POSTER PRESENTATIONS

BRAIN TUMORS/ONCOLOGY

1. Neuropsychiatric symptoms in an adolescent:Dig deeper?
Khan Mahjabeen (Saint Louis, MO, United States) Tanios Aline

OBJECTIVE: We report a case of an adolescent who presented with a cluster of vague behavioral symptoms, later diagnosed with an intra-ventricular tumor causing obstructive hydrocephalus.
METHODS: A 17 year old female presented with a three month history of mood changes, weight loss, near syncope episodes and urinary incontinence. She had fatigue, anorexia, depressed mood, anhedonia, decreased sociability and insomnia. Patient identified breakup with her boyfriend as a trigger. She also reported intermittent headaches and vomiting. Exam was notable for flat affect, staring spells, increased distractibility, slow thought processing and responsiveness, generalized hyperreflexia, bilateral Babinski's sign with hand tremors.
RESULTS: Although, symptoms were pan positive for Major Depressive Disorder with severe features, unusual findings of urinary incontinence, frequent falls, headaches and vomiting could not be explained by a mood disorder alone. Neurological signs also raised concerns for intracranial pathology. Brain MRI revealed a heterogeneous enhancing lobular mass arising from the septum pellucidum resulting in obstructive hydrocephalus. She underwent emergent resection of the tumor, which on histopathology, was identified as a Sub-ependymal Giant Cell Astrocytoma (SEGA) and tumor cytogenetics showed TSC2 mutation. She had no clinical diagnosis of Tuberous Sclerosis.
CONCLUSIONS: Major Depressive Disorder is highly prevalent among adolescents in the US. Interpersonal dysfunction is a commonly identified trigger. Psychiatric symptoms are a rare presentation of brain tumors and vice versa. Pediatricians and/or psychiatrists may encounter such patients. With atypical symptoms, a thorough exam and high index of suspicion is important for a timely diagnosis. This is a clinical conundrum with a classic neuropsychiatric interface.
KEYWORDS: Brain Tumors/Oncology, Rare Diseases, Genetics

2. Careful approach to acquired facial nerve palsies in infants: two cases of symptomatic disease
Chandler Erika (Louisville, KY, United States) Barton Chris, Puri Vinay

OBJECTIVE: Acquired facial nerve palsies in children are commonly encountered. Up to 50% are of unknown causes, often attributed to post-infectious syndromes. In rare cases, peripheral facial palsies may be secondary to underlying infections, tumors, trauma, or even leukemia. In infants, differentiating these may be difficult. We present two cases of infants with symptomatic facial nerve palsies.
METHODS: A detailed chart review and literature search.
RESULTS: We present two infants with new onset full facial nerve palsies. Patient one presented one day after falling from a 3 foot height and having persistent isolated facial

weakness over 2 days. CT head was obtained due to trauma and showed opacification of bilateral mastoids in the setting of bilateral otitis media, and mastoiditis was suspected. CBC showed a WBC count of >250k, prompting urgent leukapheresis. She was ultimately diagnosed with T-cell ALL with CNS involvement. Patient two presented with right sided head tilt, right sided full facial weakness and truncal ataxia. MRI brain showed a tumor of the internal auditory canal extending into the right cerebellopontine angle. Lumbar puncture with negative cytology, solid tumor panel negative. Electroneurography showed involvement of cranial nerve VII and VIII with chronic involvement, suggesting a schwannoma.
CONCLUSIONS: In children, facial nerve palsies are often attributed to post-infectious inflammation. However, in infants with no clear history of recent infection or trauma, alternative differentials should be considered. MRI brain with gadolinium and a CBC should be considered in individuals when indicated by history, examination or a lack of response to treatment.
KEYWORDS: Brain Tumors/Oncology

3. Trametinib for pediatric plexiform neurofibroma and recurrent low-grade glioma
Sato Aimee (Seattle, WA, United States) Millard Nathan, Oztek Murat Alp, Perez Francisco, Vitanza Nicholas, Leary Sarah

OBJECTIVE: Based on early clinical efficacy data, Seattle Children's Hospital established a standard clinical practice for MEK inhibitor therapy for children with plexiform neurofibroma (pNF) or recurrent low-grade glioma (LGG). We sought to describe the clinical experience and response to treatment for these children.
METHODS: Data were collected under an IRB-approved retrospective chart review. Trametinib was prescribed off-label at 0.025 mg/kg daily for up to two years. Physical exam and labs were monthly for 3 months, then every 3 months. Retinal examination, echocardiogram and ECG were every 3 months. Tumor response was evaluated by MRI every 3 months.
RESULTS: 30 patients received trametinib; 17 LGG, 16 PN (3 both); 22 with Neurofibromatosis Type-1 (NF1); 16 female/14 male; median age 11 (range 4.1-22.6). Most common tumor location was optic pathway (n=11) and face/neck (n=10). Most common adverse events (AE) were dermatologic and gastrointestinal. Ten had dose interruption/reduction, only one discontinued therapy for AE. Six received dermatology specialty care for AE. With median follow-up of 12 months, only 3 patients had progression, one with NF1. One-year EFS was 100% for PN and 88%+7 for LGG. Driver mutations were identified in 9 of 10 tumors tested (5 BRAF fusion, 1 BRAFV600E, 1 FGFR1+NF1, 1 FGFR1+PTPN11, 1 NF1). Central radiology review of response will be presented.
CONCLUSIONS: This real-world pediatric cohort supports efficacy and tolerability of MEK inhibitor therapy for short-term control of pNF and LGG with and without NF1. Further studies are warranted to evaluate comparative efficacy, combination therapy and duration of therapy.
KEYWORDS: Brain Tumors/Oncology, Genetics

4. A First-Reported Use of Everolimus to Reduce Seizures and Neurodevelopmental Delays in PTEN Tumor Hamartoma Syndrome With Hemimegalencephaly
Swarz Jeffrey (Boston, MA, United States) Gaitanis John, Law Jason

OBJECTIVE: To describe the first-reported use of Everolimus for the treatment of seizures and neurodevelopmental delays in a four year old girl with hemimegalencephaly and PTEN Tumor Hamartoma Syndrome (PTHS).
METHODS: Patient demographics, history, neurological findings, MRI, neuropsychiatric testing, treatment, and clinical course were reviewed. The literature was reviewed for prior case reports.
RESULTS: Our patient with PTHS (confirmed on genetic testing) was treated with the mTOR inhibitor Everolimus. The EXIST 3 studies demonstrated promise for Everolimus in tuberous sclerosis (TSC) for seizure control and neurodevelopmental improvement. The shared pathophysiology of TSC 1 and PTHS, and similar desired clinical goals of improved seizure control and neurodevelopmental outcome, led to the prescription of Everolimus after careful consideration and discussion with her parents. One year after Everolimus initiation our patient showed significant clinical improvements. She experienced improved seizure control (one seizure per year post-treatment versus a pre-Everolimus baseline of one to two per month). She also showed significant advancements in the gross and fine motor domains, cognition, and receptive language. Her expressive language showed less improvement but was likely an underestimate since her communications board was not permitted during standardized testing.
CONCLUSIONS: This first-reported use of Everolimus in our patient with hemimegalencephaly and PTHS was associated with decreased seizure activity and significant global improvement in neurodevelopment. These results are similar to the studied effects of mTOR inhibition in the treatment of TSC and supports growing evidence that a medical, rather than surgical approach, may be considered in similar patients.
KEYWORDS: Brain Tumors/Oncology, Epilepsy

COGNITIVE/BEHAVIORAL DISORDERS (INCLUDING AUTISM)

5. Amyloid Plaque Proteome in Down Syndrome

Garcia Mekka (New York, NY, United States) Faustin Arline, Askenazi Manor, Ueberheide Beatrix, Pires Geoffrey, Drummond Eleanor, Wisniewski Thomas

OBJECTIVE: The aim of the study is to compare Down Syndrome (DS) amyloid plaques and cortex proteome to that of early-onset Alzheimer's Disease (AD) in hope of finding a novel protein(s) that could elucidate the mechanism of early-onset dementia in DS.
METHODS: Protein differences were examined in cases of DS with AD neuropathology (n=5; age= 52.6±8.9yrs), AD (n=5; age=60.6±3.4yrs), and cognitively normal controls (n=5; age=56.2±1.9yrs). Amyloid plaques and non-plaque affected temporal cortex were analyzed using proteomic methods we have previously published (*Acta Neuropathologica*, 133: 933-954, 2017). Fluorescent immunohistochemistry (IHC) was used to examine levels of total Aß, pyroglutamate Aß, Aß phosphorylated at serine 8, oligomeric species, and phosphorylated tau. Further studies are being conducted to increase sample size.
RESULTS: Proteomic analysis resulted in the quantification of 1650 proteins. Comparison of the plaque proteome in DS and AD revealed similar proteins are present in DS and AD plaques, though a relative abundance of many key proteins was different (Figure 1). Network analysis suggested that DS plaques were high in proteins related to the inflammatory response (Figure 2).

IHC showed DS plaques also contained a higher amount of post-translationally modified Aß species than AD plaques. Conversely, we observed lower levels of oligomeric species in the DS cortex in comparison to the AD cortex ($p<0.01$).
CONCLUSIONS: Our preliminary data suggests that there are pertinent differences in the amyloid plaque proteome in DS and AD. Interestingly, DS plaques had higher protein content related to inflammation, suggesting a possible inflammatory mechanism in the development of early-onset dementia in DS.
KEYWORDS: Cognitive/Behavioral Disorders (including Autism)

6. OPSOCLONUS MYOCLONUS ATAXIA (OMA) SYNDROME: A TEN YEARS REVIEW
Arora Anshita (Mumbai, India) Rastogi Sanchi, Panday Ankit, Kothari Sonam, Kulkarni Shilpa, Hegde Anaita

OBJECTIVE: Opsoclonus-myoclonus ataxia (OMA) syndrome is rare neuro-immune disorder characterized by acute onset ataxia, opsoclonus, myoclonus, behavioural changes. It usually occurs in first 2 years, associated with viral infections or neural crest tumours.
METHODS: A retrospective review done at three tertiary centers of Western India.
RESULTS: Twenty patients of OMA syndrome diagnosed,managed and followed up over a decade. Median follow up(f/u) period: 12 months(6 months-10 years).Given these being tertiary centers with patients from all over India, f/u was clinical/ telephonic.14/20 had clinical f/u, 4/20 telephonic f/u, 2/20 lost to f/u. Long-term neuropsychological assessment couldn't be performed, which is a topic of an ongoing study. F:M ratio was 2.3:1. Mean age of presentation: 19 months (9-30 months). All had ataxia and motor regression, opsoclonus in 19/20, myoclonus 12/20, behavioral changes 14/20. 15/20 had neuroblastoma,2/20 post viral,3/20 idiopathic. All neuroblastoma patients underwent surgery,4/15 required chemotherapy.
3/20 treated with monotherapy(ACTH),17/20 received combination therapy, including prednisolone with ACTH(2/20),ACTH with rituximab(2/20),ACTH with IVIG(3/20), prednisolone with IVIG(2/20),dexamethasone with rituximab(5/20),ACTH,IVIG with rituximab(2/20), dexamethasone, IVIG with rituximab(1/20). 7/20 showed complete recovery of acute neurological symptoms.2/20 were lost to f/u after initial treatment. Rest showed partial resolution. Complete resolution with relation to treatment (2/3 on three drugs,5/15 on two drugs,0/3 on single drug) and with relation to etiology (7/15 with neuroblastoma, 0/5 with post viral/idiopathic).
CONCLUSIONS: OMA seen predominantly in females with late infantile presentation. Neuroblastoma was noted in 75%. Treatment included monotherapy (15%), polytherapy-two drugs (70%), three drugs (15%).35% showed complete resolution. Better outcomes noted with neuroblastoma and polytherapy (3>2 drugs). Long term neuropsychology f/u is ideally needed and ongoing.
KEYWORDS: Cognitive/Behavioral Disorders, Brain Tumors/Oncology

7. Treatment of children with Autism spectrum disorder using repetitive Transcranial Magnetic Stimulation: A multi-center randomized sham-controlled Pilot Study
Sondhi Vishal (Pune, India) Goswami Jyotindra, Chauhan Vinay, Gambhirrao Ankita, Devgan Amit

OBJECTIVE: The objective of this clinical trial was to assess the improvement in the scores of (a) Childhood Autism Rating Scale-2 (CARS-2) (b) Indian scale for Autism Assessment (ISAA) and (c) Social Communication Questionnaire (SCQ) among children with Autism Spectrum Disorder (ASD) following 12weeks of repetitive-Transcranial Magnetic Stimulation (rTMS) as compared to sham therapy.
METHODS: This was a multi-center, prospective, double-blinded, randomized sham-controlled pilot study. Children between 6 to 16years with ASD were randomized to receive either active (rTMS) vs. control (sham) settings on a weekly basis for 12weeks. The rTMS group received 12 sessions of rTMS over the left dorsolateral prefrontal cortex at a frequency of 0.5Hz for duration of 10minutes each. The primary outcome was assessed based on measures of CARS-2, ISAA, and SCQ administered before treatment and after 12weeks of intervention.
RESULTS: Twenty-seven patients underwent randomization; 24 (r-TMS=12) completed the therapy. The baseline CARS score (median (IQR)) was comparable between rTMS (42 (38-43)) and sham (40 (35-43)) groups. After 12 weeks of intervention, the median (IQR) change in CARS score with rTMS was -2.5 (-3.8 to 0.75) as compared to -0.50 (-2.0 to 2.8) with sham intervention. The median (95%CI) difference in the change in CARS score between two groups was 2 (95%CI= -1.5, 4.5, p=0.37). Similarly, the median difference between rTMS and sham group in change in ISAA score was 7 (95%CI= -11, 24, p=0.40) and in SCQ score was 3 (95%CI= 0, 7, p=0.13).
CONCLUSIONS: The intervention with rTMS did not have clinically significant impact among children with ASD.
KEYWORDS: Cognitive/Behavioral Disorders (including Autism)

8. Association of Psychiatric Disorders in Children with Epilepsy
Hossain Mohammad (Dhaka, Bangladesh) Akhter Shaheen, Rahman Md Mizanur, Fatema Kanij

OBJECTIVE: Psychiatric disorders are important aspects of epilepsy. A significant number of children with epilepsy have psychiatric comorbidities. The objective of this study is to find out the types and frequency of psychiatric disorders in children with epilepsy
METHODS: This cross-sectional observational study was conducted at the Outpatient department, Institute of Paediatric Neurodisorder and Autism (IPNA), BSMMU during September' 2018 to August' 2019. Sixty-eight epileptic children,age ranged from five to seventeen years were enrolled as case and similar number of nonepileptic healthy children were enrolled as control. Parent, teacher and self version of Development And Well-Being Assessment (DAWBA) (Validated Bangla Version) were used to assess the psychiatric disorders and diagnosis was assigned as DSM-5.
RESULTS: The mean age of both groups were comparable with slight male predominance (male 64.7% vs55.9%; p>0.05). Family history of psychiatric illnesses was found only among cases group. Level of schooling was significantly lower among the children with epilepsy (Never went to school 13.2%vs 2.9%, p <0.05). Higher proportion of psychiatric illness was found among the cases (83.8% vs 16.2%; p<0.05) with significantly increased number and broad categories of disorders, namely Neurodevelopmental (p<0.05) and emotional (p<0.05) and behavioral (p<0.05). ADHD/Hyperkinesis (20.6%), Oppositional defiant disorder /conduct disorder (17.6%), ASD (9%) and specific phobia (9%) .

CONCLUSIONS: About eighty percent of children with epilepsy had at least one different type of psychiatric comorbidities which are not associated with their demographic profile but related with duration of illness.
KEYWORDS: Cognitive/Behavioral Disorders (including Autism), Epilepsy

9. Neurodevelopment of children aged 5-8 years who were born prematurely
Zavadenko Nikolay (Moscow, Russia Federation) Davydova Larisa, Zavadenko Aleksandra

OBJECTIVE: To evaluate the characteristics of neurodevelopment by the age of 5–8 years in children born prematurely with extremely low (ELBW), very low (VLBW) or low body weight (LBW).
METHODS: 122 children aged 5-8 years were examined, including 36 born with ELBW (1^{st}), 36 with VLBW (2^{nd}), 50 with LBW (3^{rd}group), and 30 healthy peers. All were assessed by means of the Griffiths Mental Development Scales (GMDS-ER2-8). The children attended secondary school or preschool, where some were admitted according to inclusive education principles.
RESULTS: GMDS general quotient in children born prematurely was significantly lower compared to peers (80,9±2,1) in 1^{st}(73,4±2,1, p=0,036) and 3^{rd} groups (71,1±2,6, p=0,019), with the same tendency in 2^{nd} group (73,1±3,0, p=0,101). Concurrently the children demonstrated lower scores on all six GMDS scales and significant differences with controls for “Locomotor”, “Performance” in 1^{st}, “Performance”, “Practical reasoning” in 2^{nd}, “Locomotor”, “Personal-Social”, “Language”, “Performance” and “Practical reasoning” scales in 3^{rd} group.
Only 6 of 122 patients suffered from cerebral palsy (spastic diplegia). The rates of neurodevelopmental disorders were very high in the examined groups compared to populational ones, including those for developmental dyspraxia, ADHD, chronic tics disorder, autism. However, in a number of children the examination did not reveal any neurological or neurodevelopmental abnormalities, including 8,3% in 1^{st}, 16,7% in 2^{nd}, 22,0% in 3^{rd} groups.
CONCLUSIONS: Early diagnosis and characterization of neurological disorders and developmental delays in children born prematurely determines the effectiveness of therapeutic interventions based on individual approach to comprehensive medical and psycho-educational support.
KEYWORDS: Cognitive/Behavioral Disorders (including Autism), Neonatal & Fetal Neurology

10. Aftereffects of continuous theta-burst stimulation of motor cortex as a biomarker for children with high-functioning autism spectrum disorder
Jannati Ali (Boston, MA, United States) Block Gabrielle, Ryan Mary, Kaye Harper, Kayarian Fae, Bashir Shahid, Oberman Lindsay, Pascual-Leone Alvaro, Rotenberg Alexander

OBJECTIVE: A neurophysiologic biomarker for autism spectrum disorder (ASD) is highly desirable and can improve diagnosis, monitoring, and assessment of therapeutic response in ASD. We investigated the utility of continuous theta-burst stimulation (cTBS) applied to motor cortex (M1) as a biomarker for children and adolescents with high-functioning (HF) ASD compared to their typically developing (TD) controls. We also compared the developmental trajectory of long-term depression- (LTD-)like plasticity in the two groups. Finally, we explored

the influence of *BDNF* Val66Met polymorphism on cTBS aftereffects in a subset of the ASD group.
METHODS: Twenty-nine children (age range 10–16) in ASD (n=11) and TD (n=18) groups underwent M1 cTBS. Changes in MEP amplitude at 5–60 minutes post-cTBS and their cumulative measures were calculated. We also assessed the relationship between age and maximum cTBS-induced MEP suppression (ΔMEP_{Max}) in each group. Finally, we compared cTBS aftereffects in *BDNF* Val/Val (n=4) and Val/Met (n=4) ASD participants.
RESULTS: Cumulative cTBS aftereffects were significantly more facilitatory in the ASD group than in the TD group (P_{FDR}'s < 0.03; Figure 1). ΔMEP_{Max} was negatively correlated with age in the ASD group (r=–0.67, P=0.025; Figure 2), but not in the TD group (r=–0.12, P=0.65). Cumulative cTBS aftereffects were not significantly different between the two *BDNF* subgroups (P-values > 0.18).
CONCLUSIONS: The results support the utility of cTBS measures of cortical plasticity as a biomarker for children and adolescents with HF-ASD and an aberrant developmental trajectory of LTD-like plasticity in ASD. [Funding: NIH NIMH R01MH100186].
KEYWORDS: Cognitive & Behavioral Disorders (including Autism)

11. Structured remedial intervention for Indian school going children up to Class VI having Specific Learning Disorder (SLD) with Dyslexia: A longitudinal study assessing change of brain activation profile using Functional MRI and Resting state MRI and clinical severity scores using standard tools post intervention of 12 weeks.
Badal Sachendra (Pune, India) Sharma Shobha, Parveen Sana, Khan Sanjeeda, Kumar Pankaj, Kumaran Senthil, Jauhari Prashant, Chakrabarty Biswaroop, Pandey RM, Gulati Sheffali

OBJECTIVE: SLD is a neurodevelopmental disorder of biological origin manifested by deficits in phonological processing and is simply described as a gap between child's ability & performance.
METHODS: We enrolled forty four Dyslexic children and 12 controls (typical readers) between July 2018 and Jun 2019. The intervention was developed keeping in mind the salient components as recommended by National Reading Panel and available in Indian literature. All cases underwent Grade Level Assesment Device (GLAD) assessment Tool pre and post intervention. fMRI using phonological tasks was done in 25 cases pre and post along with 12 controls) .
RESULTS: The mean age was 9 years (6 yrs –12 yrs), boys were 80%. Combination of dyslexia, dysgraphia and dyscalculia was in 66% of children. Inattention, ADHD was present in 75% children as comorbidity. Post intervention there was significant improvement in the reading scores of GLAD assessment (p<0.05), mean difference 14.0 (95% CI 10.3-17.70) more so in younger children. fMRI activation clusters of language areas showed significant change post intervention and was comparable to the controls versus treatment naïve dyslexics. The deficit found in dyslexics was the poor activation of posterior reading systems namely the Left posterior Superior temporal gyrus for reading words during the functional task. Resting state MRI in Dyslexics show strong connections between Left IFG and Left pSTG.
CONCLUSIONS: An explicit phonologically based structured remedial intervention is effective in improving children's word level decoding difficulties while addressing letter–sound knowledge and phonemic awareness skills in dyslexics.
KEYWORDS: Cognitive/Behavioral Disorders (including Autism), Neuroscience

12. Comparison of symptom severity as per AIIMS Modified INDT-ADHD tool with Conner's Parent reported scale in 6-18 year old children and adolescents with ADHD

Gulati Sheffali (New Delhi, India) Sharma Sobha, Panda Prateek, Parveen Sana, Agrawal Samprati, Rakholia Vaidehi, Dahiya Vinod

OBJECTIVE: To evaluate the additional utility of AIIMS modified INCLEN Diagnostic Tool for ADHD as a symptom severity rating scale ADHD (with Conner's parent reported scale as gold standard)
METHODS: 6-18 year old ADHD children (DSM V criteria satisfying) with IQ>70 were enrolled between May 2019 and January 2020.Two well trained clinical psychologists analyzed ADHD symptom severity using Conner' s Parent Rating Scale Revised(CPRS-R), Conner's Global Index-Parent (CGI-P) and AIIMS modified INDT tool for ADHD. CPRS-R and INDT tool were applied to one participant by separate psychologists, both unaware of result of other person. The sequence was determined by block randomization, with help of computer generated random number sequence.
RESULTS: Sixty children (10.12±2.24 years, 56 boys, IQ=84.88±7.24) were enrolled. Out of these, 41 children were of combined type, 9 were of predominantly hyperactive/impulsive type and 11 were of predominantly inattentive type. There was positive correlation between total symptom severity score obtained from AIIMS modified INDT ADHD tool and T score of six Connor's 3-Parent Rating content scales: inattention, hyperactivity/impulsivity, learning problems, executive functions, defiance/aggression, and peer relationship (p=0.01), but the strength of correlation was weak. However, moderate positive correlation was observed between hyperactivity/impulsivity symptom severity score of AIIMS modified INDT ADHD tool & hyperactivity/impulsivity content scale of CPRS (correlation coefficient, r=0.31). Moreover, the strength of positive correlation was better for AIIMS modified tool than for DSM-IV-TR based INDT ADHD tool.
CONCLUSIONS: Although originally developed as a diagnostic tool, AIIMS modified INDT ADHD tool can be used successfully as severity rating scale in ADHD children.
KEYWORDS: Cognitive/Behavioral Disorders (including Autism)

13. Comparative analysis of gut microbiota between children with autism spectrum disorder and typically developing children: A PCR and metagenomic approach

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OBJECTIVE: This study was undertaken to study the comparative abundance of major gut microflora between children with autism spectrum disorder (ASD) and typically developing (TD) children.
METHODS: All children between 3 to 15 years with ASD, presenting to a tertiary care centre in India were eligible for the study. The TD siblings of ASD patients were enrolled as controls. Faecal specimens were collected in the homes of the participants by their parents. The faecal specimens were then shipped to the laboratory on the same day where each specimen was frozen at −80 °C until DNA extraction. Relative and Absolute qPCR as well as 16S rRNA diversity using High throughput Sequencing (HTS) of metagenomic DNA analysis were carried out for studying comparative abundance of the targeted microbiota.

