic with distal and proximal weakness of lower extremities. She had difficulties in going upstairs. Her walking distance was 400-500m. The clinical examination revealed a calf hypertrophy, a positive Gowers sign, hyperlordosis, foot drop and high arc feet. Deep tendon reflexes were absent. Diagnostic tests: Serum CK level was as slightly elevated. Motor nerve conduction velocity of peroneal and tibial nerves was normal. Genetic testing for SMN1-associated spinal muscular atrophy Type 3 was negative. Echocardiography and ECG were normal. A next generation sequencing panel revealed a homozygous mutation in the MYH7 gene coding for the heavy b-chain of the myosin protein.

Discussion: The clinical presentation including the leading symptoms of distal weakness and foot deformities is compatible to an early-onset distal phenotype due to a MYH7 mutation. The bioinformatic prediction and the fact that the affected domain is highly conserved in mammalian species suggest a pathogenic effect. The wide clinical spectrum of MYH7 mutations should be considered in the work-up of pediatric distal myopathies.

Disclosure: No potential conflict stated.

P11-34

Prevalence and genetic subtypes of Congenital Myasthenic Syndromes in Slovenian children

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Introduction: Congenital myasthenic syndromes (CMS) are genetically and phenotypically diverse genetic disorders of neuromuscular transmission. Data on prevalence among children are scarce with just a few studies conducted in specific countries. Whole exome sequencing facilitated discovery of novel CMS and to date over 30 genes have been implicated. Treatment varies depending on the CMS genetic subtype. Our aim was to identify the prevalence and the genetic subtypes of childhood CMS in Slovenia.

Methods: Medical records were retrospectively reviewed of all patients with CMS, referred over a 18-year period (2000-2017) to the Department of Child, Adolescent & Developmental Neurology, University Medical Centre, Ljubljana, Slovenia, which is assumed to cover all paediatric patients with CMS in our country. All patients with genetically confirmed CMS were included in the study. The population of children under 18 years of age at the end of 2017 was 358,756 according to the Statistical Office of the Republic of Slovenia.

Results: 8 children (3 males, 5 females) with a confirmed genetic diagnosis of CMS from 6 unrelated families were included. According to the genetic subtypes 4 patients (50%, n=8) have a AchR subunit mutation (3 Ⅰ and 1 Ⅰ subunit), 3 (37%, n=8) patients defects in the end potential development and maintenance due to RAPSN and MUSK mutation and 1 (12,5%, n=8) has choline acetyltransferase (ChAT) deficiency due to a mutation in the CHAT gene. Estimated prevalence of genetically confirmed CMS in Slovenian children was 22,3 cases per 1,000,000 children at the end of 2017.

Conclusion: To our knowledge this is the highest reported prevalence of genetically confirmed CMS in children and exceeds previously reported prevalence more than two-fold.

Disclosure: No potential conflict stated.
Follow-up of 13 Duchenne boys treated with Ataluren in Portugal

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Objective: Evolution of 13 boys with Duchenne Muscular Dystrophy (non-sense mutations) treated with ataluren in Portugal.

Methods: Retrospective review of files and functional measures. Clinical and functional data were analysed for age and age at start of medication. Evaluations were done at beginning, 12, 24 and 36 months. All were seen by neuromuscular specialists in tertiary hospitals. Three patients were in a phase 3 clinical trial. Literature review of natural history was made and compared with patient’s progression.

Results: Four patients are from Lisbon, 3 from Oporto and 6 from Coimbra. Mean age at the beginning of ataluren was 7 years 5 months (from 5y 10 months to 11y 6m) and mean actual age was 10 years and 6 months (from 6y 1m to 16y 8m). The duration of treatment was in average 29 months (between 9 and 58 m). One suspended treatment for noncompliance. Evolution of 6MWT was available in all, NSAA was done in 4, Rise from floor and 10 m run in all the patients from Lisboa and Coimbra. All patients remained ambulant. Most (7/13) showed an increase in 6MWT at 12th months (+35,2m avg), and decrease at 24th months (-70m avg). This improvement at 12th m was not seen in NSAA (-7p at 12 m, -18p at 24m), nor “rise from floor” (6/13 increased 2,26", 2/13 equal or decrease) or 10 m run. In this cohort, 6 patients predictably will lose ambulence in 2 years (current age- 11,5 y avg, between 9,5 and 15,5y).