RESULTS: Twenty-four children were enrolled in the study; six were excluded due to inadequacy of stool sample and eighteen children (all boys, median age=7.5 years) were included for final analysis. These included 12 children with ASD and six TD siblings of ASD patients. There was decreased gut bacterial diversity in the gut microflora of children with ASD. The phylum *Firmicutes* was significantly less and the phylum *Bacteroidetes* was significantly more in children with ASD as compared to TD siblings. In addition, *Clostridium perfringens* was significantly higher in the gut microbiota of children with ASD.
CONCLUSIONS: These results suggest that gut-microbiota-based disease analysis is able to predict novel connection between gut microbes and ASD and may play a role in revealing the pathogenesis of ASD.
KEYWORDS: Cognitive/Behavioral Disorders (including Autism)

14. Development and evaluation of Autism screening instrument (AIIMS-ASD-Infant-Screening tool) in children aged 1-18 months and DSM-5 based Autism diagnostic instrument (AIIMS-Modified-INDT-ASD tool) for children above 1 year
Gulati Sheffali (New Delhi, India) Gupta Aparajita, Sondhi Vishal, Kaushik Jayashankar, Saini Lokesh, Sharma Shobha, Pandey Ravindra

OBJECTIVE: To describe the development of (a) AIIMS-Modified-INDT-ASD Tool based on DSM-5 criteria for diagnosis of Autism-Spectrum-Disorder (ASD) and (b) AIIMS-ASD-Infant-Screening tool for identifying the early signs of ASD in children aged 1-18 months.
METHODS: This AIIMS-Modified-INDT-ASD Tool, was developed by incorporating DSM-5 related changes in INCLEN Diagnostic Tool for ASD. The psychometric property of the aforementioned tool were assessed in a cohort of children between 1 to 14years. The development of AIIMS-ASD-Infant-Screening tool was conducted in two stages. The first stage involved generation of pool of questions, using Delphi's technique, to identify early signs of ASD. The second stage consisted of applying this questionnaire in the 4 groups: ASD, global development delay (GDD), hearing loss (HL) and typically developing children (TDC) and determining cut off scores in age specific strata.
RESULTS: For determining the psychometric properties of AIIMS-Modified-INDT-ASD Tool, 225 children (159 boys, median age = 47months) were enrolled. The tool demonstrated sensitivity of 98.4% and specificity of 91.7% to diagnose ASD. A score ≥14 on the tool was suggestive of severe ASD (CARS>36.5) with a sensitivity and specificity of 80% and 80.7% respectively. The evaluation of AIIMS-ASD-Infant-Screening tool involved 200 Children (24-30 months). Out of the 62 questions in the original questionnaire,30 questions were identified with >80% sensitivity and specificity. The sensitivity and specificity of the screening tool increased from 92.1% and 85% at 6 months to 90% and 76% at 12 months, and 99% and 95% at 18 months.
CONCLUSIONS: Both AIIMS-Modified-INDT-ASD Tool and AIIMS-ASD-Infant-Screening tool have good psychometric properties.
KEYWORDS: Cognitive/Behavioral Disorders (including Autism)

15. Cluster analysis reveals sensory profile subtypes in Autism Spectrum Disorder
Lyons-Warren Ariel (Houston, TX, United States) Wan Ying-Wooi

OBJECTIVE: The diagnostic criteria for Autism spectrum disorder (ASD) includes unusual interest in sensory aspects of the environment or atypical reactivity to sensory input. Indeed, up to 94% of patients with ASD exhibit hyper or hypo sensitivity in at least one sensory modality. However, individual sensory phenotypes are heterogeneous and the distribution of affected sensory modalities remains unknown. A recent study proposed two sensory subtypes classified as uniformly elevated verses isolated impairment in sensitivity and avoiding behaviors but did not evaluate for subtypes or clusters of specific sensory modalities. We hypothesized that the short sensory profile could be used to identify sensory subtypes within ASD.
METHODS: Short sensory profile data from 378 patients with Autism spectrum disorder were obtained from the MSSNG database. We performed a k-means cluster analysis on the 7 sensory features identified in the short sensory profile. We then used correlation analysis to confirm identified associations between specific sensory modalities.
RESULTS: Our cluster analysis revealed a larger than expected subgroup (N = 145 for K = 3) that scored in or near the typical performance range in all categories. Interestingly, typical performance in movement sensitivity and low energy consistently clustered together. We also observed overlap across impairments in auditory filtering and sensory seeking (K = 4, 5 or 6).
CONCLUSIONS: Data from the short sensory profile can be used to identify sensory subtypes in Autism spectrum disorder. We propose that sensory subtypes will provide key insights necessary to identify underlying shared circuit mechanisms of ASD.
KEYWORDS: Cognitive/Behavioral Disorders (including Autism), Genetics

16. Effect of Media Exposure to Social Development in Children
Kim Sung Koo (Seoul, Republic of Korea) Seo Suk Hyun, We Da Som, Ma Chul Kyu

OBJECTIVE: Recently, many children have been exposed to media for a long time due to the development of media devices including smartphones. The prevalence of autism spectrum disorder patients, which show problems in social development, is also rapidly increasing. This study was performed in order to evaluate the association of media exposure with social developmental delay
METHODS: The sample consisted of 96 patients with autism spectrum disorder and social developmental disorder who visited the developmental disorder clinic from January 2013 to April 2019. Control group included 101 child who were visited our developmental clinic with normal result of developmental screening test for the same period. The data were collected by using self-report questionnaires.
RESULTS: The mean age of the social developmental delay group was 33.5±9.7 months and the male-to-female ratio was 2.6:1. In regard to media exposure time, 61% of the social development delay patients were exposed to media for more than 2 hours a day, as compared to 19% of the control group (P<0.001, odd ratios 8.12). Among the social development delay group, 92% of the patients were under 24 months old at the time of exposure to media, as compared to 60% of the control group (P=0.03, odd ratios 14.63). In addition, 74% of the social developmental delay group watched media alone, as compared to 39% of the control group (p=0.01, odd ratios 6.15)
CONCLUSIONS: Media exposure over 2 hours a day, before age of 24 months and watching alone respectively were risk factors for social developmental delay.
KEYWORDS: Cognitive/Behavioral Disorders (including Autism)

17. Head circumference smaller than 2 standard deviations (SD) below the mean at 2 and 10 years of age (microcephaly) is associated with poorer cognitive and neurologic outcomes at 10 years of age in a cohort of children born extremely preterm (EP, < 28 weeks)

Jonas Rinat (Jamaica Plain, MA, United States) Mabray Patrick, Heeran Timothy, Hooper Stephen, Joseph Robert, Douglass Laurie, Frazier Jean, Hirtz Deborah, Rollins Julie, O'Shea Thomas, Kuban Karl

OBJECTIVE: To evaluate the association of head circumferences (HC) at birth, 2 years, and 10 years with IQ and neurological outcomes at 10 years in a cohort of children born EP.
METHODS: We measured HC, assessed IQ using Differential Ability Scales–II, conducted validated assessments for seizures, autism, and motor function, and completed caretaker interviews when children were 10 years old. In a sample of 786 participants, we analyzed associations of HC Z-scores at birth, 2 years and 10 years with cognitive and neuro-educational outcomes.
RESULTS: 14% of children had microcephaly at 10 years (8% at birth, 10% at 2 years). A third of children with microcephaly at 2 years no longer had microcephaly at 10 years while 8.5% of those not microcephalic at 2 years, had microcephaly at 10 years. Almost half with microcephaly at 2 years had a full scale IQ<70 (Figure 1). Compared to microcephaly at birth (OR 2.4; 95%CI 1.4, 4.2), microcephaly at 2 years of age (OR 11.5; 95%CI 6.4, 20.7) is more strongly associated with IQ<70 at 10 years. Microcephaly at 2 years is strongly associated with epilepsy, impaired motor abilities, autism, and need for an individual educational plan/separate classroom at 10 years (Table 1). Compared to HC at 2 years, HC at 10 years was not more strongly associated with cognitive impairment.
CONCLUSIONS: Microcephaly at age 2 years, more so than at birth and comparable to microcephaly at 10 years, is associated with lower IQ and neurological morbidity at 10 years of age.
KEYWORDS: Cognitive/Behavioral Disorders (including Autism), Neonatal & Fetal Neurology

18. Indian Adaptation and Validation of ASQ 3 (Ages and Stages Questionnaire) in Indian children 2 to 24 months of age

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OBJECTIVE: To develop and validate an Indian adaptation of ASQ-3 (Ages and Stages Questionnaire) as a screening tool for developmental delay in children 2-24 months of age
METHODS: Input were taken from 37 Indian experts regarding sociocultural adaption of ASQ by semidelphi method. Modified ASQ was successfully piloted in 20 subjects. DASII (Developmental Assessment Scale for Indian Infants) was used as gold standard. Children with developmental concerns were subjected to assessment by DASII and modified ASQ on same day by separate experienced child psychologists (allocation done by computer generated random number and sample population was age stratified to ensure lack of bias and uniform representation of all age groups)
RESULTS: Out of 654 children screened, 568 were enrolled (420 children had developmental delay confirmed on DASII and 148 had normal development). Indian adaptation of ASQ failed to identify only 18 (4.3%) out of 420 children with developmental delay correctly. The overall

sensitivity of Indian adaptation ASQ in detecting developmental delay was 95.9% (93.6%-97.5%) and specificity was 81.7% (74%-87.9%) with a positive predictive value 94.6 % (92%-96.5%) and negative predictive value of 85.6% (78.2%-92.2%). The sensitivity of Mental domain (communication, personal social and problem solving) of Indian adaptation of ASQ-3 was 95.5% (93.1-97.2%) and specificity was 95.3% (90.1%-98.3%). The overall sensitivity of Motor domain (gross motor, fine motor) of Indian adaptation of ASQ-3 was 96.1% (93.8%-97.7%) and specificity was 92.4% (86.4%-96.3%)
CONCLUSIONS: The Indian adaptation of ASQ has excellent psychometric properties as a screening tool to detect developmental delay in children aged 2-24 months.
KEYWORDS: Cognitive/Behavioral Disorders (including Autism)

19. Gender Differences in Early Neurodevelopment Detected by WIDEA- a criterion measure of early neurodevelopmental functioning in daily activities
Mulkey Sarah (Washington, DC, United States) Persaud Reva, Hitchings Laura, Eze Augustine, Swisher Christopher, Russo Stephanie, Maxwell G, Baker Robin, Msall Michael, du Plessid Adre

OBJECTIVE: The Warner Initial Developmental Evaluation of Adaptive and Functional Skills (WIDEA) is a validated questionnaire of early neurodevelopment. The objective was to evaluate the role of gender in WIDEA scores in term and low-risk preterm infants at 6 and 12 months of age.
METHODS: We performed a prospective study of infant development at Inova Fairfax Hospital, Virginia. Healthy term newborns (n=180) and preterm infants (n=100), born between 23-36 weeks gestation were included. The premature cohort had a low prevalence of prematurity related morbidity. WIDEA total and sub-domains of self-care, mobility, communication, and social-cognition at 6 and 12 months cGA were compared between groups by t-test.
RESULTS: Of the term cohort, 151 (84%; 77 male, 74 female) completed the WIDEA at 6 months, and showed no difference in WIDEA by gender. However, by 12 months, term-born females had higher WIDEA communication (P=.03) and total WIDEA scores (P=.046). In the preterm cohort, 73 (73%; 36 male, 37 female) completed the WIDEA at 6 months, again without a gender difference in scores. At 12 months, preterm-born males had higher WIDEA social-cognition scores (P=.03), but there was no gender difference in the total WIDEA score. Furthermore, there was no significant difference in WIDEA between term and preterm-born infants at 12 months.
CONCLUSIONS: The WIDEA enabled high follow-up rates in prospectively enrolled term and preterm cohorts. Gender may play a role in early domains of neurodevelopment and should be considered in analyses. The underpinnings of the domain-specific gender differences require further study and correlation with longterm neurodevelopmental outcomes.
KEYWORDS: Cognitive/Behavioral Disorders (including Autism), Neonatal & Fetal Neurology

20. Chandelier cells and an altered GABAergic synaptic system in the human prefrontal cortex in autism
Hong Tiffany (Sacramento, CA, United States) Falcone Carmen, Amina Sarwat, Perez Castro Rosalia, Regalado Jade, Pearson Weston, Noctor Stephen, Salcedo Maria Jimena, Martinez-Cerdeno Veronica

OBJECTIVE: Autism severity has been correlated with a dysregulated excitation/inhibition balance in the cerebral cortex. We previously found a significantly decreased number of chandelier cells (Ch) in the human prefrontal cortex in autism; Ch cells are a unique subtype of gamma-aminobutyric acid (GABA)ergic inhibitory interneurons in that each Ch cell's axon forms synapses exclusively on the axon initial segment (AIS) of excitatory pyramidal cells, and does so on hundreds of pyramidal cells. Thus, to further uncover Ch cell/GABA system alterations in the anatomy of autism neuropathology, we hypothesized that in autism, Ch cells have a decreased number of terminal boutons and that the postsynaptic pyramidal cell contains fewer $GABA_A$ receptors in its AIS.
METHODS: In human postmortem prefrontal cortex tissue, we examined Brodmann Areas (BA) BA9, BA46, and BA47 in control and autism cases, as these are areas associated with the cognitive abnormalities in autism. We used immunohistochemistry to label Ch cell terminal boutons as well as $GABA_A$ receptors in the pyramidal cell AIS, and ImageJ (NIH) was utilized for bouton and protein quantification.
RESULTS: In autism, we found a decreased amount of $GABA_A$ receptor subunit α2 protein in the pyramidal cell AIS in supragranular layers of BA9 and BA47, and preliminary data shows no difference in bouton number.
CONCLUSIONS: Reduced GABA receptor protein in the AIS of pyramidal cells may contribute to an excitation/inhibition imbalance in the prefrontal cortex of subjects with autism, and our findings support the potential for GABA receptor agonists as a therapeutic tool for autism.
KEYWORDS: Cognitive/Behavioral Disorders (including Autism), Neuroscience

21. Can a home-based digital treatment improve neural biomarkers of attention for children with ADHD?
Gerdes Molly (San Rafael, CA, United States) Copeland Brianna, Silvers Elizabeth, Simon Alexander, Anguera Joaquin, Marco Elysa

OBJECTIVE: Children with impaired cognitive control have challenges in everyday life and school function. Certain types of cognitive training have been shown to improve attention, providing an alternative or adjunct to prescription medication. Based on previous work involving children with sensory processing disorders (SPD) (Anguera et al., 2017, PLOS-ONE), only children with SPD and comorbid inattention showed increased midline frontal theta (MFT) power (a neural marker of attention) after home-based digital treatment. We sought to replicate these findings in a larger cohort of children with ADHD.
METHODS: 25 unmedicated children with ADHD, 8-12 years, underwent a 4-week adaptive/personalized training using AKL-T01 (Project: EVO) on an iPad. All children met inclusion criteria on the Vanderbilt ADHD Parent Rating Scale as well as the Mini-International Neuropsychiatric Interview for Children and Adolescents. Cognitive control was assessed pre and post-intervention using the Vanderbilt, the Test of Variables of Attention (T.O.V.A.®),. and task-based electroencephalography during a perceptual discrimination task to evaluate changes in MFT power.
RESULTS: We observed significant improvements on the Vanderbilt for real-world function. Direct assessment using the T.O.V.A.®. revealed performance improvement for reaction time and reaction time variability. Finally, we evidenced increased event-related MFT

power, replicating our previous finding and providing direct support that use of AKL-T01 is associated with increased neural plasticity in this population.
CONCLUSIONS: These findings augment a positive randomized controlled multisite ADHD efficacy study with AKL-T01 by demonstrating that a video game-based cognitive training intervention can enhance attention-related behavior, performance, and neural engagement for children with inattention/ADHD.
KEYWORDS: Cognitive/Behavioral Disorders (including Autism)

22. Infant Feeding Practice and Developmental Outcomes of Children 6-59 months in Nigeria
Jimoh Adenike (Zaria, Nigeria) Anyiam Jane, Yakubu Alhassan

OBJECTIVE: The study aimed to examine the association between both cognitive and non-cognitive developmental domains and breastfeeding practice of under-five children.
METHODS: A cross-sectional, community-based study in Zaria, Kaduna state, northwestern Nigeria. Study participants included 415 under-five children in selected pre-schools and immunization centres. Developmental screening was done using the Schedule of Growing Skills II tool. Gross motor, manipulative, visual, hearing/speech/language, interactive/self-care social and cognitive skills were assessed. Developmental quotient below threshold point of 85% in a developmental domain defined developmental delay. Using pre-tested questionnaire, information on sociodemographic characteristics, infant feeding practices, family and social history was obtained from the parents.
RESULTS: Of 415 children assessed, only one child was not breastfed, while 194 (46.7%) of them were exclusively breastfed. There was no significant relationship between the breastfeeding pattern and developmental quotient across all the domains. Children who were breastfed longer than 1 year had twice the odds of developmental delay in interactive/self-care social domain compared to those who breastfed for a period of less than one year. (OR 2.0: 95% CI 1.04-3.88, $p = 0.033$).
CONCLUSIONS: Breastfeeding during infancy has been found to secure mother-child bond, in addition to other developmental outcomes. Children who breastfeed for shorter duration are however more likely to be independent of their caregivers early thus may likely establish self-regulation quicker through interaction with those around them. While we still recommend and encourage breastfeeding, directed efforts need to be made to ensure that subtle unwanted effects, as observed in this study, are compensated for.
KEYWORDS: Cognitive/Behavioral Disorders (including Autism)

23. JUVENILE ONSET NEUROREGRESSION - MTHFR DEFICIENCY: A RARE BUT POTENTIALLY TREATABLE ETIOLOGY
Arora Anshita (Mumbai, India) Patel Vishal, Rathod Nishant, Agrawal Radhika, Hegde Anaita

OBJECTIVE: MTFHR deficiency is rare potentially treatable metabolic disorder with variable presentations in different age groups. It presents commonly in neonatal and childhood period with few cases of adolescent onset reported in literature. This disorder can mimic genetic/acquired leukodystrophy or mitochondrial disorder.
METHODS: We retrospectively reviewed four patients with MTHFR gene mutation and studied clinical presentation, progression, investigations and treatment response over last 2 years.

RESULTS: All patients were males. 3/4 presented between 12-17 years while one at 5 years. Clinical presentation included varying degree of cognitive decline, neuropsychiatric symptoms, bradykinesia, spastic paraparesis/quadriparesis and intermittent encephalopathy. Transient venous sinus thrombosis was seen in one patient. 1/4 had significant history of sibling death due to similar illness. Metabolic workup showed high serum homocystine with subnormal serum B12 levels. All had normal metabolic screen. MRI brain had soft diffuse periventricular white matter changes with progressive generalized cerebral atrophy.They were treated with injectable methylcobalamine, methylfolate and betaine after diagnosis with significant clinical improvement in all patients and reversal of cerebral atrophy in 2/4.
CONCLUSIONS: Homocysteine metabolism disorders are under recognized group of disorders, which mostly present in childhood with thrombophilic spectrum. In juvenile age group, they are an important cause for cognitive and motor regression.An early diagnosis and timely initiation of treatment can prevent further complications of this potentially treatable disorder, which can be fatal if not treated on time. Serum homocysteine levels is a cost effective test for screening of MTHFR deficiency and should be included in biochemical work up for all children with cognitive and motor regression.
KEYWORDS: Cognitive/Behavioral Disorders (including Autism)

24. Clinical profile of children with attention deficit hyperactivity disorder from a tertiary care center in North India

Panda Prateek (Rishikesh, India) Verma Henuka, Sharma Vishakha, Lourembam Radhapyari, Sharawat Indar

OBJECTIVE: To describe the clinical profile and treatment outcome of children with attention deficit hyperactivity disorder from a tertiary care center in North India
METHODS: The clinical profile, socio-demographic, neuropsychological factors, co-morbidities and management outcome of children presenting with ADHD between August 2019 and January 2020 were analyzed. DSM V criteria, Conner's Parent Rating Scale-Revised (CPRS-R), Mallin's Intelligence Scale for Indian Children (MISIC), Childhood Behavior Check List (CBCL) and Childhood Sleep Health Questionnaire (CSHQ) were utilized for diagnosing and evaluating these children.
RESULTS: Total 41 children (36 boys, 79 %, 9.46±1.75 years) with ADHD were identified. Commonest subtype was combined type (27/41), followed by predominantly hyperactive/impulsive type (8/41) and predominantly inattentive type (6/41). Commonest co-morbidities were sleep disturbance (13/41, CSHQ>41), Specific Learning Disability (11/41), Oppositional Defiant Disorder (ODD, 18/41) and conduct disorder (9/41). ODD and CD were more common among boys with combined and hyperactive subtype. 15/41 children had other emotional issues on CBCL. 7/41 children had history of fever triggered or unprovoked seizures and 9/41 children had history of language milestone predominant developmental delay. Mean IQ of the group was 87.42±9.21.
37/41 children required medication, with commonest drug used were Atomoxetine (34/37, median dose 10 mg), Methyl Phenidate (3/37, median dose 5 mg), melatonin (7/41)and Clonidine (5/41, median dose 100 microgram), along with behavioral intervention. At median follow up duration of 2 months, 35/41 children had shown significant improvement as measured by CPRS-R, Pre-and Post-treatment (p=0.04).

CONCLUSIONS: Timely identification with proper pharmacological and behavioral intervention is imperative for early remediation of ADHD symptoms.
KEYWORDS: Cognitive/Behavioral Disorders (including Autism), Neurorehabiliation

25. Creation and Implementation of an Inpatient Autism Specific Care Plan to Improve Neurology Hospitalizations for Patients with Autism Spectrum Disorder (ASD)
Spence Sarah (Boston, MA, United States) Atkinson Carole, Chiujdea Madeline, Coffey Kristin, Fernandes Serena, Luercio Marcella, Miller Olivia, Nolan Michaela, Parsons Chase, Snell Matthew, Starmer Amy

OBJECTIVE: To describe the development and pilot results of a clinical pathway to improve hospitalizations for children with autism spectrum disorder (ASD).
METHODS: Interdisciplinary input was sought from neurology, pediatrics, psychiatry, nursing, child life, social work, behavioral response team (BRT), augmentative communication, occupational (OT) /physical therapy (PT), and nutritionists, working with Quality Improvement staff. An existing hospital resource for behavioral support plans which detail communication methods and accommodations to reduce stress and promote coping was utilized. The pathway was piloted on an inpatient neurology unit and 44 caregivers were surveyed about how the child's autism impacted goals of admission.
RESULTS: The clinical pathway steps include: creating/reviewing individualized behavior support plan; door signage notifying staff to review behavior support plan; guidance for consultation by child life, BRT, psychiatry, augmentative communication, OT/PT, and feeding teams; reminder for autism informed rounding; autism-specific discharge planning. Survey response rate was 32%. 86% of caregivers felt autism made the admission difficult for their child, but care teams was only asked about their child's autism 50% of the time. However, when the pathway was utilized 100% of caregivers felt it helped.
CONCLUSIONS: Hospitalizations for children with ASD can be challenging for the patient, their families and the inpatient care team. A clinical pathway to address autism-specific care needs may improve patient/family experience and help patients meet admission goals, but a culture shift on the inpatient team is necessary. Next steps are increasing provider awareness, improving integration into electronic medical record and expanding pathway use hospital wide.
KEYWORDS: Cognitive/Behavioral Disorders (including Autism)

26. Quantitative electroencephalographic changes in children with autism spectrum disorders
Azouz Hanan (Alexandria, Egypt) Khalil Mona, Abdeldayem Samia

OBJECTIVE: It has been recently suggested that autism spectrum disorders (ASD) are characterized by abnormal brain networks and connectivity The aim of this study is to analyze neurophysiological characteristics of children with ASD using quantitative electroencephalography (QEEG) and compare it with age-matched controls and to assess if QEEG analysis is sensitive and yet simple enough to aid in the diagnosis children with ASD.
METHODS: QEEG recordings of 50 children with ASD diagnosed by DSM-5 criteria between the ages of 2 and 6 years were compared with those of 50 age-matched controls under eyes-closed condition. Brain functioning and its connectivity were examined using measurements of spectral analysis of both absolute and relative power and inter-hemispheric coherence

RESULTS: There were statistically significant differences in electroencephalogram spectral power and coherence between the study and control groups. It revealed an increased absolute delta power in the frontal, anterior temporal, mid-temporal, central, and parietal regions and an increase of absolute alpha power mainly in the prefrontal and frontal regions. There was a greater beta power in mid-temporal and posterior temporal regions. In addition, inter-hemispheric coherence showed a pattern of frontal overconnectivity and temporal under-connectivity with the other brain areas in children with ASD in comparison with the control group. Moreover, statistical differences in electroencephalogram spectral power and coherence between the different grades of children with ASD were noticed.
CONCLUSIONS: These results suggested that children with ASD have QEEG dysfunctions that underlie their symptomatology. Hence, QEEG may provide a useful method that aids in the diagnosis of children with ASD.
KEYWORDS: Cognitive/Behavioral Disorders (including Autism), Neuroscience

27. Sensorimotor Therapies Improve Core Symptoms of Autism Spectrum Disorder
Shapiro Kevin (Torrance, CA, United States) Jaska Savannah, Shankula Chase, Hattangadi Neil, Marco Elysa, Goh Suzanne

OBJECTIVE: Sensorimotor therapies, including occupational and physical therapy, are often used to treat comorbid motor and sensory processing difficulties in children with autism spectrum disorder (ASD). We hypothesized that sensorimotor therapies (SMT) are also beneficial for two core deficits in ASD, difficulty with social behavior and communication.
METHODS: We retrospectively reviewed records of 32 children with ASD, ages 2;11-18;1 years (median 7;0 years), treated at our center from 2016 to 2018. All received Applied Behavior Analysis (ABA) therapy as standard of care and were assessed at least twice using the Vineland Adaptive Behavior Scales (Vineland-3), with mean interval between initial and final assessments of 376 days (range 123-598 days). Of these children, 21 received >20 hours of SMT as part of a comprehensive treatment program. We assessed the relationship between exposure to SMT, level of ASD severity, and improvement in Communication and Socialization domains of the Vineland-3, using direct t-tests and a multivariate regression model controlling for age, sex, and total duration of therapy.
RESULTS: Children who received SMT in addition to ABA showed significantly greater improvement in Socialization ($p < 0.05$) and marginally greater improvement in Communication ($p = 0.078$) than children receiving ABA alone. In the multivariate model, hours of SMT predicted improvement in Communication ($p < 0.02$) and Socialization ($p < 0.02$), independently of level of ASD severity.
CONCLUSIONS: Sensorimotor therapies, delivered as part of a comprehensive treatment program, have a significant added benefit to ABA for remediation of communication and social deficits in ASD.
KEYWORDS: Cognitive/Behavioral Disorders (including Autism)

28. Aripiprazole-Induced Seizures in children with Autism Spectrum Disorder and Epilepsy
Jan Mohammed (Jeddah, Saudi Arabia)

OBJECTIVE: Children with autism spectrum disorder are at an increased risk for developing seizures, which can be triggered by classical antipsychotics. Aripiprazole is an atypical antipsychotic that has a safer drug profile. The objective is to present the experience with seizure control in autistic children who are placed on Aripiprazole.
METHODS: Series of consecutive autistic children with comorbid epilepsy treated with Aripiprazole were identified prospectively over a 3-year period. Monthly follow up by one pediatric neurologist was performed to document seizure control.
RESULTS: 56 autistic children with comorbid epilepsy were placed on Aripiprazole. Most children (59%) were seizure free for at least 6 months. The initial Aripiprazole dose was 5 mg in all patients. Follow up ranged between 5-8 months (mean 6.9). A total of 5 (9%) children developed seizure provocation (3/5) or worsening seizure control (2/5). There were 3 males and 2 females with ages ranging between 6-11.5 years (mean 8.5). Three of these children had a previous history of seizure worsening with other antipsychotic drugs (respiridone in 2 and haloperidol in 1). One child with seizure provocation developed status epilepticus 5 days after introducing Aripiprazole that required intensive care admission. The drug was stopped in all 5 children with no long-term effects.
CONCLUSIONS: Seizure provocation or worsening seizure control is not uncommon following the introduction of Aripiprazole in autistic children with controlled epilepsy. Although the risk is low, parents should be warned and advised on what to do, particularly in the first month of therapy.
KEYWORDS: Cognitive/Behavioral Disorders (including Autism), Epilepsy, Neuroscience

29. Doxepin in Children and Adolescents with Symptoms of Insomnia: A Single Center Experience
Shah Yash (New York, NY, United States) Stringel Virginia, Pavkovic Ivan, Kothare Sanjeev

OBJECTIVE: Pediatric insomnia is a widespread problem and especially difficult to manage in children with neurodevelopmental disorders. There are currently no FDA- approved medications to use once first line therapy fails. The objective of this study was to evaluate the efficacy and tolerability of doxepin in pediatric patients.
METHODS: This is a retrospective single center chart review of children and adolescents (2-17 years of age) whose sleep failed to improve with behavioral intervention and melatonin who were then trialed on doxepin. Treatment was initiated at a median starting dose of 2mg and slowly escalated to a median maintenance dose of 10mg. Improvement in sleep was recorded using a 4-point Likert scale reported by parents on follow up visits.
RESULTS: Total of 29 patients were included in analysis (table 1). Mean follow-up duration was 6.5 months (±3.5). Out of 29 patients, 4 (13.8%) patients discontinued doxepin due to lack of efficacy or side effects. 8 (27.6%) patients showed significant improvement of their insomnia, 8 (27.6%) showed moderate, 10 (34.5%) showed mild and 3 (10.3%) showed minimal to no improvement on treatment with doxepin ($P<0.05$) Only two patients (6.8%) experienced adverse effects in the form of behavioral side effects (aggression) and enuresis.
CONCLUSIONS: Our data suggests that doxepin is effective, safe and well-tolerated in the treatment of sleep initiation and maintenance insomnia as well as psychophysiological insomnia in child and adolescents with autism spectrum disorder and ADHD. It is also an effective, safe, and well-tolerated alternative in children suffering from chronic persistent insomnia (fig.1)

KEYWORDS: Cognitive/Behavioral Disorders (including Autism), Translational/Experimental Therapeutics

30. Efficacy of combined methylphenidate and iron therapy among ADHD children with iron deficiency anemia-A randomized controlled trial

Saha Dipa (Dhaka, Bangladesh) Saha Narayan, Haque Azimul, Saha Chinmoy, Islam Ariful

OBJECTIVE: To investigate the comparative efficacy of combined use of methylphenidate with iron and methylphenidate alone among ADHD children with iron deficiency anemia.
METHODS: This study was a randomized clinical trial over 6 months period from July 2018 to January 2019, 100 moderate and severe ADHD children of 3 to 17 years (based on DSM V & confirmation by Conner's parent rating scale) with iron deficiency anemia, were enrolled in this study. All the cases of both groups of moderate and severe ADHD were randomized into two treatment groups. One group received methylphenidate (Ritalin/ Rital) and another group were treated with methylphenidate and iron for 3 months. After 1 month and 3 months, efficacy of therapy was compared between two treatment group on the basis of Conner's rating scale and iron profile. Analysis of data was done by SPSS version of 22.0.
RESULTS: Mean age was 6.4 ± 2.26 years, majority of them were male. Combined ADHD was the prominent features in all groups. T score of Conner's rating scale in oppositional, cognition, hyperactivity-impulsivity and ADHD index showed significant decremental response from baseline to 1 month and 3 months follow up in combined therapy groups of moderate and severe ADHD than methylphenidate alone groups.
CONCLUSIONS: Combined therapy of methylphenidate and iron may more effective than methylphenidate alone for treating the iron deficient child with ADHD.
KEYWORDS: Cognitive/Behavioral Disorders (including Autism)

31. Comparison between Caregiver-Reported Simons Searchlight Registry Data and Provider-Reported Published Data in SLC6A1-Related Disorders

Goodspeed Kimberly (Dallas, TX, United States) Snyder LeeAnn, Helbig Katherine, Cooper Dominique, Chung Wendy, Bain

OBJECTIVE: In this study, we aim to describe and compare caregiver- and provider-reported phenotypic data in SLC6A1-related disorder (SRD), inclusive of published literature, curated databases, and the SLC6A1 patient registry on Simons Searchlight.
METHODS: Provider-reported clinical prevalence data of neurological features of SRD were combined from the published literature, Epi25 Collaborative and referrals to the SLC6A1 Connect Foundation (n=116) and compared to caregiver medical history interview data from the Simons Searchlight registry (n=27). Simons Searchlight conducts a standardized medical history interview by phone with caregivers of all participants.
RESULTS: Based on review of the two datasets, the most prevalent clinical features reported in SRD include epilepsy, intellectual disability/developmental delay (ID/DD), autism spectrum disorder (ASD), hypotonia, and movement disorders/ataxia (Table 1). Frequencies of epilepsy, ID/DD, and ASD are similar between the two groups while hypotonia and movement disorder are higher in the caregiver-report group.
CONCLUSIONS: Provider and caregiver data sources were highly consistent in 3 of 5 conditions reviewed (epilepsy, ID/DD, and ASD) which are core clinical features commonly

discussed in the epilepsy and neurodevelopmental literature. The lower prevalence of hypotonia and movement disorders in the provider-reported dataset may reflect variable data capture in published reports, whereas standardized caregiver interviews may offer more in depth characterization. Though studies combining cohorts are challenged by sample overlap, this study demonstrates consistency between clinical features identified by both providers and caregivers. This supports use of caregiver-reported registry data to identify the core clinical features of rare disorders in a standardized manner.
KEYWORDS: Cognitive/Behavioral Disorders (including Autism), Epilepsy, Genetics

32. Assessing Cranial Electrotherapy Stimulation (CES) Benefits in a Clinical Cohort
Marco Elysa (San Rafael, CA, United States) Copeland Brianna, Gerdes Molly, Silvers Elizabeth, Steele Mary, Shapiro Kevin

OBJECTIVE: Cranial electrotherapy stimulation (CES) is a form of noninvasive transcranial pulsed-current stimulation that is presumed to modify brain activity via vagal and other cranial nerve pathways. CES has been studied in adults for anxiety, insomnia, pain, and headaches, but its effectiveness in pediatric populations is unknown. Putative effects on the vagus nerve suggest CES may be beneficial for symptoms related to autonomic nervous system dysregulation. We hypothesized that a 4-week trial of CES would lead to clinical improvement, based on parent report, in one or more of the following symptoms in children with neurodevelopmental differences: insomnia, headaches, constipation, sensory over-responsivity, and motor tics.
METHODS: This open-label study enrolled 48 individuals, aged 2-24 years, over a 6 month period. Participants underwent 4 weeks of at-home CES therapy using the AlphaStim AID device for 20 minutes/day, 5 7 days/week, at an average intensity of 50-100 microamperes. A symptom questionnaire, the Repeated CES Symptom Survey (RECESS), was completed before and after training. The RECESS evaluates clinical global impression of benefit along with specific parasympathetic-gated functions including sleep, gastrointestinal issues, headaches, involuntary movements, and sensory over-responsivity.
RESULTS: Overall, 49% of parents reported clinical benefit for their child. Parents reported resolution of insomnia (37%), constipation (55%), sensory over-responsivity (46%), and motor tics (43%), but not headache, after the 4-week trial compared to baseline (see table).
CONCLUSIONS: These findings provide preliminary evidence that CES is beneficial in a pediatric cohort and supports further study of this technique with a randomized placebo-controlled design and objective biomarkers.
KEYWORDS: Cognitive/Behavioral Disorders (including Autism), Translational/Experimental Therapeutics

33. Peripheral iron status in children with with attention deficit hyperactivity disorder (ADHD) presenting with sleep disorders – a report form a single tertiary pediatric sleep disorders centre.
Gnidovec Strazisar Barbara (Celje, Slovenia) Strazisar Lea

OBJECTIVE: To evaluate associations of peripheral iron status with sleep disorders in ADHD children and compare it with typically developing children.

METHODS: Hematological parameters indicating iron status (haemoglobin (Hb), iron, total iron binding capacity (TIBC), transferrin saturation, mean corpuscular volume (MCV) and ferritin) were assessed in 21 ADHD children referred to a tertiary pediatric sleep disorders centre in Celje, Slovenia, from January to December 2019. They were compared with those in 18 healthy, age-matched controls using two-tailed Student's t-test. Sleep disorders in ADHD children were diagnosed using standardised techniques of thorough sleep history, clinical exam and polysomnography (PSG) when indicated.
RESULTS: In ADHD children with different types of sleep disorders no significant differences in iron status parameters were found compared to typically developing controls. However, separate analysis taking into consideration specific type of sleep disorders, revealed significantly lower peripheral ferritin levels in ADHD children with sleep-related movement disorders compared to controls (16,6 ± 9.87µ/L vs. 35,53 ± 24.66µ/L; t=2.306, p= 0.030).
CONCLUSIONS: Our results do not support differences in iron status parameters among ADHD children with sleep disorders versus healthy controls but they however suggest that sleep-related movement disorders in children with ADHD are associated with lower serum ferritin levels.
KEYWORDS: Cognitive/Behavioral Disorders (including Autism)

34. Developmental and behavioral profile of children with Neurocutaneous Syndrome- a developing country perspective
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OBJECTIVE: To determine the developmental and behavioral profile in children with neurocutaneous syndromes
METHODS: Ours is a prospective observational study in which 119 patients with neurocutaneous syndromes aged between 1 years and 15 years presenting to pediatric neurology services in a north Indian tertiary care hospital were enrolled from January 2018 to July 2019.They were assessed for I.Q./D.Q. using Indian Adaptation of Wechsler's Intelligence Scale for Children and Development Profile 3. All children were subjected to Diagnostic and Statistical Manual 5 (DSM 5) criteria for Autism Spectrum Disorder (ASD), Attention Deficit Hyperactivity Disorder (ADHD) and Intellectual Deficit (ID). Screening for behavioural problems was done using an indigenous tool.
RESULTS: In our cohort, 16(13.4%) children had ASD. 5% (1/21) of Neurofibromatosis 1(NF 1) patients, 14% (10/72) of Tuberous Sclerosis Complex (TSC) patients and 19% (3/16) of Sturge Weber Syndrome (SWS) patients had ASD. 10.1% (12/119) children had ADHD. This included 5% (1/21) with NF 1, 14% (9/72) with TSC, 6% (1/16) with SWS and 1 patient of Linear Nevus Syndrome (LNS). 58% (69/119) of the total study population had ID. 93 patients could be assessed for behavioral abnormalities. 31.3% (5/16) of children with NF 1, 61.7% (37/60) of children with TSC, 45.5% (5/11) of children with SWS and 2 children with LNS had significant behavioural problems.
CONCLUSIONS: Developmental and behavioral concerns impose significant co-morbidity in children with Neurocutaneous syndromes. Their timely evaluation will therefore improve the over-all quality of life of these children.
KEYWORDS: Cognitive/Behavioral Disorders (including Autism)

35. Efficacy of Yoga as add on therapy option in reducing severity of clinical symptoms in children with attention deficit hyperactivity disorder: a systematic review and metanalysis
Panda Prateek (Rishikesh, India) Sharma Vishakha, Sharawat Indar

OBJECTIVE: To determine the efficacy of yoga as add on therapy option in reducing symptom severity in children <18 years with ADHD.
METHODS: Electronic databases like Pubmed, Scopus and Google scholar were searched in January 2020, using MeSH terms "yoga'', ''children'' and ''attention deficit hyperactivity disorder''. All articles were reviewed independently by two reviewers. Newcastle-Ottawa Scale (NOS) for nonrandomized studies and CONSORT criteria and Cochrane risk-of-bias tool for randomized trials were used for quality assessment. The review was registered in PROSPERO.
RESULTS: 19 relevant articles were identified from 124 search items, after reviewing the contents and excluding duplicate results. Total 13 studies (2 RCTs, 11 single arm prospective studies) and 3 case reports were found. One RCT had low risk of bias and another had carry over effect. Most of the single arm studies had small sample size and only 5/11 studies were of high quality (NOS score ≥7).
Out of these, 6 clinical studies(2 RCTs and 4 single arm studies) describing 93 children could be included in the analysis, as only these studies used a uniform scale for measurement (Connner's Parent/Teacher rating scale), thereby allowing comparability to combine the effect size. Combined results of both RCTs showed significant reduction in symptom severity of ADHD can be obtained as compared to control interventions (p=0.01). None of the studies reported any adverse effects.
CONCLUSIONS: Although yoga seems to be a feasible, harmless and promising add on treatment option in children with ADHD, RCTs with adequate sample size are required to provide high quality evidence.
KEYWORDS: Cognitive/Behavioral Disorders (including Autism)

36. Quantitative measures of spontaneous leg movements differentiate infants at high and low familial risk for autism spectrum disorder
Wilson Rujuta (Los Angeles, CA, United States) Vangala Sitaram, Elashoff David, Sim Danielle, Safari Tabitha, Smith Beth

OBJECTIVE: Motor impairments might be the first sign of atypical development in infants at high risk (HR) for ASD. However, studies have produced varying results due to the limitations of current standardized motor assessments. Quantitative measures of infant motor skills may improve early detection of motor differences that are associated with risk for ASD. We utilized a quantitative wearable sensor to evaluate motor function in HR and low risk (LR) infants and identify motor differences associated with ASD.
METHODS: N = 12 LR infants (no elevated concern for ASD) and 15 HR infants (one sibling with ASD). 5 HR infants with behavioral outcomes. Quantitative measurement of spontaneous leg movements was collected 4 times across the first 12 months of life. Features of the movement data were developed to measure amount of and variability in leg movement patterns. The Alberta Infant Motor Scale [AIMS] was also conducted. ASD symptoms were measured with the Autism Diagnostic Observation Schedule.

RESULTS: HR infants showed lower leg movement rates compared to LR infants (p=0.032, Figure 1). HR infants had normal AIMS scores. HR infants with severe concern for ASD showed lower leg movement rates and variability in leg movement patterns compared to those with no concern for ASD (p=0.017, Figure 2).
CONCLUSIONS: HR infants showed lower leg movements rates, a potential marker of fewer volitional movements. HR infants showed less variability in leg movement patterns, which suggests more repetitive movements (a diagnostic feature of ASD). Quantitative measures can improve early identification of motor impairments associated with risk for ASD.
KEYWORDS: Cognitive/Behavioral Disorders (including Autism), Movement Disorders (including Cerebral Palsy)

37. Associated Risk Factors of Language-Based Disorders in Sickle Cell Disease
Cannon Alicia (Baltimore, MD, United States) McIntyre Tiffany, Casella James, Lance Eboni

OBJECTIVE: The aim of this study was to identify disease-related and neurodevelopmental characteristics that can facilitate early identification of language disorders and learning disabilities in children with Sickle Cell Disease (SCD).
METHODS: We performed a retrospective chart review of patients from a pediatric SCD clinic roster in 2017 to identify patients with SCD who had participated in comprehensive neuropsychological evaluations. Data extracted from participants' charts included age at evaluation, sex, SCD type, baseline hemoglobin, highest and most recent transcranial Doppler (TCD) velocities, developmental history, school support services, testing results, and diagnoses.
RESULTS: Twenty-two participants met inclusion criteria. A majority of participants were male (n=15, 68%) and had a mean age at evaluation of 12.5 years (range 5 to 24 years). Participants had varying SCD phenotypes, including HbSS (54.5%), HbSC (18.2%), and HbS-β^+-thalassemia (9.1%). SCD phenotype was unavailable for 4 participants (18.2%). The participants with recorded TCD velocities (n=8) had a mean maximum TCD of 135 cm/sec, with 62% of maximum TCD velocities recorded in the left middle cerebral artery. Participants' highest and most recent TCD velocities correlated with Spelling and Comprehension of Instructions test scores. Parent ratings of communication skills in young children (<12 years) was predictive of language and reading scores.
CONCLUSIONS: Children with SCD are at risk for neurodevelopmental disorders, including language-based disorders. Participants with elevated TCD velocities in areas of the brain associated with language, particularly left/dominant cortical regions, may be particularly vulnerable.
KEYWORDS: Cognitive/Behavioral Disorders (including Autism)

38. Utility of Video EEG (VEEG) in the Assessment of Staring Spells (SS) in Children with Autism.
Arya Kapil (Little Rock, AR, United States) Verma Smriti, Jones Stephen

OBJECTIVE: To report on the utility of VEEG in children with autism and SS.
METHODS: We conducted a retrospective chart review of autistic children with VEEGs done at our institution during May 2010-May 2019 to characterize SS. EEG done prior to VEEG (pEEG) was divided into normal, with seizures, with focal epileptiform discharges (EDs) or with generalized EDs. SS clinical characterization prior to VEEG was recorded- complex partial

seizure (CPS), absence seizure (AS) or behavioral. Frequency tables were generated. Chi-square analysis was performed to test for any significant association between pEEG result or diagnosis prior to VEEG characterization with VEEG characterization of SS.
RESULTS: Of 75 subjects with VEEG, 33 had events, 27 without and 6 with seizures. Of 27 children without seizures, 15 had normal EEGs, 1 had non-epileptiform abnormalities on EEG, 6 had generalized EDs and 5 had focal EDs. Of 42 subjects without events, 33 had normal EEGs, 8 had focal EDs and 1 had non-epileptiform EEG abnormalities. Seizures recorded on pEEG significantly predicted seizures on VEEG (p=0.04) while normal pEEG predicted a normal VEEG (p=0.02). SS characterization as CPS or AS prior to VEEG, significantly predicted similar characterization on VEEG (p=0.045).
CONCLUSIONS: VEEG proved useful in characterizing SS in almost half our subjects. However, VEEG may not help change the diagnosis for patients with a normal pEEG, those with seizures captured on pEEG and those with prior CPS or AS clinical characterization.
KEYWORDS: Cognitive/Behavioral Disorders (including Autism), Epilepsy

39. Impact of a Behavior Analyst to Improve Care for Patients with Autism Spectrum Disorder During Inpatient Hospitalizations.
Miller Olivia (Boston, MA, United States) Coffey Kristin, Snell Matthew, Fernandes Serena, Crook Douglas, Spence Sarah

OBJECTIVE: Inpatient hospitalizations are often highly stressful for individuals with Autism Spectrum Disorder (ASD), and may contribute to increased agitation and challenging behaviors. These behaviors may result in barriers to essential medical care for patients with ASD. The goal of the current project is to describe the impact of behavioral interventions, delivered by a Behavior Analyst (BCBA), on treatment outcomes in patients with ASD during inpatient hospitalizations.
METHODS: BCBA consulted due to staff/parent concern regarding behaviors that may impede medical interventions during hospitalization. BCBA coordinated with staff/parent to complete functional assessment and developed interventions to address behaviors. BCBA provided training on behavior protocol to key members of care team including; security, nursing, child life, social work and psychiatry. Training included prevention of problematic behaviors by changing aspects of the environment, teaching skills to replace challenging behaviors, and responding to encourage positive behavior. Additionally, BCBA provided coaching to assist with implementation of behavior protocol and daily behavior monitoring.
RESULTS: Qualitative analysis of data reveals that BCBA increased medical adherence, reduced use of restraints, and contributed to improved patient outcomes in patients with ASD during hospitalizations.
CONCLUSIONS: The inclusion of a BCBA as part inpatient care team not only improves treatment outcomes for patients with ASD, but also equips staff with behavioral strategies they can implement independently. The findings of the current project suggest that behavioral intervention plays a crucial role in the delivery of essential medical care in patients with ASD.
KEYWORDS: Cognitive/Behavioral Disorders (including Autism)

40. The Autism Spectrum Ambassador Program: Enhancing a Novel Medical Student Run Program
Patel Himadri (Hershey, PA, United States) Fairfull Aubree, Tierney Cheryl

OBJECTIVE: The Autism Spectrum Ambassador Program aims to improve the healthcare experience for pediatric patients with ASD by providing the child and family with a medical student Ambassador to advocate on their behalf during a surgical procedure at the Penn State Hershey Children's Hospital. This study used a common quality improvement methodology (PDSA cycles) to improve recruitment and enrollment for the novel medical student run Ambassador program.
METHODS: Medical students were educated about autism and trained to be ambassadors by study personnel. Over the first full year of implementation, the protocol was not effective in identifying and recruiting participants. To identify potential barriers structured, open ended interviews were conducted with every member of the study team.
RESULTS: In the 2 years after the program's inception, 23 patients were identified for enrollment. Ten participants were enrolled as controls. While 13 were enrolled into the intervention group, only 4 were assigned student Ambassadors. The remaining 9 did not complete the accommodation survey despite several reminders. Based on interviews, the following changes resulted: 1) allowing student Ambassadors to create and distribute accommodation plans even if they themselves were not available to be at the child's procedure in person, 2) distributing study flyers to all clinic sites and re-educating the surgical sub-specialties about the program and 3) adding an option to consent potential recruits over the phone.
CONCLUSIONS: While the ASAP program aims to improve the healthcare experience for pediatric patients with ASD, barriers exist that prevent the positive impact of this program to be fully realized.
KEYWORDS: Cognitive/Behavioral Disorders (including Autism)

41. Weakness in Executive Abilities is a Risk for Delay in the Development of Grammar Understanding in Preschool Children
Kiselev Sergey (Ekaterinburg, Russian Federation)

OBJECTIVE: Children with specific language impairment (SLI) have deficit in grammar understanding (Bishop, 1997). The goal of this research was to examine the hypothesis that children at the age of 5 with weakness in executive abilities have a risk for delay in developing grammar understanding at the age of 6.
METHODS: 114 children at the age of 5 were assessed by 5 subtests from NEPSY (Tower, Auditory Attention and Response Set, Visual Attention, Statue, Design Fluency), which are designed to assess executive abilities. We have revealed 27 children with weakness in executive abilities. These children were included in the experimental group. The control group included 27 children with typical level of executive abilities. The children from experimental and control group were matched for gender, age and IQ. Children at the age of 6 from both groups were assessed by Grammar Understanding Test from Luria's neuropsychological assessment technique.
RESULTS: One-way ANOVA has revealed significant differences between groups for scores in Grammar Understanding Test [F(1,52)=6,65; p=0,013]. Children from experimental group had low level of grammar understanding.
CONCLUSIONS: This research has shown that weakness in executive abilities can be a risk for delay in development of grammar understanding in preschool children. The received results provided insight into cognitive mechanisms in typically developing and the underlying nature of

SLI, helping to elucidate the nature of impaired mechanism in this disorder. It can be assumed that deficit in executive abilities is one of the risk factors for emerging deficit in grammar understanding in SLI children.
KEYWORDS: Cognitive/Behavioral Disorders (including Autism), Neuroscience

42. Body-oriented training has positive effect on attention in preschool children with ADHD
Kiselev Sergey (Ekaterinburg, Russian Federation)

OBJECTIVE: It is known that children with ADHD have deficit in executive abilities and attention. We have revealed that body-oriented training has positive effect on executive abilities in 6-7 years age children with ADHD (Kiselev & Parshakova, 2018). The goal of this study was to reveal effect of body-oriented training on attention in 4-5 years of age children with ADHD. We compared the efficacy of two methods of treatment (body-oriented therapy for children vs. conventional motor exercises) in a randomized controlled pilot study.
METHODS: 16 children with ADHD between 4 and 5 years of age were included and randomly assigned to training conditions according to a 2×2 cross-over design. The body-oriented training included the exercises from yoga and breathing techniques. We used 3 subtests from NEPSY (Auditory Attention and Response Set, Visual Attention, Statue) to assess attention in children.
RESULTS: Effects of training were analyzed by means of an ANOVA for repeated measurements. The ANOVA has revealed ($p<.05$) that for all used subtests (Auditory Attention and Response Set, Visual Attention, Statue) the body-oriented training was superior to the conventional motor training, with effect sizes in the medium-to-high range (0.50-0.88).
CONCLUSIONS: The findings from this pilot study suggest that body-oriented training has a positive effect on attention in 4-5 years age children with ADHD. However, it is necessary to do further research into the impact of body-oriented training on ADHD children.
KEYWORDS: Cognitive/Behavioral Disorders (including Autism), Neuroscience

43. Evaluation and remediation of central auditory processing disorders in children with autism spectrum disorders
Kozou Hesham (Alexandria, Egypt) Azouz Hanan, Abdou Rania, Shaltout Aliaa

OBJECTIVE: This study is a non-randomized clinical experiment. 30 high functioning ASD children aged from 7 to 12 years were included in the study. They underwent comprehensive neurological and audiological measurements with behavioral assessments of CAP skills including dichotic listening abilities measurement by the Arabic version of dichotic digit test (DDT) and behavioral auditory and language processing measurements. Subsequent remediation by dichotic training therapy for the children who revealed significant dichotic deficits (14 children) was done.
METHODS: This study is a non-randomized clinical experiment. 30 high functioning ASD children aged from 7 to 12 years were included in the study. They underwent comprehensive neurological and audiological measurements with behavioral assessments of CAP skills including dichotic listening abilities measurement by the Arabic version of dichotic digit test (DDT) and behavioral auditory and language processing measurements. Subsequent remediation by dichotic training therapy for the children who revealed significant dichotic deficits (14 children) was done.