Conclusions: Despite the reduced sample, different ages and durations of treatment, we tried to compare with natural history. This follow up will continue to appreciate evolution under treatment in natural clinical conditions.

Disclosure: No potential conflict stated.

Congenital Myopathies: clinicopathological findings and genotype-phenotype correlations

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Introduction: Congenital myopathies are a group of clinically and genetically heterogenous muscle disorders characterized by hypotonia and weakness that typically present at birth or early in infancy. With an increased understanding of the genetic basis of the disease, we now have the knowledge that the mutations in congenital myopathy genes can result in different clinical phenotypes.

Methods and Results: We studied the clinico-pathological features and genotype-phenotype correlations in 62 patients with congenital myopathy. We performed whole exome sequencing in 43 and a NGS panel in 19 patients.

There were 62 congenital myopathy cases with a mean age of 68 months at diagnosis and a female/male ratio of 1. Consanguinity was present in %58 of patients. Histopathological classification yielded 12 patients with nemaline myopathy, 8 with core myopathy, 3 with centronuclear myopathy, 3 with congenital fiber type disproportion. In 36 patients, muscle biopsy showed features suggestive for congenital myopathy but not sufficient to classify into a single subgroup. The molecular diagnosis was achieved in 34 of 62 patients. Of the 34 patients with a genetic diagnosis, RYR1 was mutated in 4, RYR1 in 6, NEB in 4, PYROXD1 in 2, MYH6 in 1, KLHL40 in 1, SEPN1 in 1, TPM3 in 1, ACTA1 in 1, FBLN2 in 1, FBLN5 in 1, BTBD1 in 1, SLC12A6 in 1, SLC18A3 in 1, ATP2A1 in 1, TRIM54 in 1, AFG3L2 in 1, CCDC78 in 1, COL6A3 in 1, MYOT in 1.

Conclusion: Genetic studies in these diseases help us to identify new genes, elaborate new pathogenetic mechanisms and design new therapeutic approaches. This study provides the relative molecular frequency of congenital myopathies and proposes a diagnostic algorithm to be used in clinical practice to adress genetic investigations.

Disclosure: No potential conflict stated.
Intrathecal Nusinersen therapy in children with Spinal Muscular Atrophy. Our experience

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Introduction: Therapeutic management of Spinal muscular atrophy (SMA) has faced a new approach since the approval of the only therapy for this disease, Nusinersen.

Methods: We evaluated 13 patients that have been treated with Nusinersen in our Department. These patients are being followed up to at least 7 months. The epidemiology and clinical characteristics, lab test and functional assessment, safety issues regarding the intrathecal administration (IA) and tolerability were recorded and the following assessments were performed: motor function outcomes (ULM upper limb module, HFMSE Hammersmith Functional Motor Scale Expanded), quality of life PEDQL, ZARIT questionnaires were evaluated at baseline and after 8 months of treatment.

Results: 13 SMA patients (9 male/4 female), the type distribution: 10 type II, 2 type III and 1 type I. Age range 2 months-16 years old. Nine patients had a night biPap and physical and all respiratory physiotherapy. Five patients had surgery due to scoliosis complications. The time of follow up was at least 7 months, with minimum 4 doses (all administrations performed in the surgery room with mild sedation, without intubation). Safety findings: headache after the puncture in 3 patients, 24 hours hospital admission in one patient that suffered an aspiration due to the sedation. A intrathecal catheter with reservoir was placed in one patient. We observed in the 80% of the patients improvement in the HFMSE and ULM scales.

Conclusions: Our preliminary experience with intrathecal administration of Nusinersen in SMA patients seems to be a safe and reliable technique. An alternative administration, such an intrathecal catheter could be considered as a safe option in complex situations. The quality of life and caregiver stress evaluation can provide an useful information for assessing the evolution of these patients treated with Nusinersen.

Disclosure: No potential conflict stated.

Timed-function test data in patients with Duchenne Muscular Dystrophy from the STRIDE Registry and the CINRG Natural History Study: a matched cohort analysis

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Objective: Strategic Targeting of Registries and International Database of Excellence (STRIDE) is a multicentre, observational registry providing real-world evidence of ataluren use in patients with nonsense mutation Duchenne muscular dystrophy (nmDMD) (NCT02369731). This analysis compared patients with nmDMD receiving ataluren+standard of care (SoC) (STRIDE) with patients with DMD receiving SoC alone (Cooperative International Neuromuscular Research Group [CINRG] Natural History Study [NCT00468832]).