RESULTS: Scores of CAP skills in ASD children are wide-ranging from completely normal to substantially defective and generally lower than those of typically developing children. By auditory training, ASD children improved their dichotic deficits as well as other untrained areas of auditory and language processing skills.By comparing the mean pre- and post-training scores of weak ear (WE) the gain in mean scores of WE was statistically significant ($p = 0.005$)
CONCLUSIONS: A group of ASD children showed different degrees of abnormalities in CAP that could be measured behaviorally and achieved benefits from auditory training in improving their dichotic listening, auditory and language processing skills.
KEYWORDS: Cognitive/Behavioral Disorders (including Autism), Translational/Experimental Therapeutics

44. ADHD Awareness Among Medical Students
Jan Mohammed (Jeddah, Saudi Arabia)

OBJECTIVE: Early recognition of attention deficit hyperactivity disorder (ADHD) is needed to prevent its psychosocial and educational consequences. We aimed to study ADHD awareness among medical students and identify correlating and contributing factors to their lack of knowledge.
METHODS: A cross sectional study included 5th year medical students attending their pediatric rotation from September 15, 2012 until June 15, 2013 at King Abdulaziz University hospital, Jeddah, Kingdom of Saudi Arabia. A structured 25-item questionnaire was designed to examine their demographics , educational experience, and awareness questions about ADHD.
RESULTS: Of 120 approached students, 111 were included with ages ranging from 20-29 years (mean 22) and 69% being females. Most students 69 (62%) were enrolled during their pediatric rotation and 97 (87%) already completed their psychiatry course. Although most students (67%) recognized ADHD, only 13 (12%) categorized their level of knowledge as very good or excellent. Only 24% correctly recognized ADHD subtypes and 58% did not know what is the initial required management step. Only 19 students (17%) correctly recognized all ADHD features based on the DSM IV criteria with a mean correct score of 69% (standard deviation 14). No correlations were found with their age, gender, completing their pediatric/ psychiatry rotation, or specialty interests.
CONCLUSIONS: Medical student's level of knowledge about ADHD needs improvement. This has to be corrected in order to improve early recognition and intervention. Increased ADHD education and exposure during pediatric/neuroscience modules are needed in our region.
KEYWORDS: Cognitive/Behavioral Disorders (including Autism), Teaching of Child Neurology, Neuroscience

45. Behavioral troubles and disordered chromatin remodeling: the lessons from Kabuki syndrome spectrum and clinical presentation of four Tunisian cases
Bouayed Nouha (Sfax, Tunisia) Abdelmoula Balkiss, Sammouda Takoua, Abid Fatma, Kammoun Sonda

OBJECTIVE: Epigenetic dysregulation are gradually being identified in a variety of neurodevelopmental disorders. Kabuki syndrome (KS) is one of these disorders in which lysine degradation and chromatin organization pathways are deregulated. Here, we report four Tunisian patients, who fulfilled the classical clinical criteria of KS.

METHODS: During our genetic couselling at the medical university of Sfax (Tunisia), we recorded four patients (three females and a male) with multiple congenital anomalies including distinct facial dysmorphism of KS, neurodevelopmental disorders, congenital heart diseases, and skeletal-ectodermal malformations.
RESULTS: Neurodevelopmental disorders were severe with mental retardation in two patients whereas behavioral troubles with learning disabilities characterize the two other patients. Developmental and psychomotor delay with late speech were constant.
CONCLUSIONS: KS is a clinically recognizable syndrome and most patients have a pathogenic variant in the Lysine (K)-specific *MethylTransferase* 2D gene inherited in an autosomal dominant manner. Some cases are due to a mutation in the Lysine (K)-Specific *Demethylase* 6A gene and are inherited in an X-linked dominant manner. Since, KS results from errors in writers of the histone marks, the primary mutational events associated with this syndrome may initiate aberrant DNA methylation and then hardwire the methylation changes into the epigenome as abnormal repressive or activator signals at loci encoding relevant transcription factors involved in the developing nervous system and brain. The presence of a moderate intellectual disability and behavioral troubles as well as severe intellectual disability and mental retardation may be associated either to different specific epigenomic signature or to the mutation type.
KEYWORDS: Cognitive/Behavioral Disorders (including Autism), Genetics, Rare Diseases

46. The adaptation and utility of the Clinical Global Impression scale for studying treatment outcomes in neurodevelopmental conditions
Jaeger Judith (Wilmington, DE, United States) Adera Mathews, Tansy Aaron, Kolevzon Alex

OBJECTIVE: To review literature that describes the adaptation and utility of the Clinical Global Impression-Improvement (CGI-I) and Severity (CGI-S) scales and assess their suitability for studying treatment outcomes in various neurodevelopmental conditions. The CGI-I is a well-validated, clinician-rated scale commonly used to measure outcomes in central nervous system therapeutic development trials across multiple conditions. The structure of the scale supports reliable and valid adaptation to many different conditions and is especially well-suited for those with heterogeneous clinical presentations between individuals and across the lifespan.
METHODS: We reviewed the literature on the use of CGI-I in a wide range of neurodevelopmental conditions, including autism spectrum disorder, Angelman syndrome, Fragile X syndrome, Prader-Willi syndrome, and Rett syndrome.
RESULTS: Adapted to the unique presentations across patients and over different developmental stages, CGI-I and CGI-S can be used to measure severity and change across conditions. The CGI-I allows each individual to serve as his or her own comparator to measure the magnitude of change from baseline CGI-S. Unlike condition-specific rating scales, the CGI-I allows individual symptoms to be weighted based on functional impact/clinical meaningfulness, thus avoiding presuppositions about the clinical effect of a specific investigational treatment.
CONCLUSIONS: Our review describes the use of CGI-I to measure outcome in a wide range of clinical studies, evaluating efficacy of treatments for various neurodevelopmental conditions. This approach highlights the potential of CGI-I to be adapted for other neurodevelopmental conditions where no condition-specific symptom rating scales are available to measure severity or change associated with an intervention.
KEYWORDS: Cognitive/Behavioral Disorders (including Autism), Rare Diseases

47. Is there a relationship between reading speed, processing speed, reading accuracy and text comprehension in children with dyslexia?

Agost Carreño María (Buenos Aires, Argentina) Carullo María, Intruvini Silvia

OBJECTIVE: 1. To analyze the relationship between IQ (Intelligence Quotient) and PSI (Processing Speed Index) and performance in text reading comprehension in a group of dyslexic children. 2. To explore the relationship between PSI and word reading speed inpatients with dyslexia diagnosis. 3. To establish whether there is a correlation between reading comprehension with the measures of word reading accuracy and fluency in this group of patients.
METHODS: 45 children given a diagnosis of dyslexia participated in the study. The ages were between 7.7 and 15.6 (Average: 9 years) and schooling was between 2nd. grade and junior year of high school. Tests administered were Prolec and WISC-V.
RESULTS: Linear regression analysis were performed. The correlation between IQ, VCI, PSI and reading measures was studied. No statistically significant correlations were found between reading fluency, word decoding and reading comprehension with those cognitive measures.
CONCLUSIONS: The lack of correlation between the PSI and word reading fluency, shows that in this group the difficulties to read quickly and automatically are specific and possibly related to deficits in phonological processing and not due to the overall processing speed. On our sample low reading speed and low reading accuracy scores had no impact on text comprehension. This may be because some dyslexic patients compensate for their deficiencies in automatic reading. The IQ and the VCI were not significantly related to reading comprehension, which is consistent with the characteristic profile of patients with dyslexia that has conserved linguistic and reasoning skills, despite specific reading difficulties.
KEYWORDS: Cognitive/Behavioral Disorders (including Autism)

48. EVALUATION OF SERUM VITAMIN D LEVEL AS RISK FACTOR FOR CHILDREN WITH AUTISM SPECTRUM DISORDER

Kundu Gopen (Dhaka, Bangladesh) Akhter Shaheen

OBJECTIVE: To determine the association between serum vitamin D3 level and autism spectrum disorder (ASD) in children.
METHODS: A comparative cross sectional study was conducted in Institute of Pediatric Neuro-disorder and Autism (IPNA), Bangabandhu Sheikh Mujib Medical University (BSMMU), Dhaka from April 2017 to March 2018. Children aged 3 to 15 years presented in OPD IPNA, BSMMU who were fulfilled the diagnostic criteria of autism (DSM-5) were included in this study as a case (68). Children Age 3 to 15 years who presented to OPD of IPNA, BSMMU, Dhaka with isolated speech delay (34). Then blood sample (2.5 ml) were collected from case and control group with aseptic way to see serum 25 hydroxy vitamin D levels in the Department of Biochemistry, BSMMU. Data analysis was performed by Statistical Package for Social Science (SPSS)
RESULTS: The mean age of ASD patients were 47.6 ±23.7 months and that was 46.6 ±21.4 months in control group. The mean serum vitamin D3 level was 23.8 ±7.8 ng/ml in ASD patients and 26.7 ±9.6 ng/ml in the control group and there were no significant difference in two groups ($p>0.05$). In 73.5% ASD cases serum vitamin D3 level was below the normal level (less than 30 ng/dl) and that was 67.6% in control group.

CONCLUSIONS: The mean serum vitamin D3 level was inadequate in ASD cases than the control group.There was no significant difference between two groups. Therefore, we can conclude that there is no association with serum vitamin D3 level and autism spectrum disorder (ASD) in children.
KEYWORDS: Cognitive/Behavioral Disorders (including Autism)

49. Relationship between maternal history of asthma and autism in their children
Awad Ahmed (New York, NY, United States) Kupferman Fernanda, Springer Carolyn, Soliman Ahmad, Mallik Amara

OBJECTIVE: Autism spectrum disorder (ASD) is a neurodevelopmental disorder of unknown etiology. General consensus supports a multifactorial cause. Conflicting research data suggests role of immune system in ASD. In this study, we aim to clarify the relationship between maternal asthma and ASD in children
METHODS: This is a case-control study of children born at Brookdale Hospital between November 2013 and October 2017 with follow up at Brookdale clinics for 2 years or more. Children 2 years or older were diagnosed with ASD (Y-ASD) either by direct evaluation (n=26) or medical chart reviewed (n=4) by the developmental pediatrician. Children 2 years or older without autism (N-ASD) were matched in a 2:1 ratio based on baby's current age, ethnicity, gender, gestational age, maternal age and birth weight. Maternal history of asthma of all children was obtained from Electronic Medical Record. Data was analyzed statistically with independent samples t-tests and chi-square analyses
RESULTS: There were 30 Y-ASD who matched with 60 N-ASD. Independent samples t-tests for gestational age, current age, birth weight, maternal age and chi-square analyses for gender and ethnicity showed that there was no significant difference between Y-ASD and N-ASD samples on the matching variables (see table 1). There was no statistically significant relationship between ASD status and maternal asthma (86.7% of Y-ASD and 80.0 % of N-ASD respectively had maternal asthma, P=0.436) (see figure 1)
CONCLUSIONS: According to our study, mothers with asthma do not seem to be at increased risk of having children with autism. Further exploration is needed with larger sample sizes
KEYWORDS: Cognitive/Behavioral Disorders, Infections/Neuroimmunology, Neuroscience

50. Comparison of blood heavy metal levels in children with Autism Spectrum Disorder aged 3-12 years with typically developing children and its correlation with quantitative EEG: A cross sectional study
Gulati Sheffali (New Delhi, India) Sharma Shobha, Ahmad Asfa, Samanchi Rupesh, Sharma Ratna, Shrivastava Amita, Qadri Javed, Panda Prateek, Sehgal Rachna, Shariff Ahmadulla, Gupta Yogendra, Pandey Ravindra

OBJECTIVE: To correlate quantitative EEG spectral power of children with autism with serum level of heavy metals.
METHODS: 180 children aged 3-12 years with ASD and 117 age and sex matched typically developing (TD) controls were enrolled between June 2016 and December 2018. One ml blood sample was collected in ultrapure Metal-free EDTA coated collection tubes and subjected to elemental analysis for chromium, manganese, lead, arsenic, zinc, iron, copper, selenium, nickel, cadmium and magnesium levels by Inductively Coupled Plasma Mass Spectroscopy.

Quantitative EEG (qEEG) correlates of neuronal processing were analyzed using neural synchrony and time-frequency analysis, in resting state and using tasks for evaluating executive function.
RESULTS: ASD subjects (153 boys/27 girls, 6.5±1.6 years, CARS-36.59±2.38, DQ-59.94±5.86) had significantly higher level of following metals in blood compared to controls: mercury, chromium, manganese($p=0.01$ for all three) and lead ($p=0.001$) and lower iron levels($p=0.014$).
The spectral power of gamma, beta, lower alpha1, theta and coherence of gamma, lower alpha1 during eyes closed condition was significantly ($p < 0.0005$) lower and the spectral power of theta and coherence of lower alpha 1, theta, delta was significantly lower ($p < 0.0005$) during eyes open condition in ASD compared to TD children. Gamma band had positive correlation with Cr, Zn, Pb and negative correlation with Ni. Beta band had positive correlation with Fe, Se, Ni, Pb and negative correlation with Cu, Mn, As.
CONCLUSIONS: ASD children have different qEEG correlates, as well as, significantly higher blood mercury, chromium, manganese and lead levels as compared to typically developing children.
KEYWORDS: Cognitive/Behavioral Disorders (including Autism)

51. MOVEMENT DISORDER AND EPILEPSY: A NOVEL GENETIC ENTITY: A CASE SERIES

Arora Anshita (Mumbai, India) Patel Vishal, Rathod Nishant, Rastogi Sanchi, Hegde Anaita

OBJECTIVE: GNAO1 encodes α-subunit of heterotrimeric guanine nucleotide-binding proteins(Gαo), which is extremely abundant in the brain tissue and modulate neuronal excitability. Three different phenotypes have been reported so far with GNAO1mutation: Early infantile epileptic encephalopathy (EIEE): severe form, EIEE with involuntary movements (moderate variant) and Development delay and involuntary movements (mild variant). GNAO1 associated movement disorders are usually refractory to medical treatment. Few studies have highlighted role of deep brain stimulation for movement disorder in GNAO1 mutation which can be a promising treatment option in future. Here,we describe 4 newly identified patients with GNAO1 mutations with different phenotypes.
METHODS: We reviewed clinical information, video recordings, and neuroimaging of four patients with GNAO1 mutations, detected by next-generation sequencing with Sanger confirmation.
RESULTS: By Next generation sequencing, we identified four unrelated patients with GNAO1 variants. All patients presented in infancy with wide range of clinical symptoms ranging from milder phenotype, featuring moderate developmental delay with involuntary movement to severe motor and cognitive impairment with choreoathetosis and early infantile epileptic encephalopathy. All four patients had delayed development, seizures were present in two out of four patients. Three patients had choreo-athetoid movements and dystonia. All patients had normal MRI Brain except one with mild cerebral atrophy on follow up.
CONCLUSIONS: Genetic testing for GNAO1 should be considered in all patients with infantile onset epilepsy and movement disorder in varying severity with relatively preserved cognitive milestones, so that parents can be given deep brain stimulation as an option for treating movement disorder and improving functional status of the patient.
KEYWORDS: Cognitive/Behavioral Disorders (including Autism)

52. Do children with ADHD have specific deficit in memory?
Kiselev Sergey (Ekaterinburg, Russian Federation)

OBJECTIVE: It was shown that children with ADHD have cognitive deficit, particularly deficit in memory (Martinussen et al., 2012). In our previous research we have revealed that ADHD children have deficit in visual memory in delayed recall condition in comparison to immediate condition (Kiselev, 2018). The goal of this research was to examine the hypothesis that children with ADHD have deficit in verbal memory in delayed recall condition.
METHODS: The experimental group included 20 children with ADHD at the age of 5-6 years. The control group included 20 typically developing children. The children from groups were matched for IQ, gender and age. Children from both groups were assessed by verbal memory subtest from Luria's neuropsychological battery. This subtest is designed to assess reproducing the 6 words in immediate and delayed recall conditions. ANOVA with repeated measures was used to reveal group differences in reproducing the words in two conditions.
RESULTS: We have not revealed significant differences between children from experimental and control group in reproducing the words in immediate condition. However, the interaction of condition type and group was significant [F(1,38)=4,44; p=0,04)]. Children with ADHD performed worse the reproducing the words in delayed recall condition in comparison to children from control group.
CONCLUSIONS: In view of our previously received results in children with ADHD concerning visual memory, we can propose that deficit in memory in delayed recall condition can be one of the key symptoms in this disorder. It is possible that children with ADHD have specific (not global) deficit in memory.
KEYWORDS: Cognitive/Behavioral Disorders (including Autism)

53. Clinimetric follow-up in a patient with molecular confirmation of CLN2
Arias Mauricio (Armenia, Colombia) Tavera Lina, Espitia Oscar

OBJECTIVE: Clinimetric follow-up in a patient with Neuronal Ceroid Lipofusicinosis2(CLN2) in treatment with Cerliponase alfa
METHODS: Comprehensive clinimetric monitoring of patient with CLN2 is performed with GMCS, MACs, FIM, HAMBURG, CLN2, before and after 4 doses of treatment.
RESULTS: *Gross Motor Function Classification Scale(GMCS)* level IV, with a total score 1st evaluation 47.9 in a P90, IC 45.7-50.1. And in 2nd evaluation, score of 44.4 IC 42.3 -46.4 P75. Manual Ability Classification System(MACs) III corresponds to manipulation of objects with difficulty. In 2nd evaluation level IV; She executes activities with effort and with limited success. *Function Independence Mesure(FIM)*, total 33/126,and in 2nd evaluation 24/126. in 1st CLN2 Clinical scoring System total score of 7/12 and in 2nd evaluation a total of 6/12 and Hamburg Clinical Assesment Scale total score 3/6 and 2nd 1/6.
CONCLUSIONS: We use GMCS because it´s designed to assess the motor function in cerebral palsy(PC), it has in common with lipofuscinosis the involvement CNS, which with treatment the progression should be stopped and thus be able to establish prognosis, similar in PC. In 1st evaluation within P90 at level IV, suggests that it could change its functional level to III, that is greater independence. But in 2nd evaluation, a functional deterioration was found with P75, due to delay 1y at the beginning of treatment. In the other scales there is a significant deterioration.