Methods: Propensity score matching was performed to identify patients from STRIDE and CINRG who were comparable in established predictors of disease progression: age at first symptom; duration of deflazacort use; and duration of other corticosteroids (34.8% vs 34.8%). Median (95% confidence interval, CI) age at transition, to both ≥5 seconds (s) and ≥10s to stand from supine and climb four stairs.

Results: Matched patients (n=187/cohort) had a mean age at first symptom of 2.7 and 2.9 years in STRIDE and CINRG, respectively. The majority of patients (STRIDE vs CINRG) received corticosteroids for ≥12 months (56.7% vs 55.1%), with a similar proportion receiving deflazacort (24.6% vs 23.5%) or other corticosteroids (34.8% vs 34.8%). Median (95% confidence interval, CI) age at transition, to both ≥5s and ≥10s to stand from supine, was higher in STRIDE vs CINRG (≥5s, 11.9 [8.5, 14.6] vs 8.6 [8.3, 9.7] years, p=0.0028; ≥10s, 14.0 [11.8, 18.6] vs 10.3 [9.5, 11.2] years; p=0.0164). In addition, for ≥5s and ≥10s to climb four stairs, median (CI) age at transition was higher in STRIDE vs CINRG (≥5s, 12.3 [10.9, 14.0] vs 9.7 [8.5, 11.3] years, p=0.0359; ≥10s, not calculable, NC [15.4, NC] vs 13.2 [11.1, NC] years; p=0.0118).
Novel ANO5 homozygous mutation causing mild myalgia and unprovoked hyperCKemia in an athlete teenager

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Introduction: Anoctaminopathies are a group of autosomal recessive skeletal muscle disorders with various clinical phenotypes, caused by the abnormal expression of anoctamin 5 (ANO5) protein due to ANO5 gene mutations, mainly divided into 3 clinical phenotypes: limb-girdle muscular dystrophy 2L, Miyoshi phenotype of distal muscular dystrophy 3 and asymptomatic hyperCKemia.

Methods: Clinical, genetic and biochemical retrospective data review.

Results: A 16-year-old male patient, born to consanguineous parents, was referred for evaluation of hyperCKemia and post-exercise myalgia. He has been in swimming competitions since 11 years old with no complaints. Around 16 years old, a routine biochemical examination showed very increased CK. Patient did not refer any symptom of weakness, nevertheless reported occasional myalgia after a more prolonged exercise training. Clinical examination showed normal strength but increased tendon reflexes. Extensive investigation for causes of hyperCKemia showed no abnormal findings. Electromyography was compatible with myopathic features. Muscle biopsy with respiratory chain enzymes analysis was also normal. Whole Exome Sequencing (WES) was performed and a homozygous intronic mutation c.1013+1 G>A in ANO5 was identified.

Discussion: Recently, mutations in the ANOS had an expansion in its clinical phenotype, including presentations associated with intolerance to physical activity, hypertrophic cardiomyopathy and even asymptomatic hyperCKemia. ANO5 function may be involved in repair of muscle membranes following injury, similar to dysferlin, with ANO5-deficient animal models showing dysfunctional sarcolemmal repair, delayed regeneration and myoblast fusion defects. So, it is becoming apparent that excessive exercise, resulting in damage to sarcolemmal membranes, may be one of the clinical triggers of increased CK in patients with mutations in such gene. In conclusion, ANOS mutations should be looked for in patients with persistently high CK levels even without muscle weakness.

Disclosure: No potential conflict stated.
P11-40

Pontocerebellar Hypoplasia Type 1 (PCH Type 1): different phenotypes in patients with EXOSC3 mutations

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Introduction: PCH type 1 is characterized by the combination of hypoplasia/atrophy of the cerebellum and pons associated with degeneration of motor neurons of the anterior horn of the spinal cord. Mutations in the EXOSC3 gene are a major cause of PCH type 1.

Methods: Cross-sectional study including clinical and neuroimaging studies of patients carrying EXOSC3 mutations.