At the moment it already has 9th doses, so it has a new clinical evaluation pending, to evaluate the response and relevance of continuing with treatment.
KEYWORDS: Cognitive/Behavioral Disorders (including Autism)

54. Mental Health Disorders among Children: Experiences from Bangladesh
Salwa Zeena (Dhaka, Bangladesh) Shilpi Asma, Ahmed Helal, Ahmed Nizam

OBJECTIVE: Mental disorders constitute a major public health problem and contribute to 13% of the global burden of disease. In Bangladesh, it is increasing among children from 13.4% to 22.9%. There is negative attitude towards treatment seeking and usually affected by social stigma in Bangladesh. Square Hospitals Ltd is implementing Child Development Center for effective & child friendly treatment, management and care through multi-disciplinary team. Objective of this study is to improve the mental health services through integrated approaches for increasing awareness and strengthening case management at hospital.
METHODS: We have collected hospital-based data from Nov 2017 to Sep 2019 with a total 1159 cases. Age of the patient ranges up to 16 years and collected from Square Child Development Center, Square Hospitals ltd, Bangladesh. Data analysis was conducted for presenting information.
RESULTS: We have identified 637 (55%) children had mental health disorders, ASD (22.21%), ADHD (10.35%), anxiety disorder (5.61%), ID (4.14%), somatoform disorder (3.28%), Oppositional defiant disorder (2.67%), attachment disorder (2.42%), learning disorder (1.73%) & others (2.59%). There is a negative attitude towards treatment due to social stigma and is yet to get priority in health care services. Limited awareness among population and yet to integrate mental health services in the mainstream of government and private health care facilities.
CONCLUSIONS: The burden of mental disorders among children is high in Bangladesh and it is largely unrecognized. Integrated mental health services are need in all settings for reducing stigma and improving awareness among population.
KEYWORDS: Cognitive/Behavioral Disorders (including Autism), History of Child Neurology, Neurorehabilitation

55. Low-Cost Eye Tracking Biomarker for Psychological Evaluation of Neuropsychiatric Attention Disorders
Shah Alay (Plano, TX, United States)

OBJECTIVE: Neuropsychiatric attention disorders such as ADHD affect 8% of all adolescents and 2% of all adults; however, about 20% of this population is considered misdiagnosed and only 20% receive proper treatment. Attention disorders suffer a prolonged diagnostic process that this research proposes to solve by analyzing eye-movement patterns in response to unique visual stimuli sequences in a broader effort to classify erratic behavioral interactions.
METHODS: The developed tool uses computer vision techniques like eye-tracking and gaze-estimation to accurately assess the neurological and psychological deficiencies of patients. An infrared camera sensor (a) tracks eye movements and (b) analyzes the intent of these movements; in both cases, deep learning is employed to identify abnormal patterns in the patients' data. Dot animations induce patients' saccadic, smooth pursuit, and convergence movements.
RESULTS: The first pattern occurs in ~97% of the patients, showing a lagged movement of the eyes during smooth pursuits indicating difficulty in predicting events in tracking. A second

pattern surfaces in ~98% of the patients, showing that when a second moving object is introduced, patients tend to indecisively deviate their gaze between the objects. The last pattern occurs in ~95% of the trials during the changes of direction of the animation, resulting in rapid horizontal eye tremors.
CONCLUSIONS: The biomarker yields a 95% sensitivity rate and a 99% specificity rate for ADHD detection, proving this tool's capability in understanding human behavior, intent, and actions. More research needs to be done in the use of psychological eye-tracking for understanding Neuropsychiatry and human behavior at large.
KEYWORDS: Cognitive/Behavioral Disorders (including Autism), Translational/Experimental Therapeutics, Neuroscience

56. A Comparative Study of the Visual Field Test and the Quotient Computer Test in Adolescents with Attention Deficit Hyperactivity Disorder (ADHD)
Sehgal Rachel (Maywood, IL, United States) Gable Eileen, Shindollar Joyce, Schnitzler Eugene

OBJECTIVE: ADHD affects up to 10% of American adolescents. The Quotient computer test (QT) provides quantitative measures of hyperactivity, attention span, distractibility, and impulsivity. Visual Field Testing (VFT) aids in the diagnosis of central nervous system disorders that affect the visual pathways, however, there is very little literature in visual field testing in children with ADHD. This pilot study compares VFT and QT tests in 14 participants aged 12 - 20 with suspected ADHD. Specifically, we hypothesized that adolescents with ADHD would be expected to have difficulty maintaining visual fixation for the VFT.
METHODS: Participants with ACTeRS self-report scores suggestive of ADHD were selected to participate in this study based on specific inclusion and exclusion criteria. A Spearman's correlation analysis was conducted on our sample size of 14 participants using bivariate scatter plots between VFT and QT metrics.
RESULTS: The sample demonstrated no significant bivariate correlations in this analysis using 95% confidence intervals. However, there were some correlations that demonstrated trends toward significance. Specifically, there was a moderately positive strong correlation between left eye false negative errors (VFT) and omission errors (QT) (0.49 (-0.06, 0.81)) (Fig. 1). There was also a weak negative correlation between hyperactivity/impulsivity (ACTeRS score) and motion score (QT) (0.15(-0.63,0.42)) (Fig. 2).
CONCLUSIONS: In this pilot study, there was no significant difference in the error profiles between the QT and VFT in adolescents with suspected ADHD. Further investigation is required to understand these correlating trends in the error profile variables between QT and VFT testing.
KEYWORDS: Cognitive/Behavioral Disorders (including Autism)

57. Sleep Dysfunction in Rett Syndrome
Bricker Katelyn (Chapel Hill, NC, United States) Fan Zheng

OBJECTIVE: Rett syndrome (RTT) is an X-linked dominant severe neurodevelopmental disorder mostly affecting females and is usually linked to mutations in the methyl-CpG-binding protein 2 (MeCP2) gene. Hyperventilation, breath-holding spells and sleep disruptions were reported, however scarce objective data are reported in this population.
METHODS: A retrospective review of consecutive 14 diagnostic polysomnograms (PSG) of 9 patients with Rett syndrome in a tertiary care facility over 15 years was conducted. Descriptive

data of sleep architecture, sleep disordered breathing parameters and demographics were analyzed.
RESULTS: Seven of nine patients (77%) have had elevated apnea-hypopnea index (AHI) that fulfills the diagnostic criterial for sleep apnea, ranging from mild to severe. Central apnea is more common than obstructive apnea and is seen mostly in the older patients and in the very young. These patients also have decreased sleep duration, sleep efficiency, and REM sleep.
CONCLUSIONS: Sleep disordered breathing is common in patients with Rett Syndrome. Central apnea can be severe and is common in older patients and the very young. It is unclear if this finding is due to their underlying brain disease (aberrant respiratory control) versus medication effect. Patients with Rett Syndrome have disrupted sleep architecture manifested as decreased sleep duration, poor sleep efficiency, and reduced REM sleep. Sleep disorders screening should be a standard of care for all patients with Rett Syndrome.
KEYWORDS: Cognitive/Behavioral Disorders (including Autism)

58. A Home-based Digital Intervention as Adjunct to Stimulant Medication for Pediatric ADHD: Benefit of Repeated Administration, Stability of Effects and Relation to Academic Performance
Kollins Scott (Durham, NC, United States) Heusser Andrew, Lutz Jacqueline

OBJECTIVE: AKL-T01 is an investigational digital intervention delivered through a videogame interface, designed to improve attention. Previous studies showed that AKL-T01 significantly improved objective measures of attention in children not on ADHD-medication after 1 month. The present study explored the effects of additional treatment in children on or off stimulant medication.
METHODS: 236 children with ADHD (8-14yo) enrolled in the open-label STARS-Adjunct study: 130 on stimulant medication, and 76 off any ADHD medication. Children used AKL-T01 for 1-month (days 0-28), followed by a pause (days 29-56) and then a 2nd treatment month with AKL-T01 (days 57-84). Primary outcomes were within-group changes in the Impairment Rating Scale (IRS) from baseline to day 28. Secondary/exploratory outcomes included changes in the IRS, ADHD-RS and objective attention (TOVA-ACS) at different time points. We also explored how objective attention improvements related to academic performance measures (ToSREC, MFACTS).
RESULTS: In both cohorts, IRS improvements after 1-month were significant (ps <0.001). Changes from baseline to day 56 remained significant and further increased from baseline to day 84 (ps<0.001) (Figure-1). Similar patterns were observed for ADHD-RS. Improvement in objective attention was related to improvements in academic performance measures (Figure-2).
CONCLUSIONS: The findings suggest that improvements in symptoms/impairment remained stable after a treatment pause and further increased with a second month of treatment, independent of medication status. Further, improvements in objective attention were related to improvements in academic performance measures. Within the caveats of an open label trial, AKL-T01 may be a viable treatment option for children on or off ADHD medication.
KEYWORDS: Cognitive/Behavioral Disorders (including Autism), Translational/Experimental Therapeutics

59. Correlations of possible TMS biomarkers of cognitive and emotional dysfunction in ADHD

Zea Vera Alonso (Cincinnati, OH, United States) Horn Paul, Mostofsky Stewart, Gilbert Donald

OBJECTIVE: To determine, in children with ADHD and typically developing (TD) controls, if primary motor cortex (M1) short-interval cortical inhibition (SICI) and task-related up-modulation (TRUM) of motor evoked potentials (MEPs) correlate with each other, suggesting they capture commonly disrupted neurobiological circuits, or do not correlate, consistent with their reflecting distinct circuits. Physiological biomarkers in Attention Deficit/Hyperactivity Disorder (ADHD) might identify relevant subgroups relating to areas of cognitive and emotional dysfunction.
METHODS: A case-control study comparing TMS-evoked SICI and TRUM in 8-12 year-old children with ADHD and TD controls during 1) a stop-signal reaction time (SSRT) task testing cognitive control (n=43 ADHD; 40 TD) and 2) a reward cue task evaluating positive valence (n=33 ADHD; 31 TD). TRUM is the ratio of the mean task (SSRT 80; Reward 105 pulses/trials) to the mean baseline (20 pulses, resting) MEP. The primary outcomes were the age-adjusted Spearman correlations between TRUM and SICI in the two tasks.
RESULTS: Both SSRT and Reward tasks significantly reduced SICI and induced TRUM; both were significantly reduced in ADHD. In the response inhibition task, SICI correlated modestly with TRUM (r=-0.29; p=0.01) for the entire cohort but not within diagnostic groups. In the reward cue task, SICI correlated at trend level with TRUM ($r = -0.21$, $p = 0.09$) for the entire cohort but not within diagnostic groups.
CONCLUSIONS: In children with ADHD, SICI correlates only modestly with TRUM across two important domains of dysfunction. Further investigation could validate SICI and TRUM as distinct biomarkers for precise treatment selection.
KEYWORDS: Cognitive/Behavioral Disorders (including Autism), Neuroscience

60. A continuum of learning and attention difficulties in females, extending from FMR1 premutation to full mutation

Gabis Lidia (Tel Hashomer, Israel) Banet Levy Yonit, David Sivan, Leon Attia Odelia, Shefer Shahar

OBJECTIVE: Carriers of Fragile X premutation may have associated medical comorbidities, such as Fragile X Associated Tremor and Ataxia (FXTAS) and Fragile X Associated Premature Ovarian Failure (FXPOI). Fragile-X premutation effect on cognition is investigated. We assume that there is a continuum of specific learning and attention deficits that correlate with increased number of CGG repeats on FMR1 gene.
METHODS: 98 women were referred to our center due to a related Fragile X Syndrome (FXS) patient, 79 women carried premutation of 56-199 repeats and 19 women carried a full mutation of more than 200 CGG repeats on the FMR1 gene. Genetic results of CGG repeats, demographic information, structured questionnaires for ADHD, learning disabilities of language and mathematics, and independence was analyzed in females carrying FMR1 premutation and compared to the group carrying full mutation. Females with fully symptomatic Fragile X Syndrome, were excluded.
RESULTS: When analyzed as a continuum, there was a significant increase in the following complaints correlated with higher number of repeats:
labor difficulties and CSection FXPOI Not being able to drive a car ADHD severity
Learning disabilities and specifically language difficulties, dyscalculia, nattentiveness, spelling

difficulties Executive dysfunction When observed within the premutation group as compared to full mutation group, we found a linear correlation FXPOI, ADHD, spelling and organization skills. Distractibility correlated inversely with CGG repeats.
CONCLUSIONS: ADHD and learning difficulties correlate with increased number of CGG repeats and are prevalent features of premutation and of full mutation in females.
KEYWORDS: Cognitive/Behavioral Disorders (including Autism), Genetics, Neuroscience

61. Behavioral Abnormalities and Early Media Exposure
Numata-Uematsu Yurika (Sendai, Japan) Sakamoto Masaki, Sato Hiroki, Uematsu Mitsugu, Nara Chieko, Kubota Yuki, Kure Shigeo, Yokoyama Hiroyuki

OBJECTIVE: Many studies have reported many adverse effects of excessive media exposure in children, showing reduced cognitive development, disinhibited behavior and inattention. Although it has been recommended that child be kept away from the media during the early developmental period, modern parents use the media as a way to calm their children. We reported a child case with autism like symptoms that showed dramatic improvement by avoiding media and introducing the parents and the child to physical exercise. We examined whether this method could reduce media exposure period.
METHODS: From April 2017 to December 2018, children under 9 years old who visited our hospital due to suspected developmental disorders were included. At the first visit of the patients, we approached their parents to keep the children out of the media and instructed how to play physical exercise using some illustrations. We surveyed the average media exposure period at first visit of the patients and more than one year after the intervention.
RESULTS: Fifty-five children were included. The average exposure period at first consultation and after the intervention was 2.3 and 0.9 hours, respectively. The children after the intervention were able to sustain a conversation with others.
CONCLUSIONS: It is sometimes difficult for children with developmental disabilities to restrict the media exposure. However, we believe it is important to teach adequate parent-child engagement forming their attachment, and then the method can restrict the media, as a result. Our physical exercise could be effective in forming the attachment of children-parents.
KEYWORDS: Cognitive/Behavioral Disorders (including Autism)

62. The weak link- Hypotonia in infancy and the Autism Spectrum
Gabis Lidia (Tel Hashomer, Israel) Shaham Meirav, Leon-Attia Odelia, Deloya Michal, Halevy Avner

OBJECTIVE: To assess early developmental milestones in a cohort of children diagnosed with autism spectrum disorder in order to find an objective and reliable early marker. We suggest that low muscle tone- hypotonia, is a
sign that meets the above criteria of consistency and reliability.
METHODS: We compared age distributions of ASD diagnosis in the presence of hypotonia in a dataset of 5280 children diagnosed ant Keshet center, 1659 children (1280 males) were diagnosed with ASD and compared to other diagnoses. Within the ASD cohort we further analyzed for gender and prematurity differences.
RESULTS: in the presence of hypotonia the age diagnosis of ASD is significantly lower by 1.5 years (using non parametric as well as parametric statistics), exhibiting p values <<0.05, and this

difference is persistent when for males and females separately, but not significant in prematurity. We analyzed a sub cohort diagnosed below age 12 years, 1373 with ASD, 1100males) and we found the same significance.
CONCLUSIONS: Hypotonia is a recognizable marker of ASD and may serve as an early "red flag" to prompt neurodevelopmental evaluation and autism diagnosis.
KEYWORDS: Cognitive/Behavioral Disorders (including Autism), Neonatal & Fetal Neurology

63. Spatial association of the diagnosis of autistic regression and timing of industrial chemicals emitted to air
Nielsen Charlene (Edmonton, Alberta, Canada) Osornio-Vargas Alvaro, Bryan Sean, Clark Brenda, Zwaigenbaum Lonnie, Goez Helly

OBJECTIVE: Among autism spectrum disorders (ASD), children who demonstrate developmental regression around 24 months of age are diagnosed with autistic regression (AR). An emerging theory in the unknown etiology involves impaired immunity. Emissions of immunotoxicants may be a potential risk factor that has not been explored. Our objective was to determine association between the geographical distribution of industrial chemicals released to the air surrounding homes where children have been diagnosed with ASD and AR.
METHODS: We mapped the residential street addresses from chart reviews of children diagnosed with ASD in Alberta, Canada, 2014-2018. We mapped their potential exposure to industrial chemicals in the outdoor environment by calculating the kernel density of tonnes emitted around all facilities. Annual estimates were available from the National Pollutant Release Inventory (NPRI) database, 2003-2017. We assigned acute (birth and diagnosis years) and chronic (average and cumulative) exposures as tonnes/km^2 of 135 industrial chemicals – 23 of which are suspected immunotoxicants. We correlated the proportion of children diagnosed as AR with acute or chronic chemical exposures.
RESULTS: Three chemicals had correlations with AR ($r >= 0.4$): Diethanolamine (diagnosis year), Hydrogen cyanide (diagnosis year), and Quinoline (birth year and average across years); none are immunotoxcants.
CONCLUSIONS: Our initial results demonstrate that primarily acute exposures to certain industrial chemicals may be associated with AR. Regression analysis continues by comparing ASD (n=946) with the AR (n=143) in regression (covariates on sex and age at diagnosis) to determine if there was more air pollution related to one versus the other.
KEYWORDS: Cognitive/Behavioral Disorders (including Autism)

64. The correlation of EEG abnormalities and core symptoms as well as co-morbidities in children with Attention-Deficit/Hyperactivity disorder
Du Jung Chieh (Taipei, Taiwan) Lee Kun Mei, Lee Min, Chiu Ting Fang

OBJECTIVE: Electroencephalography (EEG) has played certain role in the assessment of neurological function in children with Attention-Deficit/Hyperactivity Disorder (ADHD). Therefore, we investigated the EEG characteristics in children with ADHD and reviewed its utility for predicting prognosis.

METHODS: We've enrolled children diagnosed as ADHD from the pediatric outpatient clinics for EEG study. EEGs were classified as abnormal based on the presence of focal or generalized epileptiform discharges and/or background slowing.
RESULTS: From Jan, 2007 to Dec, 2019, we've enrolled 158 children with ADHD (M/F=126/32, aged 3~15) and 65 (41.1%) revealed paroxysmal abnormality on EEG. Children with abnormal EEG (n=65) were slightly older than those with normal EEG(n=93) (8.0±3.0 v.s. 7.8±2.4 yr, p=0.03). 35 (53.8%) of those with abnormal EEG also diagnosed as tic disorders (TD), and 4 (6.2%) developed epilepsy later. However, less children with normal EEG had TD (n=36, 38.7%) and no one developed epilepsy. Children with abnormal EEG had higher comorbid rate with TD then those with normal EEG (53.8% v.s. 38.7%, p=0.05, OR: 1.85, 95%CI: 0.98-3.57). As to the abnormality on EEG, 56 (86.2%) had focal discharges, with most common foci over central regions (n=28, 43.1%), 10 (15.4%) revealed generalized discharges and 8 (12.3%) showed background slowing. More children with hyperactive-impulsive or combined type had abnormal EEG than those with inattentive type. (47.5% v.s. 29.8%, p=0.01, OR: 2.60, 95% CI: 1.29-5.03).
CONCLUSIONS: ADHD Children with abnormal EEG had higher probability to be comorbid with TD. Their hyperactive-impulsive symptoms also seemed being highly correlated with EEG abnormalities, especially focal discharges over central areas.
KEYWORDS: Cognitive/Behavioral Disorders (including Autism), Movement Disorders (including Cerebral Palsy)

65. Fetal Alcohol Spectrum Disorder – Is it a Ciliopathy?
Urquhart Joshua (Edmonton, Alberta, Canada) Wishart David, Berjanskii Mark, Wincott Leigh, Andrew Gail, Islam Bonnieca, Goez Helly

OBJECTIVE: Fetal Alcohol Spectrum Disorder (FASD) is a term used to describe a constellation of neurodevelopmental and physical presentations resulting from alcohol exposure in utero. The mechanism by which alcohol exposure results in FASD has not been fully illustrated. Currently the diagnosis of FASD requires a multidisciplinary team approach engaging in a process which is time and resource intensive, as there is no laboratory biomarker associated with FASD. We hypothesized that alcohol exposure can lead to dysfunction in the ciliary system, resulting in the abnormalities seen in FASD.
METHODS: 7 healthy children, and 5 children with FASD were recruited for a pilot study. Urine metabolomic analysis was performed to determine if there are unique urine metabolic markers associated with ciliary pathways which would allow for differentiation between children with FASD and healthy controls based on laboratory investigations.
RESULTS: Urine metabolomics revealed 19 different metabolites which were elevated (>1.5 fold) or reduced (<0.77 fold) in the FASD group when compared to the controls. The most prominently increased metabolites based on our univariate analysis, raw p-value were alpha-ketoglutaric acid by 4.26-fold (p = 0.0025), C16-1OH by 2.07-fold (p = 0.0051) LYSOC26-0 by 5.32-fold (p = 0.0092) and acetyl ornithine by 4.16 (p=0.01).
CONCLUSIONS: Several metabolic markers might be associated with ciliary pathways but more specifically mitochondrial energy metabolism which might be altered in children diagnosed with FASD. Larger cohort studies to elucidate these findings are necessary for future development of biomarkers to assist in the diagnosis of FASD.
KEYWORDS: Cognitive/Behavioral Disorders (including Autism)

66. Response to social stimuli in young children with ASD: an fNIRS study
Akinsanmi Danielle (New York, NY, United States) Ahuja Abhilasha, Huberman Harris, Frye Richard, Barbour Randall

OBJECTIVE: There is critical need for research of the developing brain concerning the characteristic alterations in "social brain" functioning that define autism spectrum disorder (ASD). We will use non-invasive, mobile neuroimaging, functional near-infrared spectroscopy (fNIRS), to demonstrate differences in connectivity and cortical activity of children with ASD and typically developing (TD) children in response to social and non-social stimuli. Our hypothesis is that TD and ASD children will exhibit differences in cortical activity to social stimuli but be similar in response to non-social stimuli.
METHODS: The experimental design is a between-group, single time point comparison of 2.5–5 year olds with ASD vs. control (TD). The primary measure will be fNIRS neuroimaging. Secondary measures to characterize the sample will include standard assessments of social function and ASD related behaviors as well as language and cognitive ability. We will use REDCap for data collection/management, general linear mixed models for continuous measures and SPSS for fixed.
RESULTS: Our study will replicate findings in earlier studies of increased connectivity between both prefrontal cortices but reduced network efficiency in ASD. Additionally, both primary and secondary measures will demonstrate reduced response/signaling to social stimuli but similar or enhanced response to non-social stimuli.
CONCLUSIONS: Our study replicates results of previous studies but in a distinct population and age group. Further, it will provide data to advance understanding of brain functioning in ASD and help to establish fNIRS as an outcome measure for future and larger projects. Finally, these results will bring us closer to finding effective early treatments for autism.
KEYWORDS: Cognitive/Behavioral Disorders (including Autism), Neuroimaging

CRITICAL CARE

67. Is Sedation Associated with Reduced Motion during Neonatal MRI Exams?
Wisnowski Jessica (Los Angeles, CA, United States) McKinstry Robert, Juul Sandra, Wu Yvonne

OBJECTIVE: Motion degrades magnetic resonance images (MRI), limiting diagnostic quality. We determined whether sedation was associated with reduced motion in neonates undergoing clinical brain MRI in a multisite, phase III clinical trial.
METHODS: After rewarming, neonates with moderate or severe HIE underwent 3T MRI using harmonized T1-weighted, T2-weighted, and Diffusion Tensor Imaging (DTI) sequences at 17 US tertiary care hospitals (HEAL Trial, NCT 02811263). Use of sedation was determined clinically. Motion was scored qualitatively as none, mild, moderate (may impact interpretation) or severe (obfuscates interpretation). Chi-square was used to determine whether motion differed by sedation use.
RESULTS: 377 neonates (mean gestation 38.7 weeks; 22% severe HIE) underwent MRI at 5.7 (± 2.9) days. 44% received sedation. Frequency of sedation differed by site (range 0 – 81%).

Mild (33% T1; 21% T2; 16% DTI) or moderate (6% T1; 8% T2; 3% DTI) motion was common. Severe motion was rare (<0.5%). T1 motion was less common in neonates with severe HIE than moderate HIE (26% vs. 43%, *p*=0.005) and in those receiving antiepileptic drugs (AEDs; 16% vs. 42%, *p*=0.003). Frequency and severity of motion did not correlate with opioid or benzodiazepine use. Sites that used sedation infrequently (<20% of patients), and sites that sedated often (>50%), both exhibited similar rates of motion (24% vs. 33%, *p=0.29*).
CONCLUSIONS: MRI motion was less common in neonates with severe HIE and those treated with AEDs. Despite wide practice variation, degree of MRI motion was no different in hospitals that do and do not commonly use sedation.
KEYWORDS: Critical Care

68. Prevalence and management of seizures in children with posterior reversible encephalopathy syndrome: single center experience
Galardi Maria (St. Louis, MO, United States) Grant Cori, Orandi Amir, Barton Kevin, Pandey Vivek, White Andrew, Agner Shannon

OBJECTIVE: To determine the prevalence of seizures as a presenting feature of posterior reversible encephalopathy syndrome (PRES) in children and investigate the use of antiepileptic drugs (AEDs) in this population.
METHODS: Probable and confirmed cases of PRES seen from 2000 to 2018 in a tertiary care children's hospital were identified from electronic medical records and retrospectively reviewed.
RESULTS: Forty-one cases of pediatric PRES were included in the study. Median age at presentation was 11.93 years. 65.9% were female. Thirty-eight (92.7%) patients had a primary diagnosis in one of the following categories: solid organ transplant (12), autoimmune disease (10), renal disease (8), hematopoietic stem cell transplant (6), and malignancy (2). Thirty-two patients (78%) had seizures as part of their initial presentation, 10 (24%) of which presented with status epilepticus. Anti-seizure therapy was initiated in 22 (68.8 %) of the patients presenting with seizures. Three patients with seizures that were on AEDs at time of presentation had doses increased. AEDs were administered for less than 1 week in 3 patients, 1-3 months in 8 patients, 3-6 months in 6 patients, and over 6 months in 6 patients. Duration was unclear in 2 cases.
CONCLUSIONS: In this retrospective study of pediatric patients with PRES, the majority had seizures as part of their presentation. Status epilepticus may be more prevalent in pediatric PRES patients than adult patients with PRES.
KEYWORDS: Critical Care, Epilepsy

69. Neonatal resting state functional MRI for disorders of consciousness, brain death, and neuro-prognostication
Boerwinkle Varina (Phoenix, AZ, United States) Sussman Bethany, Bonnell Alexandra, Mirea Lucia

OBJECTIVE: Discriminating between transient verses permanent causes of decreased consciousness is imperative for recognition and treatment of recoverable brain functions after acute brain insult. There are no pediatric resting state fMRI (RS) studies on disorders of conscious or consciousness, with the exception of a case report. We aim to determine if resting state fMRI (RS), acquired in the early acute brain injury period, correlates with level of

consciousness, progression to recovery verses death, and seizure prospectively in neonates after suspected acute brain insult resulting in encephalopathy.
METHODS: RS was acquired prospectively 1-22 days after suspected brain insult in 23 human neonates. RS were analyzed by independant component analysis, which has been shown to detect the resting state networks in adults, and neonates. Networks including the basal ganglia, language, default mode network, Clinical care team exams, test interpretations (including EEG, anatomical MRI, passive-task based fMRI, and RS), diagnoses, and follow up condition/exam were assigned ordinal scores by two blinded study personnel.
RESULTS: Significant association between individual network condition and test/exams were as follows: Basal Ganglia: anatomical MRI, neuro exam, condition at discharge, follow up condition, follow up tone Language: task-fMRI, MR Spectroscopy, condition at discharge Default mode: HIE grade, neurological exam, death, condition at discharge, follow up condition, follow up tone RS-Seizure: anatomical MIR, follow up condition, follow up tone, on-going concern for seizure disorder at follow up
CONCLUSIONS: Individual RS network health is predictive of death, recovery of consciousness, and follow up condition in neonates after acute brain insult.
KEYWORDS: Critical Care, Neonatal & Fetal Neurology, Neuroimaging

70. Quantitative electroencephalography for early detection of elevated intracranial pressure in critically ill children- case series
Sansevere Arnold (Boston, MA, United States) DiBacco Melissa, Pearl Phillip