Results: Four unrelated patients (age range: 0.6-12 years) were assessed. All patients presented early-onset psychomotor retardation associated with the following clinical signs in variable severity: strabismus, nystagmus, axial hypotonia, bulbar dysfunction, pyramidal signs and axonal neuropathy. All patients had a GMFCS=5, except for one who presented autonomous gait by age 3. EEG with beta rhythms was found in one patient. Muscle biopsy showed signs of anterior horn damage in one case. Neuroimaging studies showed cerebellar atrophy with variable involvement of pons in all cases. Progressive cerebellar atrophy was present in 2 cases. The mutation c.395A>C/p.D132A in homozygous status in the EXOSC3 gene was identified in 3 patients.

Conclusion: The RNA metabolism is implicated in various spinal motor disorders. The patients carrying homozygous c.395A>C/p.D132A variant had a milder phenotype compared with the patient carrying the mutation in compound heterozygous status. The genotype-phenotype correlation of our cohort agrees with the cases reported. To consider, unlike other reports, the mildest case of this cohort evolves favorably, with maintained autonomous gait.

Disclosure: No potential conflict stated.

P11-41

The Identification of CHRNE 1267delG mutation in Greek Roma patients with Congenital Myasthenia

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Introduction: Congenital myasthenic syndromes form a heterogenous group of genetic disorders. Mutations in CHRNE are one of the most common causes of them. 1267delG mutation in the AChR ε subunit causes an autosomal recessive myasthenic syndrome which leads to a variable phenotype characterized by ophthalmoplegia, bilateral ptosis and potentially facial weakness, bulbar symptoms, neck muscle weakness and proximal limb weakness. The symptoms are usually mild and there is a good response to pyridostigmine and 3,4-DAP. The diagnosis of a cms is based on a combination of the patient’s history, electrophysiological testing, response to acetylcholine-inhibitors, muscle biopsy and more recently by genetic testing.

Methods and results: We present the cases of four Greek patients (two females, two males) of Gypsy ethnic origin, who have been diagnosed with congenital myasthenia at infancy and are being treated with pyridostigmine ever since. All four patients presented with progressive ptosis, external ophthalmoplegia, swallowing and respiratory problems at infancy. They had positive response to the administration of edrophonium and started treatment with pyridostigmine. At present they are eight to fifteen years of age and present mild symptoms, most frequently respiratory infections. We took blood samples from these patients and their parents and had it analyzed. The mutation 1267delG was identified in an homozygous state in all of them. The parents were carriers of the mutation.

Conclusions: The identified mutation, situated in exon 12 of the AChR ε subunit, is quite frequent among patients of Gypsy ethnic origin, which complies with findings of similar studies. The identification of the mutation confirms the diagnosis. This is crucial as misdiagnosis occurs quite often, a fact that leads to treatment delay and unnecessary exposure to immunotherapy, thymectomy or muscle biopsy.

Disclosure: No potential conflict stated.
The importance of the establishment a register for monitoring children with Neuromuscular Disorders

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Introduction: Neuromuscular diseases are rare, chronic, genetic, still incurable diseases. That is why continuing all research and development activities on the path of finding and developing new treatments for children with neuromuscular diseases is of great importance.

Methods and Results: A consistent overview of the patients with neuromuscular diseases is key for studying the course, progression or regression of the disease during treatment with new drugs. At the University Children’s Hospital, Department of Child, Adolescent and Developmental Neurology in Ljubljana we created a registry of patients with neuromuscular diseases in 2016 to provide this key overview.

With the registry we invite children and adolescents to a two day visit at least once a year to our department. The frequency of the visits varies depending on the stage of the disease, because the needs for care are changing. Data from the visits allows providing more adequate treatment, which can slow down the disease progression and avoid complications that require additional treatment. Visits of subspecialists from different fields and numerous standard tests are being carried out according to protocol and time plan to ensure that we complete all tests the patient needs in a narrow time frame.

Conclusion: With monitoring of patient condition and use of rankings for specific diseases we can assess the rate of progression of the disease and recognize potential deviation from the expected course. At the same time, we can measure the efficiency of treatment with drugs that are used to treat the basic disease of the patient. All of the mentioned activities are important to predict potential complications and to prevent them in as many cases as possible and provide useful data for future research activities.

Disclosure: No potential conflict stated.