OBJECTIVE: To describe changes in the quantitative EEG (qEEG) suppression ratio (SR) in patients with increased intracranial pressure (ICP).
METHODS: We retrospectively reviewed a continuous EEG (cEEG) database of patients in the pediatric ICU. Patients from 1 month to 21 years of age that had neuroimaging findings of increased ICP after being placed on cEEG were included. Patients admitted for epilepsy surgery, those that required invasive ICP monitoring or patients with confirmed diffuse cerebral edema or herniation prior to cEEG were excluded. qEEG variables included the time from the first documented change above 0% (T1) on the SR that led to maximum suppression (T2). The time of change was compared to examination, neuroimaging findings and / or time of administration of ICP lowering agents (e.g. 3% normal saline). The time to maximum suppression was described.
RESULTS: 14 patients were included with a median age of 3.08 years (IQR 1.6-8.7). The most common etiology was cardiac arrest with the sole indication for EEG to detect subclinical seizures or assess for epileptiform discharges (Table 1). The median time from identification of cerebral edema on neuroimaging was 6 hours (IQR 1:49 – 40:34) after the first increase in the SR. The median time to maximum suppression was 3:17 hours (IQR 2:20-9:30) (Table 2).
CONCLUSIONS: Acute changes in the SR are seen prior to examination and imaging findings of increased ICP. With further study, this signal can be targeted with ICP lowering measures and agents to prevent morbidity and mortality associated with increased ICP.
KEYWORDS: Critical Care, Epilepsy, Neuroimaging

71. Rapid neurodegeneration in infant due to homozygous NAXE mutation
Wiegand Sarah (Los Angeles, CA, United States) Tamrazi Benita, Ho Eugenia

OBJECTIVE: Neurodegenerative disorders have previously been associated with mutations affecting the reactive oxidase species protection mechanisms. We describe a likely pathogenic gene mutation involving NAD (P)HX epimerase (NAXE) presenting as a progressive rostrocaudal neurodegenerative disease provoked by metabolic stress.
METHODS: An 11 month-old previously healthy, developmentally appropriate female presented with hypotonia and poor feeding in the setting of febrile illness. She had rapidly progressive decompensation over several months with associated quadriparesis, ascending loss of brainstem reflexes, and seizures. Initial brain MRI was normal, but spine MRI showed central gray matter involvement. Spectroscopy had mildly increased lactate and decreased choline peaks. Serial MRIs showed progressive rostrocaudal progression of disease involving grey matter as well as deep and subcortical white matter. Infectious and metabolic evaluations were unrevealing. The patient's sibling died at age 18 months with a similar clinical and neuroimaging course.
RESULTS: Clinical trio-exome sequencing identified a homozygous c.206A>G (p.Asp69Gly) variant of uncertain significance in the NAXE gene. This has not been previously reported in individuals affected with NAXE-associated disease. It occurs at a position that is evolutionarily conserved and multiple in silico algorithms predict that it may be damaging to protein structure and function.
CONCLUSIONS: The NAXE gene encodes an epimerase involved in cellular metabolite repair; pathogenic variants have been associated with progressive encephalopathy with brain edema and/or leukoencephalopathy-1 (PEBEL1). This novel homozygous mutation involving NAXE is likely pathogenic in the setting of two siblings developing a progressive neurodegenerative disease provoked by illness.
KEYWORDS: Critical Care, Genetics, Neurometabolic Disorders

72. Utility of Short-term EEG Monitoring in the Pediatric Intensive Care Unit
Günbey Ceren (Ankara, Turkey) Öncel İbrahim, Kesici Selman, Bayrakçı Benan, Haliloğlu Göknur, Anlar Banu, Yalnızoğlu Dilek

OBJECTIVE: The study aims to explore the underlying etiologies and outcome in children who underwent EEG monitoring at pediatric intensive care unit (PICU).
METHODS: Critically ill children who underwent EEG monitoring (0.5-1 hours) in the PICU at Hacettepe University Children's Hospital between January 2019 and June 2019 were retrospectively studied. Functional outcome was assessed with the modified Rankin Scale (mRS) at final follow up visit.
RESULTS: Thirty-five patients aged 2.2–12 years, median 4.5 years, 24 (68.5%) of them male, were included. The most common underlying condition was encephalitis (10/35, 28.6%) followed by hypoxic/hypercapnic respiratory failure, acute traumatic brain injury, systemic infection/disease, and others. Six patients (17.1%) had preexisting neurological disorders including epilepsy (n=2). Indications for EEG monitoring were altered mental status (n=17), seizures (n=11), and abnormal movements or fluctuations in vital signs (n=7). Normal background activity was observed in 6 patients, one patient had burst-suppression pattern; in the remaining cases EEG background was slow/disorganized in 12 patients, and low-suppressed voltage was noted in 16 patients. Four patients (11.4%) had epileptiform discharges, three (8.5%) had electrographic seizures without clinical signs. The PICU length of stay was 24 (3–60) days; 15 patients (42.8%) had excellent outcome (mRS 0-1).

CONCLUSIONS: Our results suggest that short-term EEG monitoring may detect electrographic seizures and background changes, and may help to guide management of critically ill children with diverse etiologies when continuous EEG is not available.
KEYWORDS: Critical Care, Epilepsy

73. Paroxysmal sympathetic hyperactivity in a child with malignant MCA stroke
Singh Sonali (New Delhi, India) Kamila Gautam, Jain Agam, Jauhari Prashant, Chakrabarty Biswaroop, Gulati Sheffali

OBJECTIVE: Sympathetic system hyperactivity is frequently encountered in critically sick children especially in those with neurological decompensation. A case of tubercular meningitis with malignant middle cerebral artery (MCA) infarct developed unexplained persistent fever. He was ultimately found to have paroxysmal sympathetic hyperactivity.
METHODS: A six-year old boy with tubercular meningitis on antitubercular drugs for two months presented with headache with sudden onset altered sensorium, left hemiparesis and seizures. Serial neuroimaging suggested diagnosis of malignant right MCA infarct. An emergent decompressive craniectomy was performed. Clinical signs of raised ICP became passive however, the child became febrile from post-operative day four. Initially fever was intermittent in nature and was associated with episodic hypertension, tachycardia, tachypnea and localised diaphoresis over face. Investigations to rule out an infectious etiology were sent on multiple occasions. By third postoperative week fever intensified in duration and frequency along with episodes of status dystonicus. In view of an unyielding infectious work up, non-infectious etiology such as autonomic dysfunction was considered. The ongoing clinical problems suggested a heightened sympathetic activity. The child satisfied the PSH assessment measure was diagnosed as moderately severe paroxysmal sympathetic hyperactivity (PSH) syndrome likely due to central nervous system damage.
RESULTS: Child dramatically responded to parenteral fentanyl and propranolol and became afebrile within 48 hours.
CONCLUSIONS: Neurointensivists must be aware of this entity. Other than traumatic brain injury, stroke and encephalitis are important entities predisposing to paroxysmal sympathetic hyperactivity. Early recognition and intervention reduces hospital stay and long term morbidity.
KEYWORDS: Critical Care, Infections/Neuroimmunology

74. EEG Monitoring Duration to Identify Electroencephalographic Seizures in Critically Ill Children
Fung France (Philadelphia, PA, United States) Fan Jiaxin, Vala Lisa, Jacobwitz Marin, Parikh Darshana, Donnelly Maureen, Topjian Alexis, Xiao Rui, Abend Nicholas

OBJECTIVE: Determination of the optimal duration of continuous EEG monitoring (CEEG) for electrographic seizure (ES) identification in critically ill children.
METHODS: We performed a single-center prospective observational cohort study of 719 consecutive critically ill children with acute encephalopathy. We evaluated baseline clinical risk factors (age and prior clinically evident seizures) and time-dependent risk factors observed during CEEG (epileptiform discharges and ictal-interictal continuum patterns) using a multi-state (entry, EEG risk, ES) survival model. For each subgroup, we determined the CEEG duration for which the risk of ES was <5%.

RESULTS: ES occurred in 184 children (26%). Patients achieved <5% risk of ES: (1) after 6 hours if aged >1 year without prior seizures or EEG risk factors; (2) after 1 day if aged <1 year without prior seizures or EEG risk factors; (3) after 1 day if aged >1 year with either prior seizures or EEG risk factors; (4) after 2 days if aged >1 year with prior seizures and EEG risk factors; (5) after 2 days if aged <1 year without prior seizures but with EEG risk factors; and (6) after 2.5 days if aged <1 year with prior seizures irrespective of the presence of EEG risk factors.
CONCLUSIONS: A model derived from two baseline clinical risk factors (age and prior clinically evident seizures) along with time-dependent emergence of EEG risk factors would allow clinicians to implement personalized strategies that optimally target limited CEEG resources. This would enable more widespread use of CEEG-guided management as a potential neuroprotective strategy.
KEYWORDS: Critical Care, Epilepsy

75. Expanding access to continuous-EEG monitoring in neonatal intensive care units using a remote EEG monitoring program
Fitzgerald Mark (Philadelphia, PA, United States) Massey Shavonne, Fung France, Abend Nicholas

OBJECTIVE: Neonatal seizures are common and difficult to identify clinically because most are subclinical and correct identification of the remainder based on semiology is unreliable. Therefore, continuous EEG monitoring (CEEG) is critical for seizure identification in neonates and is recommended as the gold-standard method in American Clinical Neurophysiology Society guidelines. Despite these recommendations, barriers to implementing widespread CEEG exist.
METHODS: In order to expand access to CEEG for at-risk neonates, we established a framework for providing remote CEEG at two regional affiliate hospital NICUs within our care network. We tracked utilization and clinical impact as a quality improvement initiative.
RESULTS: In a 27-month period from June 2017 through September 2019, 76 neonates underwent CEEG between the two network NICUs. Electrographic seizures occurred in about one-quarter of records (18/76; 24%) across CEEG indications (seizure burden assessment: 1/1 (100%) with seizures; unexplained encephalopathy/subclinical seizure screening: 4/10 (40%) with seizures; HIE undergoing therapeutic hypothermia: 10/44 (23%) with seizures; differential diagnosis of movements of concern: 3/21 (14%) with seizures). Care notes indicated that CEEG impacted clinical care in three-quarters of cases (57/76; 75%). CEEG impacted decisions to treat with anti-seizure medications in approximately one-half of patients [impact: 28/57 (49%); no impact 29/57 (51%)], and CEEG impacted prognostic discussions in approximately two-thirds of patients [impact: 39/57 (68%); no impact 18/57 (32%)].
CONCLUSIONS: We demonstrate that establishing a program of remote CEEG is feasible, effective at identifying seizures, and impactful in improving the quality of care provided to neonates hospitalized at these network hospitals.
KEYWORDS: Critical Care, Epilepsy

76. Spinal Cord Compression Secondary to Aneurysmal Bone Cyst in a Pediatric Patient
Dechnik Andzelika (New York, NY, United States) Parikh Karishma, Segal Devorah

OBJECTIVE: A previously healthy 13-year-old female presented to our emergency room with sudden inability to move her legs after collapsing to the floor while getting out of bed. Her

neurological exam was significant for flaccid paralysis in both legs along with absent reflexes and sensation to all modalities below T4. MRI spine revealed severe cord compression at T4 secondary to a fracture of the T4 vertebral body with associated retropulsion of the fracture fragments, presumed to be secondary to an aneurysmal bone cyst at that level (Figures 1 and 2).
METHODS: The patient underwent urgent surgical decompression and resection, and pathology confirmed an aneurysmal bone cyst.
RESULTS: The patient recovered remarkably well with physical therapy. She was able to stand without assistance for 45 seconds was walking independently within 2 months, and was able to ride a bicycle independently one year after her surgery.
CONCLUSIONS: To our knowledge, this is the first report describing spinal cord compression due to an aneurysmal bone cyst in a pediatric patient. Aneurysmal bone cysts are rare osteolytic lesions that are benign but expansive and locally destructive. They are often found in long bones (50-60%) but are present in the spine 20-30% of the time [1]. 34% of spinal lesions are in the lumbar spine, versus 23 % in the thoracic spine [2]. The evidence is equivocal on best management to prevent recurrence, but several studies have found that total excision of the aneurysmal bone cyst is the most important factor in preventing recurrence [3-4].
KEYWORDS: Critical Care, Neuroimaging, Neurorehabilitation

77. Implementation of a quantitative electroencephalography curriculum for seizure detection in the pediatric intensive care unit- A quality improvement initiative
Kielian Agnieszka (Boston, MA, United States) Davila-Williams Daniel, Fialkow Alexandra, Chiujdea Madeline, Sansevere Arnold

OBJECTIVE: To evaluate the effectiveness of a standardized curriculum on the accurate identification of electrographic seizures (ES) amongst child neurology residents and EEG technologists using quantitative EEG (qEEG) in the pediatric intensive care unit (PICU).
METHODS: Child neurology residents and EEG technologists of varying levels of training completed a pre-training survey that included examples of common background patterns, artifacts and seizure patterns using proprietary qEEG software (PERSYST). After completion of the pre-training survey, a 25-minute on-line education module focused on principles of qEEG and pattern recognition was completed followed by a small group training sessions with a pediatric epileptologist. Residents and technologists who completed the video module received a printed reference card with common images and descriptions of EEG trends. A post-training survey was then completed to assess accuracy of seizure and background identification of common patterns in the ICU using quantitative EEG. Utilization of EEG quantitative EEG software was assessed using written audits and with pre-and post-surveys.
RESULTS: Eighty-one percent (17/21) of EEG technologists and 62% (8/13) of child neurology residents completed the pre-test with 90% (19/21) and 38% (5/13) completing the post-test. The average test scores improved by 41% for EEG technologists and 61% for residents. Audit data showed an increased frequency of EEG trend software use by EEG technologists and residents.
CONCLUSIONS: qEEG has the potential to improve seizure identification and subsequent time to treatment. Standardized teaching modules are effective in teaching qEEG patterns.
KEYWORDS: Critical Care, Epilepsy, Neuroscience

78. Establishment and outcomes of a continuous EEG monitoring protocol in ECMO patients in the pediatric ICU at a large tertiary referral center

Herman Isabella (Houston, TX, United States) Erklauer Jennifer, Riviello James, Ontaneda-Perez Andrea

OBJECTIVE: Children in the pediatric ICU are at high risk of neurologic decompensation and cerebral injury, which is challenging to clinically diagnose in the setting of sedative and paralytic use. In particular, children undergoing ECMO therapy often suffer from neurologic complications which are frequently diagnosed after completion of ECMO therapy. cEEG monitoring allows for a real-time insight into cerebral function, providing opportunity to diagnose cerebral injury prior to clinically evident findings. Clinical guidelines have been established to broaden the role of cEEG monitoring in the pediatric ICU, including establishment of a continuous EEG monitoring protocol in all patients undergoing ECMO therapy, which has correlated with the establishment of a dedicated neuro ICU and expansion of available EEG services at our large tertiary referral center. Here, we discuss neurologic outcomes in ECMO patients prior and after the initiation of a dedicated cEEG monitoring protocol.
METHODS: A retrospective chart review was performed on all patients undergoing ECMO therapy between 2017 to 2019 to determine outcomes prior to and after the initiation of an ECMO continuous EEG monitoring protocol.
RESULTS: The initiation of a dedicated cEEG monitoring protocol at TCH has allowed for identification in background patterns over time, allowing diagnosis of cerebral injury prior to being clinically apparent.
CONCLUSIONS: cEEG monitoring is a powerful tool providing real time insight into cerebral function, and is important in cases in which a proper neurological exam cannot be performed. cEEG monitoring in ECMO patients has allowed for identification of cerebral injury prior to clinically apparent signs.
KEYWORDS: Critical Care, Stroke (including other Vascular Disorders, Epilepsy

79. The Management of Vasospasm in Pediatric Arterial Ischemic Stroke

Siddiq Adil Ishita (Toronto, Ontario, Canada) Muthusami Prakash, Guerguerian Anne-Marie, Bhathal Ishvinder, Pulcine Elizabeth, MacGregor Duane, DeVeber Gabrielle, Dlamini Nomazulu

OBJECTIVE: Pediatric treatment approaches to cerebral vasospasm are mostly derived from adult practices in the setting of aneurysmal subarachnoid hemorrhage (aSAH) with the use of calcium channel blockers (CCBs). We report four cases of children with etiologically heterogenous cerebral vasospasm in the context of arterial ischemic stroke (AIS) and discuss management strategies.
METHODS: We reviewed all patients admitted to our hospital's Intensive Care Unit from 2000-2017 with radiographically identified vasospasm and ischemic stroke. Children with hemorrhagic stroke were excluded. Four children met inclusion criteria. Charts, imaging, treatment and outcome was evaluated.
RESULTS: Diagnosis included: 1) left MCA and ACA AIS secondary to desmoplastic infantile astrocytoma 2) left MCA AIS secondary to focal cerebral arteriopathy 3) right basal ganglia and rolandic AIS due to substance abuse and 4) right MCA AIS due to vasculitis. Vasospasm in the MCA +/- ACA or ICA was identified in all 4 children. Treatment with a CCB was considered in all, and received in one patient. Symptomatic and radiologic extension of the ischemic stroke occurred in the patient treated with an oral CCB 24 hours post treatment temporally correlating

with a drop in blood pressure. The remaining children received standard antithrombotic treatment.
CONCLUSIONS: CCBs have vasodilatory properties which can cause systemic hypotension or steal phenomenon theoretically resulting in hypoperfusion of the vulnerable penumbra. We suggest caution in the use of CCB treatment in vasospasm cases not attributed to aSAH due to the lack of clarity regarding risk-benefit ratio.
KEYWORDS: Critical Care, Brain Tumors/Oncology

DEMYELINATING DISORDERS

80. Response to Immunomodulatory Treatment in Pediatric Patients with MOG-Antibody Associated Disease

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OBJECTIVE: Evidence-based guidelines are sparse in pediatric MOG-Ab disease, including type and duration of treatment to prevent relapses. We aim to describe our cohort of children with MOG-Ab disease and characterize responses to first and second-line immunomodulation.
METHODS: Retrospective review was performed on pediatric patients with positive MOG-Ab testing between 11/2017-7/2019. Demographics, clinical characteristics, and immunomodulatory data were extracted from clinical records. Time to first relapse and total annualized relapse rate (ARR) were calculated. For patients treated with second-line immunomodulation (i.e. rituximab, Cellcept) for >3 months, ARR was also calculated pre- and post-initiation. Relapses occurring within 3 months after the initiation of second-line therapy were excluded in the calculation of ARR.
RESULTS: 15 patients with MOG-Ab disease were identified (53% female). Mean age at onset was 6.95 years (range 1.3-14). Clinical phenotype at presentation included ADEM (9/15, 60%), ON (4/15, 27%), and NMOSD (2/15, 13%). 9/15 patients responded fully to first-line immunomodulatory treatment with IV steroids +/- IVIG. Of the 6 non-responders, 5 demonstrated a progressive decline requiring additional steroids +/- IVIG, rituximab, or Cellcept. 10/15 patients relapsed with a mean time to first relapse of 2 years (range 0.25-5) and mean ARR of 0.51 (range 0.16-1.07). In patients maintained >3 months on second-line immunomodulation to control relapsing disease, ARR was reduced by 85% (mean ARR pre-initiation 0.93, post-initiation 0.14).
CONCLUSIONS: Second-line immunomodulatory therapy reduces the ARR of pediatric patients with MOG-Ab disease. Our data suggests that earlier escalation of treatment should be considered in the management of patients with a relapsing disease course.
KEYWORDS: Demyelinating Disorders

81. Clinical, imaging and follow-up study of myelin oligodendrocyte glycoprotein associated demyelination in children: A Multicentric study

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OBJECTIVE: The objective of this study was to characterize the clinico-radiological phenotype of children with myelin oligodendrocyte glycoprotein (MOG-IgG) related demyelination.

METHODS: The records of all children (≤12 years) admitted in the three medical centers with MOG-IgG positive demyelination between Jan 2018 through Feb 2020 were reviewed. MOG-IgG positivity was tested by cell-based-assay using transfected cell lines for in-vitro semiquantitative determination in serum of human IgG antibodies to MOG antigen by indirect immunofluorescence at a titer of 1:10 dilution.
RESULTS: Nine patients tested positive for MOG-IgG antibody (5 females), with a median age of 64 (range= 32 to 120) months. The phenotypes included optic neuritis (5, 55.6%), acute demyelinating encephalomyelitis (2, 22%), isolated longitudinally extensive transverse myelitis (1, 11%), and neuromyelitis optica spectrum disorder (1, 11%). There was no correlation of presenting phenotype with age of child. Relapsing disease occurred in 5 (55.6%) children during a median follow-up of 22months. Neuroimaging revealed brain involvement in 9 (100%) patients with cortical gray/juxtacortical white matter involvement in 4 (44.4%) patients. A total 18 orbits were imaged; in 9/18 orbits optic nerve involvement was identified, with the predominant pattern being involvement of pre-chiasmatic optic nerve (9 eyes). The spinal cord lesions were identified in 3 patients (two short segments).
CONCLUSIONS: Our findings suggest that MOG-IgG associated childhood demyelination most frequently presents with optic neuritis phenotype. WM lesions in brain are most often located in cortical gray/juxtacortical white matter and optic nerve involvement is most frequently pre-chiasmatic. Spinal MRI could be of interest in detecting silent suggestive lesions.
KEYWORDS: Demyelinating Disorders

82. Increased Likelihood of Relapse in Pediatric Anti-MOG Acute Disseminated Encephalomyelitis (ADEM) and Optic Neuritis (ON) vs. Seronegative ADEM and ON Patients

Fisher Kristen (Houston, TX, United States) Balasa Alfred, Shukla Nikita, Lotze Timothy

OBJECTIVE: To determine correlation between MOG antibody status and symptom recurrence within three months of presentation. We present 22 patients who presented to Texas Children's Hospital January 2018 - September 2019 diagnosed with ADEM and/or ON, characterizing presentation, presence of ant-MOG antibodies, and relapse rates.
METHODS: Retrospective chart review of patients diagnosed with ADEM and/or ON and tested for MOG antibodies. Charts reviewed for evidence of new MRI lesions or new symptoms.
RESULTS: 22 patients were identified with a mean age of 8.0 years. 16 patients (72.7%) were found to be antibody positive. At presentation, 17 patients were diagnosed with ADEM (12 MOG Ab positive), 3 with ON (2 MOG Ab positive), and 2 with ADEM and ON (both MOG Ab positive). 5 patients developed recurring attacks, with new symptoms and MRI findings of new lesion with contrast enhancement. Of these, all were positive for anti-MOG antibody, with an overall rate in the anti-MOG antibody population of 31.2%. 4 of these had new symptomatology within 3 months from presentation. All patients with recurrent attacks had an initial diagnosis of ADEM, with subsequent events including ADEM, ADEM and ON, and solely ON. Additionally, 3 patients have had more than one subsequent attack.
CONCLUSIONS: Higher rates of relapse were seen in anti-MOG ADEM and ON in comparison to those who are seronegative. It was also found these patients are at increased risk of recurrent attacks less than 3 months from presentation, which is varying from the current classification of multiphasic ADEM.
KEYWORDS: Demyelinating Disorders, Infections/Neuroimmunology

83. MOG Antibody Associated Demyelination in Children - A Single-Site UK Tertiary Paediatric Experience

Sharma Richa (Lancashire, United Kingdom) Ram Dipak, West Siobhan, Pavaine Julija

OBJECTIVE: Myelin Oligodendrocyte Glycoprotein Antibody (MOG-Ab) positivity has been widely identified in Acquired Demyelinating Syndromes (ADS) such as Acute Disseminating Encephalomyelitis (ADEM), Optic Neuritis (ON), and Longitudinally Extensive Transverse Myelitis (LETM). We aim to determine the range of radiological patterns in comparison with distinctive imaging features in published cohorts.
METHODS: We present a cohort of 11 patients with MOG-Ab associated demyelination from Royal Manchester Children's Hospital. MR brain, spine and orbits were obtained based on the presentation. Imaging findings were assessed by neuroradiologists in correlation with the clinical history. The course of disease was classified as either monophasic, prolonged monophasic (radiological progression within first month of presentation), or relapsing.
RESULTS: The age range at the first presentation was 3-13 years with a M:F ratio of 6:5. Seven patients presented with monophasic disease, two with prolonged monophasic, and two with relapsing courses with at least two distinct episodes. Although we found imaging similarities with comparison cohorts, there were also some unique features. Two of our patients presented with cerebellitis. One relapsed further with a patchy "lace-like" enhancement pattern and cortical enhancement. In the other child, cerebellitis was accompanied by significant cerebellar oedema with resultant supratentorial hydrocephalus. To our knowledge, these findings of cerebellitis have not specifically been reported in literature before.
CONCLUSIONS: Our study demonstrates the wide range of neuroimaging patterns in paediatric MOG-Ab positive ADS, mostly in concordance with comparison cohorts. Cerebellitis has not been specifically mentioned in published cohorts, and is presumably a new imaging pattern in MOG-Ab associated demyelination.
KEYWORDS: Demyelinating Disorders, Rare Diseases

84. Balo's concentric sclerosis mimicking acute stroke in an adolescent

Huff Hanalise (Boston, MA, United States) Stredny Coral, Rivkin Michael, Jaimes Camilo, Gorman Mark

OBJECTIVE: To describe a case which highlights the similarity in initial presentation and MRI of Balo's concentric sclerosis (BCS) to acute ischemic stroke.
METHODS: Case report
RESULTS: A 16-year-old girl presented with hyperacute slurred speech, right hemiparesis, and right arm numbness with last known well four hours prior. Stroke stat was called and MRI/MRA showed a focal area of reduced diffusivity and T2 hyperintensity involving the left frontal centrum semiovale and corona radiata interpreted by neuroradiology as consistent with an acute ischemic infarct. Symptoms improved, but then worsened over several days prompting serial MRIs which showed rapidly evolving findings, leading to an expanded diagnostic workup. PET showed low-level fluorodeoxyglucose uptake and crossed cerebellar diaschisis, felt to be most consistent with an inflammatory lesion interrupting the adjacent white matter tracts. CSF revealed elevated IgG index of 0.80 (normal 0.28-0.66) and six CSF-restricted oligoclonal bands. She was treated with methylprednisolone 1000mg IV daily for 5 days and plasma exchange.