Enlargement of peripheral nerves in late-onset Krabbe’s Disease as demonstrated by nerve ultrasound

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Introduction: Thickening of peripheral nerves has been demonstrated in a variety of demyelinating disorders such as metachromatic leukodystrophy (MLD). Nerve ultrasound has become a valuable diagnostic measure for this evaluation. Up to date, nerve ultrasound data has not been shown for Krabbe’s disease.

Methods: Nerve ultrasound was performed in accordance to standard protocols (Grimm et al.): Nerve cross-sectional area was measured at anatomically defined landmarks and compared to an age- and gender- matched control. An ultrasound pattern sum score was calculated.

Results: On initial presentation at the age of 13 years, the girl showed motor difficulties and progressive pes cavus. Nerve conduction studies gave abnormal results, indicating a demyelinating nerve pathology. Nerve ultrasound of the peripheral nerves showed a distinct homogeneous thickening. Brain MRI, neurometabolic and genetic testing gave typical results of Krabbe’s disease.

Conclusion: Krabbe’s disease is known to lead to extensive demyelination of the central and peripheral nervous system. Peripheral neuropathy has been observed in about 60% of patients with late-onset Krabbe’s disease (Malandrini et al.). Thickening of the cauda equine roots in patients with Krabbe’s disease has been demonstrated by MRI (Hwang et al.). Also, thickening of peripheral nerves has been demonstrated in other demyelinating disorders (MLD). However, little imaging data of peripheral nerves is available for Krabbe’s disease. Here, we demonstrate a particular homogeneous enlargement of peripheral nerves in a girl with late-onset Krabbe’s disease, in accordance with her neuropathological data of demyelination of peripheral nerves. As early diagnosis is crucial for the prognosis in Krabbe’s disease in terms of initiating effective treatment, we suggest nerve ultrasound (as an easily available diagnostic tool) to become part of the routine evaluation when Krabbe’s disease is suspected.

Disclosure: No potential conflict stated.
P11-44

Extending the phenotype of the Hypotonia-Ataxia-Developmental Delay – Tooth Enamel Defect Syndrome (CTBP1 gene)

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Introduction: Heterozygous missense variants in the CTBP1 gene have been associated with the hypotonia- ataxia- developmental delay- tooth enamel defect syndrome (Beck et al., 2016; first description of four patients). Here, we present the case of a girl aged 5 years with a similar phenotype with the same, de-novo mutation in the CTBP1-gene. We further extend the known phenotypic spectrum by specific neurophysiological findings, suggesting a myotonic- dystrophic myopathy.

Methods: Trio- whole- exome sequencing and genetic testing of the DMPK gene were performed. Brain MRI, extended laboratory tests, muscle and nerve ultrasound, nerve conduction study and electromyography were conducted.

Results: The patient presented with a distinct gait ataxia, marked muscle hypotonia and muscle weakness with proximal predominance. She had wide spaced incisors with slight brown discoloration. Brain MRI showed moderate atrophy of the cerebellum with vermian predominance. Muscle ultrasound showed distinct diffuse hyperechogenicity while nerve ultrasound and nerve conduction study were unspecific. Electromyography showed abnormal spontaneous activity, complex repetitive and myotonic discharges.

Conclusion: Up to date, neurophysiological findings have not been described in the four reported patients with hypotonia-ataxia- developmental delay- tooth enamel defect syndrome (Beck et al.). Here, we present a 5 year old girl with a CTBP1- mutation with a similar phenotype and a marked diffuse muscle hyperechogenicity on muscle ultrasound and distinct pathological changes on electromyography, suggesting a chronic myotonic- dystrophic myopathy. Beck et al. reported myopathic or dystrophic changes in the muscle biopsy in some of the four patients. With reference to these described histopathological changes we hereby add specific neurophysiological findings suggestive of a myotonic- dystrophic myopathy in this syndrome, thereby stressing the importance of muscle ultrasound and electromyography in these patients.

Disclosure: No potential conflict stated.

P11-45

One-year follow-up of Slovenian DMD patients treated with Ataluren

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Introduction: Ataluren is used to treat nonsense mutation Duchenne muscular dystrophy (DMD). It most probably works by making ribosomes less sensitive to premature stop codons (“read-through” mechanism).

Methods: We analyzed data on DMD patients treated with ataluren from our neuromuscular disease registry, to determine the outcomes after one year of treatment.

Results: Of the 25 DMD patients, 5 had the nonsense mutation amendable to treatment with ataluren, but only 3 met the clinical criteria for treatment. All patients were on steroid treatment before ataluren and continued steroids for the duration of our follow-up. Their ages ranged from 5.5 to 8.5 years. The initial 6 minute walk distance (6MWD) was below 400 m (360, 250 and 360 meters respectively), so a significant motor decline would be expected in the natural course of the disease during follow-up. The 6MWD remained stable or even improved after the first year of treatment (360, 300, 380 meters respectively). No other factors seemed to effect outcome.

Conclusion: Ataluren was well tolerated by our patients and showed a clear clinical effect in modifying the progressive decline expected in the natural course of DMD. Age did not seem to play a role in our patient’s outcome, as some authors have suggested. It is still too early to evaluate the long-term effects, so further follow-up is needed, but the information gathered this far supports the use of ataluren in these patients.

Disclosure: No potential conflict stated.
From upper respiratory tract infection and myocarditis to the diagnosis of a child female carrier of Duchenne Muscular Dystrophy: a case report

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Introduction: Dystrophinopathies are a group of distinct neuromuscular diseases that result from mutations in the structural cytoskeletal dystrophin gene. They include Duchenne muscular dystrophy (DMD), Becker muscular dystrophy (BMD), X-linked dilated cardiomyopathy as well as DMD and BMD female carriers. (1) It is known that some female carriers with a dystrophin mutation have symptoms of cardiomyopathy and that heart dystrophinopathy is a risk factor for myocarditis. (2,3).

Methods: We report a case of an otherwise healthy 17 years old girl who was transferred to our tertiary center for further diagnostic of chest pain which began after a mild upper respiratory tract infection 14 days before and high levels of serum troponin I.

Results: At admission laboratory results showed low inflammatory markers, high serum troponin I and elevated (3x above normal) serum creatine kinase (CK) levels. Electrocardiogram and echocardiogram were normal while cardiovascular magnetic resonance imaging (CMR) showed signs of focal myocarditis. She was transiently treated with non-steroid anti-inflammatory drugs and b-blocker, the latter was later switched to angiotensin-converting-enzyme inhibitor and she also received azithromycin due to positive serology tests (positive IgM) for M. pneumoniae (all other extensive microbiological results were negative). Chest pain resolved after 3 weeks but high levels of troponin I and CK persisted. Control CMR still showed signs of focal myocarditis; she received intravenous immunoglobulins after which levels of troponin I normalized. Due to persistently high levels of CK additional tests (screening for metabolic diseases and metabolic cardiomyopathies, Pompe disease, rheumatological diseases) were done and they were all normal; genetic test showed heterozygote deletion of exons 45 – 50 in the dystrophin gene.

Conclusion: Myocarditis with prolonged high levels of CK should raise suspicion of dystrophinopathy in an otherwise healthy girl.

Disclosure: No potential conflict stated.

Evaluation of Slovenian children with Spinal Muscular Atrophy Type I–III six months after treatment with Nusinersen

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Introduction: Spinal muscular atrophy (SMA) is characterized by muscle weakness, atrophy and paralysis. Nusinersen is an antisense oligonucleotide, designed to alter splicing of SMN2 pre-mRNA and thus increase the amount of deficient functional survival motor neuron protein in SMA patients.

Aims: To evaluate a motor - milestone response defined according to the results of The Children’s Hospital of Philadelphia Infant Test of Neuromuscular Disorders - CHOP – INTEND, Hammersmith functional motor scale (HFMS) and treatment adverse events (AE).

Methods: We conducted a prospective, longitudinal data collection of all children aged 0 – 19 years treated with nusinersen. Intrathecal injections of nusinersen were given according to the protocol. Standardized assessment with CHOP – INTEND and HFMS was performed at baseline and 180 days after the start of treatment. AE were regularly recorded.

Results: 26 patients (46.2% boys) were included. 19.2% have SMA type 1, 65.4% type 2 and 15.4% type 3. The mean age was 8.4 years (range 0.2 – 18.8 years). 7.7% of patients have invasive and 30.8% non-invasive ventilation; 23.1% have been operated for scoliosis. 14 (53.8%) patients were evaluated with CHOP – INTEND and 12 (46.2%) with HFMS. After 6 months of treatment, 4 patients (28.6%) improved by ≥ 4 points in CHOP INTEND score. The mean change in the CHOP INTEND score was 3.8±6.4 points. Two (16.7%) patients improved by ≥ 4 points in HFMS. Reported AE were post puncture headache and pain at the site of lumbar puncture. In 3 patients cerebrospinal fluid leakage was detected but it resolved spontaneously.