MRI on hospital day 19 showed concentric rings of alternating facilitated and restricted diffusion in the lesion consistent with BCS. She was then treated with two doses each of rituximab 1000mg and cyclophosphamide 750mg. At most recent follow up three months after presentation, right hemiparesis had resolved and the lesion was smaller on MRI.
CONCLUSIONS: BCS can present with acute onset focal weakness and MRI findings that mimic stroke. Serial MRIs may show evolution and lesion patterns ultimately diagnostic of BCS that requires dramatically different treatment modalities.
KEYWORDS: Demyelinating Disorders, Neuroimaging, Infections/Neuroimmunology

85. Acquired Childhood CNS Demyelination associated with Anti-MOG Antibody: A Retrospective Cohort
Gupta Juhi (New Delhi, India) Badal Sachendra, Jauhari Prashant, Chakrabarty Biswaroop, Gulati Sheffali

OBJECTIVE: We aimed to review the spectrum of anti-MOG (Myelin Oligodendrocyte Glycoprotein) IgG antibody associated acquired demyelination in children.
METHODS: Case records of all children presenting with CNS demyelination were reviewed from December 2018 to January 2020 and those positive for anti-MOG antibody were included.
RESULTS: Thirty children presented with CNS demyelination out of which ten children (mean age 10.5 years,7 males) were positive for anti-MOG antibody. Clinical presentation during the first episode of demyelination was optic neuritis in 7 cases (unilateral in 2, bilateral in 5) and acute disseminated encephalomyelitis (ADEM), longitudinally extensive transverse myelitis (LETM) and diplopia with hypersomnolence in one case each. All children except one (treated outside with oral steroids) were given steroid pulse (dexamethasone/methylprednisolone). MRI revealed contrast enhancement in anterior portion of optic nerves in all (Image). The child presenting with ADEM had 3 episodes of demyelination over 14 years (ADEM at 3, LETM at 5 and optic neuritis at 16 years age) with complete recovery in all episodes. The case presenting with LETM developed bilateral optic neuritis 3 months later and had complete recovery in both episodes. Another child presented with headache, convergent squint, diplopia and hypersomnolence with T2/FLAIR hyperintensities in dorsal pons and had complete recovery at 3 months follow-up. Majority cases (10/16 eyes,62.5%) of optic neuritis were able to achieve best corrected visual acuity of at least 6/9 at 3 months follow-up.
CONCLUSIONS: Children with Anti-MOG antibody positive demyelination have varied presentations, majority have anterior optic nerve involvement and show remarkable response to steroids.
KEYWORDS: Demyelinating Disorders, Neuroimaging

86. Updates to CANinform – A Multi-Center, Multi-National Retrospective and Prospective Natural History Study of Canavan Disease
Eichler Florian (Boston, MA, United States) Lau Heather, Bley Annette, Kirby Kathleen, Laforet Genevieve, Shaywitz Adam, Balser John

OBJECTIVE: Canavan Disease (CD) is a rare, autosomal recessive, leukodystrophy caused by aspartoacylase deficiency, leading to brain accumulation of its substrate N-acetylaspartic acid (NAA) and severe impairment of psychomotor development beginning in the earliest months of life. There is a paucity of longitudinally collected data from CD patients and no approved

therapies for CD exist. Therefore, the objective of the CAN*inform* study is to rigorously collect data from patients with CD, define endpoints for future interventional trials, and identify current gaps in disease understanding and management across ranges of ages and disease severity.
METHODS: This study represents a multi-center effort to identify and enroll CD patients for prospective, longitudinal collection of data using a battery of standardized developmental instruments and intervals and for retrospective collection of medical record data as well. Additionally, a CD-specific scale has been developed and is being used. Laboratory assessment of blood and urine will help further characterize known aspects of the disease and may identify additional aspects of the disease not yet reported.
RESULTS: CAN*inform* is actively enrolling participants. To date, twenty-three families have signed up for record retrieval; 8 have signed consent and initiated assessments. Retrospective data extraction and prospective data collection are on going. Enrollment status, demographics, and early insights into neurologic and non-neurologic impacts of CD will be presented.
CONCLUSIONS: CAN*inform*, the natural history study of CD is expected to continue for 3 years. The natural history database will be made available for meaningful research towards the treatment of patients with Canavan disease.
KEYWORDS: Demyelinating Disorders, Rare Diseases, Genetics

87. MOG antibodies associated CNS disease
Hundallah Khalid (Riyadh, Saudi Arabia)

OBJECTIVE: MOG antibody associated CNS disease is an autoimmune diseases of the central nervous system associated with a serological antibodies against Myelin Oligodendrocyte Glycoprotein. It is a relatively new disorder and the full clinical spectrum is not fully described yet. our aim is to investigate the clinical characteristics of pediatric MOG antibody associated CNS disease.
METHODS: We conducted a retrospective review of children presenting with MOG antibody positive neurological illness. Case records of patients following up in the pediatric neurology clinics in a tertiary care center in Saudi Arabia, from January 2014 to December 2019 were reviewed for MOG antibody positivity and those patients with positive antibody result were included in this study.
RESULTS: 9 patients were found to be positive for MOG antibody. Median age was 10.6 years. 77% were females. Clinical presentations included a combination of optic neuritis, transverse myelitis and acute disseminated encephalomyelitis (optic neuritis 66%, transverse myelitis 22% and acute disseminated encephalomyelitis 11%) Clinical relapses occurred in 4 of 9 children (44%) who remained persistently seropositive. All these 4 patients had good was started on long-term immunomodulatory therapy and had a good outcome.
CONCLUSIONS: MOG antibody associated CNS disease presents predominantly as optic neuritis, transverse myelitis and acute disseminated encephalomyelitis. Many of the patients had relapses, but had good outcomes with long-term immunomodulatory therapy
KEYWORDS: Demyelinating Disorders

88. Visual Outcome in Pediatric Optic Neuritis Cohort from a Tertiary Care Centre in India
Gupta Juhi (New Delhi, India) Badal Sachendra, Sinha Rahul, Jauhari Prashant, Chakrabarty Biswaroop, Kumar Atin, Jana Manisha, Gulati Sheffali

OBJECTIVE: Demyelinating optic neuropathy is a treatable cause of vision loss and early treatment leads to better outcome as shown in adults (1). We aimed to correlate visual outcome with time to treatment in children.
METHODS: Records of all children (<18 years age) presenting to us with demyelinating optic neuropathy from January 2018 to January 2020 were reviewed. Best corrected visual acuity at 3 months (BCVA3m) was correlated with time to therapy (Intravenous Methylprednisolone/Dexamethasone pulse) in days.
RESULTS: Twenty-five children (41 eyes) (mean age 9.5 ± 3 years, 15 males) were included. Nine children were positive for Anti-MOG (Myelin oligodendrocyte glycoprotein) IgG antibody and one for Anti-aquaporin-4 (NMO) IgG antibody. Eight (33.34%) children had fever at presentation and 10 (41.67%) children had painful vision loss. Fourteen children (56%) had T2/FLAIR lesions in brain [8(32%) white matter, 3(12%) grey matter, 1(4%) cerebellum and 2 (8%) white matter, grey matter and brainstem together]. Eight children (32%) had spinal lesions (6(24%) longitudinally extensive transverse myelitis). Seven (28%) patients had elevated cells/protein in CSF suggestive of inflammation. Fourteen children (24 eyes) (58.5%) presented within 7 days of vision loss and were treated with methylprednisolone/dexamethasone pulse. Odds ratio of gaining 20/20 BCVA3m for children treated within 7 days was 7.14 (95% CI 1.68-30.27, p = 0.008) compared to treatment after 7 days (Addendum 1). Four children (2 MOG positive) had recurrence.
CONCLUSIONS: Initiation of steroid pulse within 7 days of vision loss is associated with better visual outcome in childhood optic neuritis which should be managed as an ophthalmological emergency.
KEYWORDS: Demyelinating Disorders

89. Pediatric acquired demyelinating syndromes in 176 patients: a retrospective study in a tertiary center, southern Taiwan
Chang Ying-Chao (Kaohsiung, Taiwan) Huang Chao-Ching, Hsu Mei-Hsin, Hung Pi-Lien

OBJECTIVE: To analyze the range of demographic, clinical, MRI, and CSF features of pediatric acquired demyelinating syndromes (ADS) and analyze long-term outcomes as well as competing diagnoses.
METHODS: We identified ADS diagnostic groups using International Classification of Diseases (ICD) codes 9 and 10 and reviewed medical records to validate the diagnoses during 2000-2019.
RESULTS: A total of 1420 patients younger than 20 years old were diagnosed with one of the following disease: acute disseminated encephalomyelitis (ADEM), chronic inflammatory demyelinating disease (CIDP), encephalitis/encephalopathy (EN), chronic inflammatory demyelinating disease (AIDP), multiple sclerosis (MS), neuromyelitis optica spectrum disorder (NMOsd), optic neuritis (ON), transverse myelitis (TM). After reviewing the medical record and excluding those patients with EN but with normal or unavailable neuroimages, 176 patients had a validated initial ADS diagnosis: ADEM (n=86, F/M= 34/51, age of onset=7.5±4.1), CIDP (n=2, F=2, 10 ±7.1 yr), AIDP (n=37, F/M=10/27, 10.2 ±6.1 yr), MS (n=9, F/M = 6/3, 16.1 ±4.9 yr), ON (n=31, F/M= 13/18, 10.7±4.8) and TM (n=11, F/M= 7/4, 10.1±6.0 yr). In patients with initial diagnosis of ADEM, 33 had other diagnoses concluded in follow-up (total follow up rate: 84.9%, duration: 8.2 ±6.2 yr), including acute necrotizing encephalitis (n=7), MS (n=6), neurometabolic

disorders (n=6), NMOsd (n=3), anti-NMDA-receptor encephalitis (n=3), febrile infection-related epilepsy syndrome (n=6), vasculitis (n=1) and neurocysticercosis (n=1).
CONCLUSIONS: Among pediatric ADS, ADEM had the highest prevalence rate and youngest age of onset. However, long-term follow-up and vigilance for other, mostly rare, diseases in ADEM is imperative.
KEYWORDS: Demyelinating Disorders, Infections/Neuroimmunology

90. No One Really Plans to Have MS: Transition Readiness and Quality of Life in Pediatric MS

Veras Julissa (New Brunswick, NJ, United States) Thoby Estherline, Nallapati Spandana, Jimenez Manuel, Bhise Vikram

OBJECTIVE: Pediatric multiple sclerosis (MS) is a progressive demyelinating disease of the central nervous system. Due to increasing incidence, there has been growing interest in its effects on the quality of life of children. We sought to understand the experiences and perceptions of quality of life in pediatric MS patients as they transition into adulthood.
METHODS: We conducted in-depth semi-structured interviews to understand patients' experiences with MS. We sampled pediatric onset MS patients between the ages of 15-26 from a pediatric subspecialty practice. We recruited participants until reaching thematic saturation after 17 interviews. We identified themes using immersion/crystallization.
RESULTS: We identified four major themes: (1) Patients needed time to accept their diagnosis and adjust to a life with MS. (2) Quality of life was most impacted by physical symptoms affecting participants' activities of daily living. (3) A positive outlook and resilient attitude provided a sense of control that enhanced participants' perceived quality of life. (4) Barriers to disease management and transition readiness included lack of knowledge of available social services, limited self-management, and delay in transition.
CONCLUSIONS: Pediatric patients with MS provided insight into quality of life and transition challenges they encounter as a result of this progressive disease. Autonomy in disease management, adequate control of physical symptoms and sufficient support impacted perceptions of quality of life. A dedicated transition visit including the patient and parents should be incorporated early in adolescence to provide appropriate anticipatory guidance regarding available services, independent medical management, and continuity of care.
KEYWORDS: Demyelinating Disorders

91. HOSPITAL BASED FUNCTIONAL OUTCOME OF ACUTE DISSEMINATED ENCEPHALOMYELITIS IN CHILDREN

Rehman Muhammad (Lahore, Pakistan) Sultan Tipu, Ali Shaila

OBJECTIVE: To determine functional outcome of acute disseminated encephalomyelitis in children and factors affecting outcome at The Children's Hospital Lahore, Pakistan.
METHODS: 15 Patients with acute disseminated encephalomyelitis (ADEM) fulfilling the inclusion criteria were enrolled during the study period of November 2016 to October 2018. Detailed history, examination, prior febrile illness and modified Rankin scale (mRS) score for functional disability at presentation and discharge were recorded through study proforma. All patients underwent lumber puncture and neuroimaging. Data was analysed in spss(v.20) and chi square test was applied to find p value.

RESULTS: Out of 15 patients, there was male predominance (10 male 66.7%) with mean age 7.4±2.5. Encephalopathy (100%) followed by fever, fits (73.3%), and motor deficit(60%) were common presentation. 46.7% cases had prior febrile illness. MRI brain had >5 lesions in 86.7% with sub-cortical area (93.3%), periventricular area (86.7%). Functional outcome was good in 80% (mRS score of 2 or less at time of discharge). Consciousness level and disability score at presentation were statistically significant factors affecting the outcome (p value (0.004 &0.002 respectively).
CONCLUSIONS: Acute disseminated encephalomyelitis in children had variable clinical presentation with encephalopathy as the hall mark. Neuroimaging showed disseminated lesions involving subcortical and periventricular areas. It has good outcome with level of consciousness and disability score as being significant factors affecting outcome.
KEYWORDS: Demyelinating Disorders

92. Spectrum of Acquired White Matter Disorders in Children and their Outcomes
Saini Arushi (Chandigarh, India) Chauhan Vikas, Sankhyan Naveen, Vyas Sameer, Singh Paramjit, Muralidharan Jayashree, Saini Lokesh, Suthat Renu, Sahu Jitendra

OBJECTIVE: We studied the clinical presentation, radiological features, comorbidities and outcomes in children children aged between 1 month and 14 years with acquired white matter disorders
METHODS: All consecutive children from 1 month to 14 years of age with a diagnosis of acquired white matter disorder were prospectively enrolled, between January 2018 and December 2019, with Gross Motor Function Classification System (GMFCS) and Expanded Disability Status Scale (EDSS) assessed outcomes.
RESULTS: Amongst n=139 children enrolled, sub-classification was acquired demyelinating encephalomyelitis (ADEM) (24.5%, n=34), acute encephalopathy with diffusion restriction (AESD) (7.2%, n=10), acute necrotizing encephalopathy (ANEC) (12.9%, n=18), congenital CMV (18.7%, n=26), subacute sclerosing panencephalitis (15.8%, n=22), posterior reversible encephalopathy syndrome (PRES) (2.8%, n=4) and unclassified (17.9%, n=25). In ADEM subgroup, mean age of presentation 5.2 ± 3.17 years, with multifocal deficits and bilateral white-matter changes (100%). Most (92.3%) had complete recovery, mean EDSS was 1.4. Similar mean EDSS for AESD and ANE were 1.8 and 4.7 respectively. However, higher EDSS was noted for children with congenital CMV (4.97) with median GMFCS level IV, and children with SSPE in follow-up (3 patients died, mean GMFCS level 5, mean EDSS 9.5) suggesting severe confinement of activities and poor functional outcomes.
CONCLUSIONS: Demyelinating disorders with good functional outcomes (ADEM and AESD) are major causes of acquired white matter disorders in children. CNS infections contribute significantly in developing countries and fare poorly in functional outcomes. ANEC exceptionally has poor outcomes in the demyelinating group.
KEYWORDS: Demyelinating Disorders, Neuroimaging, Infections/Neuroimmunology

93. Pediatric CLIPPER: Does this entity exist
Patel Vishal (Mumbai, India) Agrawal Radhika, Arora Anshita, Rathod Nishant, Hegde Anaita

OBJECTIVE: Chronic Lymphocytic inflammation with pontine perivascular enhancement responsive to steroids (CLIPPERS) is rare central nervous system inflammatory disorder . *It*

is distinct form of brainstem encephalitis responsive to immunosuppression with Glucocorticosteroids. We present case of 13 year old boy who presented as relapsing multiphasic demyelinating encephalomyelitis was initially diagnosed as CLIPPERS after extensive workup. Final Diagnosis of Familial Hemophagocytosis Lymphohistiocytosis (FHLH) was made after 6 years when child finally presented with systemic manifestation .Genetic etiology confirmed by Next Generation sequencing(NGS)
METHODS: We reviewed clinical information, neuroimaging of our patient diagnosed as FHLH, detected by NGS and compared it with recent review of literature of other four cases of Pediatric CLIPPERS who were subsequently identified as F-HLH.
RESULTS: We present 13 year old boy with intermittent episodes of ataxia and diplopia commencing at 6.5 years. Extensive workup over several years including that for HLH was negative. Clinical, radiological and brain biopsy confirmed diagnosis of CLIPPERS.He was dependent on steroids & immune modulators. Twist to the tale was seen when he presented with clinical, hematological and confirmation of HLH -2004 criteria associated with secondary CMV infection. Genetic testing identified compound heterozygous pathogenic mutations in PRF1 gene causative of FHLH-2 with Sanger & parent confirmation.
CONCLUSIONS: Pediatric CLIPPERS is rare neuroinflammatory disorder. It is predominantly an adult neuro, radiological, histopathological entity. Review of the 4 pediatric cases shows evolution into familial HLH over time. We propose that in cases of Pediatric CLIPPERS even in absence of classical HLH markers, isolated CNS familial HLH should be considered.
KEYWORDS: Demyelinating Disorders

94. Anti-myelin oligodendrocyte glycoprotein antibody in hereditary citrullinemia
Inci Asli (Ankara, Turkey) Oncel Ibrahim, Arslan Nur, Altunbasak Sakir, Karaca Meryem, Kor Deniz, Unal Ozlem, Tumer Leyla, Gucuyener Kivilcim, Anlar Banu

OBJECTIVE: Citrullination is a post-translational modification altering antigenic properties of proteins. Anti-cyclic citrullinated peptide is an antigen for synovial T and B lymphocytes in rheumatoid arthritis, and citrullinated myelin basic protein elicits stronger T lymphocyte responses in patients with multiple sclerosis. A hereditary citrullinemia (HCitr) patient was reported with increasing titers of serum anti-myelin oligodendrocyte glycoprotein (MOG) antibody (Di Pauli et al 2011).These suggest citrullinated epitopes of myelin can elicit anti-MOG antibody response. We tested patients with HCitr, a urea-cycle disorder characterized by high blood citrulline levels, for anti-MOG.
METHODS: Serum samples from HCitr (n=15, median age 90 months) and, as control group, phenylketonuria (n=15, median age 123 months) patients were analyzed for MOG-IgG levels by a live cell-based assay using HeLa cells transfected with plasmids expressing EGFP or MOG-EGFP. Meanfluorescence intensity (MFI) was counted in the Alexa Fluor 647 channel. DeltaMFI=MFI(hMOG)-MFI(EGFP only) was calculated, andcut-off for DeltaMFI, determined as 547 using mean DeltaMFI of 30 healthycontrols+5SDs.
RESULTS: All patients were negative for anti-MOG antibody. DeltaMFI was <300 in all healthy control and phenylketonuria cases and >2000 in positive control cases while three HCitr patient had DeltaMFI>300.
CONCLUSIONS: Although our results did not support the hypothesis of high citrulline levels enhancing the antigenicity of MOG in HCitr, the young age of our patients and the report of anti-MOG increasing in time suggest follow-up of HCitr cases for anti-MOGserology.

KEYWORDS: Demyelinating Disorders

95. A 9-year-old child with subacute parkinsonism and oral apraxia

Rossi Gian (Memphis, TN, United States) Rivas-Coppola Marianna, Shah Namrata

OBJECTIVE: Though several autoantibody-mediated movement disorders have been described in adults, apart from N-methyl-D-aspartate receptor (NMDAR) antibodies, these entities are rarely seen in children. We describe a child who developed progressive parkinsonism and oral apraxia with minimal encephalopathy over one month leading to hospitalization. The clinical scenario could suggest a neurometabolic crisis, however, he was eventually diagnosed with myelin oligodendrocyte glycoprotein (MOG) antibody disease and fully recovered with immunotherapy.
METHODS: We detail our patient's history, clinical presentation, diagnostic work-up, and response to treatment. A literature review of MOG antibody disease presenting as a movement disorder is provided.
RESULTS: A 9-year-old boy, the offspring of consanguineous Middle Eastern parents, presented with progressive speech difficulty with loss of motor control over one month immediately following a febrile illness. Neurological examination revealed severe bradykinesia with cogwheel rigidity. He could not voluntarily open his mouth to command but was able to yawn spontaneously. He communicated primarily with eye blinks and eye gaze toward picture cards. Magnetic resonance imaging illustrated T2-weighted fluid-attenuated inversion recovery hyperintense signal involving the bilateral deep gray nuclei, hypothalamus, periaqueductal gray matter, subinsular region and medulla, without contrast enhancement. Biotin and thiamine supplementation and high dose intravenous steroids were started while awaiting SLC19A3 gene analysis (biotin-thiamine-responsive basal ganglia disease) and autoantibody titers, respectively. Investigations were negative apart from MOG antibody positivity.
CONCLUSIONS: MOG antibody disease can present with a subacute profound movement disorder with minimal encephalopathy. Neuroimaging and MOG antibody testing are keys to the diagnosis.
KEYWORDS: Demyelinating Disorders, Movement Disorders (including Cerebral Palsy), Neuroimaging

96. Two cases of anti-Myelin Oligodendrocyte Glycoprotein (MOG) antibody disease with atypical presentations

Rashid Khan Tuba (Dallas, TX, United States) Wang Cynthia

OBJECTIVE: MOG positivity has been primarily associated with ADEM, optic neuritis, and transverse myelitis, and less commonly with aseptic meningitis and seizures. We report two children with novel clinical syndromes for anti-MOG disease: severe dystonia and Guillain-Barre-like syndrome, respectively.
METHODS: Case presentation of two children with anti-MOG associated disease and their clinical course, laboratory and neuroimaging features.
RESULTS: Case 1: A 3-year-old boy presented with new onset seizure preceded by malaise and fever. MRI showed multifocal brain and spinal cord lesions, most prominently in bilateral insula and putamen (image 1). He developed severe orofacial and limb dystonia. He received high dose steroids, plasma exchange and IVIG. Dystonia was treated with diazepam, baclofen, and

botulinum injections. Serum MOG antibody titer was 1:1000. His abnormal movements improved over several weeks and he required intensive inpatient rehabilitation but was able to return largely to baseline. Case 2: A 3-year-old previously healthy boy presented with leg weakness, pain, and constipation in setting of febrile illness. He had flaccid, areflexic weakness of both legs. MRI showed longitudinally-extensive cord edema and enhancement of the ventral cauda equina and dorsal/ventral conus medullaris (image 2). CSF showed 19 nucleated cells/mm3 and 140 mg/dL protein. He received high dose IV steroids and plasma exchange. Serum anti-MOG antibody was 1:1000. He received inpatient rehabilitation and was able to walk independently after 2 months.
CONCLUSIONS: We report two atypical presentations of MOG antibody related disease in very young pediatric patients. Their unique symptoms highlight the heterogeneity of phenotypes associated with anti-MOG disease.
KEYWORDS: Demyelinating Disorders, Infections/Neuroimmunology

97. Primary Infection Triggering Myelin Oligodendrocyte Glycoprotein (MOG) Encephalomyelitis
Ahsan Nusrat (Los Angeles, CA, United States) Santoro Jonathan