Conclusion: Our short – term data did not show regression of motor function. No serious AE were observed. Further studies are needed to evaluate the long-term efficacy and side effects of nusinersen.

Disclosure: No potential conflict stated.
Eculizumab as a long-term treatment in Congenital CD59 Deficiency: single-centre experience

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Objective: Eculizumab, is a humanized C5 monoclonal antibody. Our aim was to report our experience in pediatric patients with congenital CD59 deficiency.

Methods: Protocol was administered according to FDA approved doses for atypical hemolytic uremic syndrome. Treatment response was evaluated by clinical and neurological examination, laboratory features, frequency of relapses, continuation of IVIg/corticosteroids, and hospital admissions.

Results: Eight patients, from 6 families (6 girls, 2 boys) with a mean current age of 9 y (12 months–14 years–4 months), a follow-up period of 24 months (1 month–55 months), and total three hospital admissions were included. One patient was lost to follow-up after 9 months of treatment. An asymptomatic sibling was treated at the age of 2 months. There was total cessation of IVIg within less than 1 month (n=4), 1-2 months (n=1), and 21 months (n=1). IVIg was reintroduced after 1-year for a patient with missing eculizumab dose (n=1). One patient who had a very recent diagnosis is on corticosteroids and IVIg. A patient with neonatal-onset presentation is wheelchair dependent and had nocturnal hypoventilation syndrome. Maximum motor capacity is walking with a neuropathic gait (n=4), with aids (n=2). Axial, upper extremity, respiratory functions improved in all. Two patients received blood transfusion at presentation and during an attack accompanied by hematuria. One patient developed Type 2 diabetes which may be independent, drug-related or due to disease course.

Conclusions: Stabilization and improvement of neurologic symptoms in varying degrees were observed with cessation of IVIg infusions almost within initial 4 weeks of treatment. Improvement of axial, bulbar, respiratory and upper extremity functions was remarkable. Eculizumab treatment seems to modify natural course of CD59 deficiency.

Disclosure: No potential conflict stated.

Clinical course, outcome and autoantibody status in children with Chronic Demyelinating Polyneuropathy (CIDP)

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Objective: Chronic inflammatory demyelinating polyradiculoneuropathy (CIDP) is a chronic autoimmune disorder characterized by monophasic or relapsing clinical course.

Aim: To analyse the clinical course, outcome and presence of autoantibodies in children with CIDP. Patients and Methods. Cerebrospinal fluid (CSF), nerve conduction studies, severity at nadir (Hughes Score), therapy and outcome (modified Rankin Scale), ganglioside and paranodal autoantibodies (e.g. Neurofascin155, Contactin1, CASPR1) were analysed in 14 CIDP patients.

Results: We studied 14 patients with chronic demyelinating polyneuropathy, 8 females (57.1%) and 6 males (42.9%), aged 3.3–18 years (mean age 9.9 years) in 4 patients infection preceding CIDP onset was reported. The Hughes Score at presentation was 4 in 6/14, 3 in 2/14, 2 in 3/14 and 1 in 3/14 patients. Cranial nerve involvement was revealed in 4/14 patients (1 unknown), 5/14 patients (1 unknown) presented with ataxia and/or tremor. Signs of demyelinating and axonal injury were detected in all patients. Nerve biopsy confirmed CIDP in 5 patients with mostly axonal degeneration. Mean CSF protein content was 112mg/dl (18–507 mg/dl) mean cell count 3 /µL (0–10/µL). Two patients were positive for GM1-, GD1a- and GD1b IgG ganglioside antibodies. Two children had neurofascin 155 IgG and one had contactin1 IgG autoantibodies. Patients were treated with repeated courses of intravenous immunoglobulins, steroids or mycophenolate mofetil and rituximab in 1 patient with contactin1 antibodies. Modified Rankin score at follow up was 4 in 1/13, 3 in 6/13, 2 in 2/13 and 1 in 4/13.

Conclusion: A substantial number of children with CIDP harbour autoantibodies against gangliosides and paranodal antibodies. In particular the latter might benefit from anti-B-cell therapies in the future.

Disclosure: No potential conflict stated.
P11-50

Genetic and nongenetic modifiers – Possible treatment targets in Spinal Muscular Atrophy

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Objective: Until recently neuromuscular diseases (NMD) including spinal muscular atrophy linked to chromosome 5q (SMA-5q) were defined as disabling conditions with high unmet medical need and no disease-modifying treatment. Although the approved treatment Spinraza (nusinersen) has changed the clinical course and outcome, and several experimental therapies are in late development, it is unknown if cure is possible. More research is needed to understand the genotype-phenotype correlation in SMA. SMA-5q may not be only a result of SMN protein deficiency but include the impact of calcium signaling, impaired mitochondrial function, and cytoskeleton dynamics.

Aim: Besides the crucial role of SMN gene product SMN protein, genetic modifiers which activities are SMN protein level dependent or independent, are possible targets for the treatment.

Methods and Results: Besides the known genetic modifiers (SMN2 gene copy number, specific SMN2 mutation and plastin-3 (PLS3) for patients with 3 or more SMN2 copies) endocytosis rescue presents a promising target. Endogenous calcineurin inhibitor neurocalcin delta (NCALD) function associated with actin dynamics is an SMN independent protective modifier which may rescue endocytosis. Downregulation of calcineurin-like EF-hand protein 1 (CHP1) which is in direct interaction with plastin present potential therapeutic target. microRNAs are important for motorneuron differentiation, axonal growth, and NMJ formation. microRNAs (miRS) can also be SMA disease modifiers and potential biomarker for clinical response to therapy. Increase of miR-183 reduces mTOR activity in SMA cells and represents another possible therapeutic target.

Conclusion: Rational treatment of SMA requires early genetic diagnosis. Knowledge of pathomechanisms in NMD, the role of gene product and natural disease history is essential for the development of next generation treatments.

Disclosure: No potential conflict stated.

P11-51

Phenotypic variability in siblings with Spinal Muscular Atrophy

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Objectives: Spinal muscular atrophy (SMA) is caused by homozygous loss of the SMN1 gene. Genetic homogeneity and phenotypic variability seen in type 1, 2 and 3 suggests the involvement of disease modifiers. Herein we describe very unusual and rare SMA families with siblings of discordant phenotypes.

Methods: From our database we selected families with 2 or more genetically confirmed SMA siblings with identical SMN2 and SERF1A copy numbers.

Results: The greatest discordant phenotypes were found in 3 families with SMA type 3: In two families we found males with 3a and 3 subtype who lost ambulance at the age of 9 and 16 years, respectively, whereas their sisters with identical genotypes have normal neurological findings at the age of 9 and 25 years. In the third family with 3 affected females, we found continuum of nonambulatory status in the first and second decades and ambulatory status in fourth decade.

Conclusion: Intrafamilial variability in siblings with SMA, particularly type 3, implies the necessity of finding novel disease modifiers and defining new prognostic biomarkers. Our effort in defining all possible disease modifiers and prognostic biomarkers would be of great importance for further therapeutic decision and evaluation.

Disclosure: No potential conflict stated.
Dynamic Thiol/Disulphide homeostasis in children with Duchenne Muscular Dystrophy

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Objective: Duchenne muscular dystrophy (DMD) is a disorder that alters the expression of the dystrophin protein. Dystrophin deficiency alters the structural integrity of the contractile apparatus/sarcolemmal integrity, leading to dystrophic changes. Dystrophin deficiency results in an increase in oxidative stress. We aimed to investigate the thiol/disulfide balance as an oxidative stress marker in children with DMD.

Methods: We included 24 DMD, and 22 healthy control group subjects in the study. The total thiol, native thiol, and disulphide levels were measured and the disulphide/native thiol, disulphide/total thiol and native thiol/total thiol ratios were calculated in DMD patients and healthy subjects.

Results: The mean age distribution of the patients and the healthy control group subjects was similar. The total thiol, native thiol, and disulfide levels were lower in DMD group than the healthy controls.

Conclusion: The markers and ratios were measured and calculated in the blood, and we detected that the total thiol, and native thiol levels were lower in DMD group than the healthy controls. These results indicate that dynamic thiol-disulphide homeostasis can be used as a marker of oxidative stress in clinical trials with DMD.

Disclosure: No potential conflict stated.
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