OBJECTIVE: We present three patients, who initially presented with infectious encephalitis and were subsequently found to have MOG encephalomyelitis with recurrence of symptoms.
METHODS: Case 1: A 3-year-old, immunocompetent male, with HHV-6 encephalitis, presenting with anorexia, altered mental status, and seizures. His MRI brain demonstrated extensive T2 signal in the cortex, subcortical white matter, and thalamus. He was treated with 21 days of ganciclovir, foscarnet and 5 days of IVIg. Three months later he presented with new diplopia, disconjugate gaze, leg weakness, and a new enhancing pontine lesion, requiring IV methylprednisolone (IVMP). MOG antibody testing showed a titer of 1:100. Patient was continued on monthly IVIg without further recurrences. Case 2: A 9-year-old male was admitted with fever, AMS, seizures found to be related to Coxsackie B5 meningoencephalitis. As no improvement in his condition was noticed, MOG Ab testing was done with a titer of 1:1000. He was started on monthly IVIG with dramatic improvement.
RESULTS: Case 3: A 5-year-old girl presented with influenza B associated postinfectious ADEM with bilateral optic neuritis, completely recovered with administration of IV methylprednisolone. One month later she re-presented with bilateral optic neuritis, requiring IVMP 6-week oral steroid taper with no further recurrence. About 1 year later her first time MOG antibody testing was positive with 1:100 titer.
CONCLUSIONS: Infectious encephalitis can be a predisposing factor for MOG associated encephalomyelitis. The role of this autoantibody and need for treatment to reduce recurrence requires further evaluation although our patients have improved with maintenance IVIg without recurrence.
KEYWORDS: Demyelinating Disorders, Infections/Neuroimmunology, Neuroimaging

98. A rare case of Mild Encephalopathy with Reversible Splenial lesion (MERS) in an eight year old girl of East Asian descent in the United States
Swarz Jeffrey (Boston, MA, United States) Rodrigues Anthony

OBJECTIVE: To describe the rare case of Mild Encephalopathy with Reversible Splenial lesion (MERS) in an eight year old girl of East Asian descent in the United States.
METHODS: Patient demographics, history, neurological findings, MRI, CSF analysis, serum antibodies, treatment, and prognosis were reviewed. The literature was reviewed for prior case reports.
RESULTS: An eight year old girl of East Asian descent living in the United States presented with acute onset of confusion, urinary incontinence, and inability to walk upon waking that morning. She had a sore throat and mild fever 5 days prior to admission with resolution of symptoms two days prior to admission. Neurological exam found mild encephalopathy, mild dysarthria, and an isolated motor disturbance bilaterally in the lower extremities. Strength was 5/5 globally, all sensory modalities were intact, and there was no limb dysmetria or truncal ataxia. However she exhibited a severely ataxic gait and was unable to stand or take steps without support. MRI showed a measuring approximately 1.2 cm (SI) by 0.7 cm (AP) by 1.5 cm (TV) T2/FLAIR hyperintense, T1 hypointense lesion in the splenium of the corpus callosum with restricted diffusion and without significant enhancement. CSF analysis showed no PMNs, no organisms, with lymphocytic pleocytosis and atypical lymphocytes suggesting a recent viral infection. NMO/AQP4 and MOG antibodies were negative. Five days of high dose steroids resulted in complete resolution of neurological findings.
CONCLUSIONS: Children of East Asian descent are susceptible to MERS though living in North America.
KEYWORDS: Demyelinating Disorders, Infections/Neuroimmunology, Neuroimaging

99. A Demyelinating Disorders Mimic: Strictly Nutritional Optic Neuropathy Presenting as Unilateral Vision Loss
Tarhan Bedirhan (Gainesville, FL, United States) Winesett Parrish, Joseph Nancy, Hyder Douglas

OBJECTIVE: The clinical presentation of nutritional optic neuropathy is indistinct from other causes of optic neuropathies with painless, bilateral, symmetric progressive loss of central visual acuity, dyschromatopsia and cecocentral scotoma. This condition is reversible if treated early. Knowing which individuals who are at risk and understanding specific features of nutritional neuropathies could lead to earlier recognition and treatment.
METHODS: A retrospective review of the clinical history, physical exam, laboratory studies, and neuroimaging.
RESULTS: 12-year-old Caucasian female with history of repaired duodenal stenosis and a diet restricted to chicken nuggets and potatoes presents with 2 months of progressive painless left eye vision loss. The patient noticed central vision loss in her left eye extending to the temporal field of the left eye with no other neurologic or visual symptoms. Initial eye exam revealed 20/25 vision in right eye and only light perception in left eye with bilateral bitot spots and bilateral optic neuritis. The working diagnosis in this adolescent female was optic neuritis. Investigations including testing for autoimmune, infectious and inflammatory diseases as well as imaging of brain and optic pathways was normal except for mildly increased signal in both optic nerves. Further diagnostic workup revealed a diagnosis of nutritional neuropathy in which the asymmetric degree of vision loss is unusual for strictly nutritional optic neuropathy.

CONCLUSIONS: Nutritional deficiencies should be considered when evaluating for vision changes especially in patients with restricted diets and previous bowel surgery. To prevent irreversible damages, dietary history should be obtained in optic neuropathy.
KEYWORDS: Demyelinating Disorders, Neurometabolic Disorders, Neuroimaging

100. Identifying the Spectrum of neurological sequela in Anti-MOG Autoimmune Disease
Ilana Kahn (Washington, DC, United States) Kousa Youssef, Doslea Alyssa Beth, Suslolvic William, Fleming Mellissa, Parker Margaret, Sady Maegan, Wells Elizabeth

OBJECTIVE: To describe the neurological sequela in the spectrum of Anti-MOG disease.
METHODS: Retrospective chart review of pediatric patients with serum positive anti- MOG antibodies diagnosed and treated at a quaternary referral center from Jan 2010 to April 2020.
RESULTS: Twenty-six children and adolescents (15 female) with anti-MOG autoimmune disease were identified, with average follow up of 25 months (maximum of 109 months). Of these, 14 (54%) patients presented with acute disseminated encephalomyelitis (ADEM) (average age 4.2 +/- 2.9 years). The remaining 12 patients (46%) presented with other acquired demyelinating syndromes (ADS); including primarily optic neuritis (8) with neuromyelitis optica spectrum disease (2), transverse myelitis (1), and cerebellitis (1) (average age 12 +/- 5.1 years). Half of the children with ADEM (7/14) developed relapsing autoimmune disease, including multiphasic ADEM (MDEM) and ADEM-Optic Neuritis. In contrast, only 25% (3/12) of children with ADS developed chronic autoimmune disease. The majority of patients who presented with ADEM (9/14) developed one or more chronic neurological sequelae; including 50% with cognitive and memory impairments, 21% with epilepsy, 14% with episodic headaches, and 14% with motor apraxia and sensory deficits. Only 2 patients (16%) with ADS had any impairment.
CONCLUSIONS: Here, we identified the spectrum of sequela in Anti-MOG autoimmune diseases. We found that patients who present with more severe and diffuse CNS disease appear to be at higher risk for relapsing chronic autoimmune disease and neurological sequala, including cognitive deficits, epilepsy, and motor/sensor deficits.
KEYWORDS: Demyelinating Disorders, Infections/Neuroimmunology, Cognitive/Behavioral Disorders (including Autism)

101. ANALYSIS OF PLASMA PROTEIN BIOMARKERS IN CHILDHOOD ONSET MULTIPLE SCLEROSIS
Solmaz Ismail (Ankara, Turkey) Kocak Engin, Kaplan Ozan, Celebier Mustafa, Anlar Banu

OBJECTIVE: Multiple sclerosis starting before 18 years (pMS) differs from adult-onset disease in prevalence, extent of inflammation and course. Definition of biomarkers can assist in diagnosis and management. We aimed to analyze plasma proteins in pediatric MS (pMS) by an untargeted proteomic approach.
METHODS: The pMS group (n=33), patients with demyelinating disease not meeting diagnostic criteria of pMS (unclassified demyelinating disease, Group U, n=4) and an age-matched healthy control group (Group C, n=40) were included. Plasma proteomic analysis was performed using Q-TOF LC/MS followed by principal component analysis (PCA). Proteins showing fold change >1.2 at Log 2 level and statistical difference ($p<0.05$) between groups were determined.

RESULTS: Proteins at higher concentration in Group pMS compared to than Group C were: alpha 1B glycoprotein (A1BG), complement factor B (CFB), plasminogen (PLG), alpha 2 antiplasmin (a2AP, SERPINF2) and inter alpha trypsin inhibitor heavy chain H2 (ITIH2). Those at lower concentrations in pMS were: centrosomal protein of 290 (CEP 290) and F-box/LRR-repeat protein 17 (FBXL17). The results of Group U were statistically close to those of Group MS.
CONCLUSIONS: Proteins involved in the pathways of inflammation, coagulation and oxidative stress were found to differ between pMS and control groups. Patients with clinically unclassified demyelinating diseases overlapped the pMS group using protein markers.
KEYWORDS: Demyelinating Disorders, Infections/Neuroimmunology, Neuroscience

102. MOG ASSOCIATED DISORDERS (MAD) IN CHILDREN- A SINGLE CENTER EXPERIENCE FROM INDIA

Desai Neelu (Mumbai, India) Badheka Rahul, Udani Vrajesh

OBJECTIVE: MOG associated disorders (MAD) have been increasingly recognised in last few years. Data in children from developing world is scarce. This study retrospectively reviewed 24 children from a tertiary centre in India with MAD over last 3 years.
METHODS: All children with neurological disorder and MOG antibody positivity were searched in database. Pertinent data was entered in pre-designed format highlighting age, initial symptoms, syndrome (ADEM/others), acute and long term treatment, relapses and long-term outcome (Expanded disability scale). Long-term follow-up (> 2 years) and serial MOG status were recorded.
RESULTS: 24 patients were enrolled over 3 years (1/1/2016 to 31/12/2019). ADEM was diagnosed in 13 and non-ADEM (ON, TM, ON-TM, aseptic meningitis) in 11. A bimodal age distribution was seen with median age of 48 months in ADEM group and 96 months in Non-ADEM group ($p<0.009$). Male: female ratio was 3.3:1 in ADEM and 1.2:1 in Non-ADEM. Fever was strikingly present in both groups, lasting more than two weeks in 58% cases. Long-term treatment given was steroids (21), IV Immunoglobulin (2) and no treatment (1). Illness was monophasic in 67% and relapsing in 33%. Though relapses occurred more with prolong fever (50% vs10%) and non-ADEM compared to ADEM (45% vs 23%); it was not statistically significant. More than 12 months follow-up was seen in 19 (median 30 months) with EDSS score of 0 in all.
CONCLUSIONS: MAD is a distinct syndrome with age-dependent phenotypes. High association with prolong fever is previously unknown. Long-term outcome is excellent in both monophasic and relapsing course.
KEYWORDS: Demyelinating Disorders, Infections/Neuroimmunology, Teaching of Child Neurology

103. Comparative study of clinical and imaging for anti-NMDAR receptor encephalitis and MOG antibody associated autoimmune demyelinating

Shulei Liu (Changsha, China) Hongmei Liao, Liming Yang, Zhi Jiang

OBJECTIVE: To compare the clinical features between NMDAR-IgG positive and MOG-IgG positive patients.

METHODS: Retrospectively analyze the gender, age, antibodies, EEG, MRI, treatment, relapse and prognosis of 37 NMDAR-IgG positive and 18 MOG-IgG positive patients.
RESULTS: The age in both group had no difference, Female were more common in NMDAR group($\chi2$= 4.080, P = 0.043). The blood routineand CSF leukocyte: MOG group[（14.62±5.712）] x10^9/L] [30（10，50）10^6/L],NMDAR group[（10.29±4.29）x10^9/L][8（2，18）10^6/L]，（t = 3.125,P =0. 003）（Z=3.062，P=0.002）. Serum and CSF antibody titer:MOG group (1:26.19) (1:15.75), detection time (16±6 days)；NMDAR group (1:8.55) (1:25.58), detection time (33±29 days). EEG:NMDAR group was more seriously affected in the acute phase($\chi2$ = 27.398, P = 0.000),but recover quicker ($\chi2$ = 8.388, P = 0.039). Imaging: NMDAR group：12 cases had typical intracranial lesions;MOG group:16 cases had atypical intracranial lesions. After immunotherapy,both groups improved to varying degrees, but the disease progressed rapidly in NMDAR group, and the occupancy rate of ICU was 13.5% (5/37)in NMDAR group and 5.5%(1/18) in MOG group. Sequelae residual rate in MOG group was 22.2% (4/18,) and 5.4% in NMDAR group (2/37).
CONCLUSIONS: Female were more common in NMDAR group. The antibody titer of NMDAR group was higher in CSF and appeared later; in MOG group was higher in serum and appeared earlier. In NMDAR group, EEG involvement was more severe, but recovery was better; Head MRI showed that NMDAR group had typical intracranial lesions;in MOG group, the intracranial involvement was extensive, but the lesions were atypical. The NMDAR group had a more severe condition but the prognosis was better than MOG group.
KEYWORDS: Demyelinating Disorders, Infections/Neuroimmunology

104. Analysis of clinical, laboratory, imaging and electroencephalogram for 24 children with MOG antibody encephalomyelopathy
Hongmei Liao (Changsha, China) Shulei Liu

OBJECTIVE: To investigate the clinical, imaging and EEG characteristics of MOG antibody mediated encephalopathy in children.
METHODS: Retrospectively analyzed the clinical, imaging, EEG characteristics of 24 cases with MOG antibody encephalomyelopathy.
RESULTS: There were 8 males and 16 females.The first symptoms included: fever (11 cases), headache (5 cases), blurred vision (9 cases), seizures (8 cases), urinary retention (3 cases), ataxia (6 cases), language (2 cases), claudication (2 cases), eye movement dysfunction with drooping eyelids(1 case). 19 cases had abnormal head MRI, 3 cases had no abnormal signal,7 cases had abnormal spinal cord MRI, the optic nerve MRI was obviously abnormal in 8 cases. Most of the MRI changes in the head were ADEM-like lesions, 3 cases were combined with positive anti-nmda antibody,2 cases were combined with positive GFAP antibody . All children had a good response to glucocorticoid and gamma globulin.The longest history was five and a half years in 11cases.During the follow-up, 1 patient relapsed.
CONCLUSIONS: The clinical manifestations of MOG antibody encephalomyelopathy included visual impairment, convulsions, abnormal gait, and dysuresia. The most common prodromal symptom was fever. There was no specificity in imaging changes, the main changes were ADEM-like lesions(involving cortex or/ and subcortex).EEG change was relatively milder than the imaging change.Immunosuppressive therapy was effective and most had a good prognosis. Therefore, MOG antibody encephalomyelopathy was a type of immune-related disease with a

good prognosis, but the diagnosis of the disease need to exclude other diseases. Anti-NMDA antibody and GFAP antibody were detected in some cases at the same time.
KEYWORDS: Demyelinating Disorders, Infections/Neuroimmunology

105. Is it CLIPPERS? It is CNS Hemophagocytic Lymphohistiocytosis - an expanding spectrum of Paediatric Demyelination
Parida Amitav (Birmingham, United Kingdom) Wassmer Evangeline, Hemingway Cheryl, Eleftheriou Despina

OBJECTIVE: We describe five children with familial Hemophagocytic Lymphohistiocytosis (fHLH), who presented with atypical demyelination and a working diagnosis of 'CLIPPERS' (Chronic lymphocytic inflammation with pontine perivascular enhancement responsive to steroids).
METHODS: Retrospective case series
RESULTS: Case 1 and 2: 11-year-old girl presented with diplopia and ataxia. MRI showed white matter lesions in the pons, medulla and cerebellum as seen in 'CLIPPERS'. Symptoms responded partially to steroids. She has a compound heterozygote RAB27A mutation, Griscelli Syndrome type 2. Her 16 year old brother has the same. Case 3: 5-year-old boy presents with headaches and squint. MRI showed demyelination of cerebellum. He improved with steroids, followed by recurrence on weaning. Brain biopsy was consistent with 'CLIPPERS'. He has heterozygote variants in the STXBP2. He is well post bonemarrow transplant. Case 4: A 9-year-old girl presented with optic neuritis. MRI brain shows demyelination. CSF Oligoclonal bands positive. Later she developed a pleural effusion, high ferritin, deranged coagulation, lymphadenopathy and a cutaneous T-cell lymphoma. She has a homozygous mutation in the UNC13 gene. She is well post bone marrow transplant. Case 5. A 17-year-old boy presented with acute ataxia and demyelination of the cerbellum and pons. He had a previouse episode of demyelination age 4. He has abnormal perforin expression.
CONCLUSIONS: Familial HLH can present with an isolated atypical demyelinating illness or 'CLIPPERS'. There may be no systemic inflammation. We propose that all children with atypical recurrent CNS inflammation and 'CLIPPERS' undergo genetic panel testing for fHLH and Natural Killer cell functional testing.
KEYWORDS: Demyelinating Disorders, Genetics, Infections/Neuroimmunology

106. Predictors of Diagnosis and Outcome in Pediatric Myelin Oligodendrocyte Glycoprotein (MOG) Antibody Associated Disorders
Hardy Duriel (Philadelphia, PA, United States) McGuire Jennifer, Banwell Brenda, Hopkins Sarah

OBJECTIVE: To characterize a cohort of MOG-antibody positive (MOG+) patients and identify clinical, laboratory, and radiographic predictors of diagnosis, relapse and treatment response in MOG+ patients.
METHODS: We retrospectively reviewed records of patients between the ages of 0-20 that had MOG-antibody testing between January 1, 2014 and December 30, 2019. Logistic regression modeling was used to identify determinants associated with a MOG-related disorder diagnosis and response to treatment.

RESULTS: Of 42 MOG+ patients, 26 (61.9%) were female with a median age of 7 (5-10) years. The most common presenting phenotype was acute disseminated encephalomyelitis (ADEM) (38.1%). 39 of the 42 MOG+ patients (92.9%) had an abnormal brain MRI with the most common findings being cerebral white matter lesions (64.1%) and deep gray matter involvement (64.1%). 17 out of 32 MOG+ patients had abnormal spinal imaging (53.1%) with longitudinally extensive lesions being the most common finding (70.6%). Positive cerebrospinal fluid (CSF) oligoclonal bands (OCBs) occurred in a subset of MOG+ patients (16.1%). 20 of the 42 MOG+ children (47.6%) had clinical relapses and these patients were treated with disease modifying therapies (DMTs).
CONCLUSIONS: MOG-related disorders present with a spectrum of phenotypes with ADEM being most common in our cohort. Cerebral white matter lesions, deep gray matter involvement, and longitudinally extensive cord lesions were common in MOG+ children. Positive OCBs in CSF is uncommon in MOG+ children. Treatment with DMTs were utilized in children with relapses leading to cessation in relapses in the majority.
KEYWORDS: Demyelinating Disorders

107. Serial Neuropsychological Testing in MOG Antibody-Associated Disease to Improve Understanding of Outcomes
Kornbluh Alexandra (Columbus, OH, United States) Bradstreet Lauren, Hutchinson Melissa, Wilson Camille

OBJECTIVE: Neurocognitive outcomes in patients with myelin oligodendrocyte glycoprotein (MOG) antibody-associated disease are unknown. Within MOG cohorts, outcomes data typically utilize gross cognitive measures or EDSS (extended disability severity score), a measure most representative of physical disability. Our multidisciplinary team examined serial neuropsychological data in a patient with MOG-mediated disease.
METHODS: Serial clinical, neuroimaging, and neuropsychological data are presented in a pediatric case of relapsing encephalomyelitis, ultimately diagnosed with MOG-mediated demyelination. Detailed serial neuropsychological domains including intelligence, verbal and nonverbal language, attention, executive functioning, and fine motor performance abilities were assessed.
RESULTS: A twelve-year-old African American boy with premorbid history of ADHD and learning disability presented in 2017 with seizures and fevers. He was found to have CSF lymphocytic pleocytosis. MRI brain revealed patchy restricted diffusion (Figure 1, A - B). An outpatient neuropsychological evaluation eight months later documented below average neurocognitive abilities, with deficits in expressive language and fine motor speed (Figure 2). The patient re-presented in 2019 with fever, back pain, rapidly progressive weakness, and urinary retention. CSF pleocytosis was re-demonstrated. Neuroimaging showed new enhancing multifocal lesions including longitudinally extensive spinal cord inflammation (Figure 1, C – F). MOG antibody titers were positive. Inpatient neuropsychological evaluation found improved nonverbal skills with new deficits in fine motor speed and dexterity (Figure 2).
CONCLUSIONS: Despite clinically heterogenous events and a high burden of neuroinflammation, our patient's neurocognitive assessments indicated a generally stable profile. Systematic and serial neuropsychological testing in populations with MOG-mediated disease can elucidate neurocognitive outcomes and facilitate multidisciplinary management to improve recovery.

KEYWORDS: Demyelinating Disorders, Cognitive/Behavioral Disorders (including Autism), Infections/Neuroimmunology

108. Pediatric NMO presenting as hypersomnolence in a 4-year-old female
Suleman Saher (Phoenix, AZ, United States)

OBJECTIVE: To report a unique case of pediatric NMOSD presenting with isolated hypersomnolence in a 4-year-old female.
METHODS: This was a 4-year-old, previously healthy female brought to the ED for a history of progressive hyper somnolence. CSF showed a lymphocytic pleocytosis and a minimally elevated protein of 46. Her brain MRI was remarkable for FLAIR/T2 hyperintensity in medial thalami, hypothalamus, and central optic pathway. MRI C- and T-spine were unremarkable. She was seronegative for AQP-4 antibodies but positive for AQP4 antibodies in the CSF.
RESULTS: She was diagnosed with NMOSD and treated with high dose steroids followed by plasmapheresis and then rituximab. She showed some improvement in mental status.
CONCLUSIONS: Neuromyelitis optica spectrum disorders (NMOSD) is an inflammatory demyelinating condition affecting the central nervous system and typically presents with episodes of optic neuritis, transverse myelitis, and brainstem/cerebellar syndromes. Only 3-5% of cases have pediatric onset, usually between ages 10-12. It is most often associated with presence of serum aquarporin-4 (AQP4) antibodies. Pediatric NMOSD is less common and isolated presentation of hyper somnolence has not been previously reported in a pediatric patient. This patient did not technically fit the criteria for NMOSD, however, lesions of the thalami and hypothalamus have been previously reported with NMOSD and associated with presentation of narcolepsy. She only demonstrated presence of AQP4 antibody in the CSF and was seronegative. This case demonstrates that presentations of NMOSD can be varied and unusual especially in the pediatric population, and often requires a high clinical suspicion to obtain work-up for diagnosis and treatment.
KEYWORDS: Demyelinating Disorders

EPILEPSY

109. Comparison of subdural grid and stereoelectroencephalography monitoring in pediatric patients
Talai Afsaneh (Aurora, CO, United States) Stence Nicholas, Chapman Kevin, O'Neill Brent, Alexander Allyson, Bird Wynne, Joshi Charuta, Eschbach Krista

OBJECTIVE: To compare adverse events between stereoelectroencephalography (sEEG) and subdural electrode (SDE) implantation in children.
METHODS: Retrospective analysis of intracranial epilepsy monitoring procedures with sEEG or SDE implantation at Children's Hospital Colorado between January 2011 and June 2019.
RESULTS: There were 47 patients with 53 sEEG implantations and 59 patients undergoing 61 SDE implantations. The average age was 12.45 years (range: 1.22-19.96). Post-implantation imaging was performed in all sEEG implantations and 46 SDE implantations. Any type of hemorrhage was identified in 37.74% and 78.26% of sEEG and SDE implantations, respectively (p=0.0001). The average number of days spent in the intensive care unit after implantation for

sEEG patients was 0.45 compared to 1.69 for SDE patients (p=0.0005). No patient undergoing sEEG implantation received blood products compared to 20% of SDE patients (p=0.0012). The rate of infection in sEEG patients was 2.13% compared to 29.51% for SDE patients (p=0.0002). Resection was completed in 59.57% of sEEG patients versus 93.44% for SDE procedures (p<0.0001). Seizure freedom rates between the two groups were similar, with 52.38% of sEEG patients and 56.14% of SDE patients (p=0.77) seizure free for at least 12 months at last follow-up.
CONCLUSIONS: In pediatric patients sEEG is associated with less adverse effects yet similar rates of seizure freedom compared to SDE implantation. This includes significantly lower rates of hemorrhage and infection associated with sEEG monitoring.
KEYWORDS: Epilepsy

110. Automated Identification and Quality Measurement for Pediatric Convulsive Status Epilepticus
Hess-Homeier David (New York, NY, United States) Parikh Karishma, Basma Natasha, Vella Adam, Grinspan Zachary

OBJECTIVE: Treatment delays for refractory convulsive status epilepticus (RCSE) are associated with worse outcomes. In the US, pediatric RCSE treatment is slower than guidelines recommend. To address this gap, the American Academy of Neurology & Child Neurology Society developed a quality measure: the percentage of RCSE patients that receive 3rd line treatment within 60 minutes. We aimed to develop computable phenotypes for convulsive status epilepticus (CSE) and RCSE to automate calculation of the quality measure.
METHODS: From an observational cohort of children presenting to the emergency department for seizures or epilepsy, we identified presentations with CSE, CSE requiring a 2nd line agent (CSE2), and RCSE by gold standard chart review. Multivariate statistical models were developed to automate case identification and serve as computable phenotypes for calculation of time to treatment.
RESULTS: From 664 charts, we identified 56 patients with CSE, 36 with CSE2, and 18 with RCSE. Five predictors were used: the term “status epilepticus” in radiology reports, ICD codes, and receiving 1st, 2nd, or 3rd line agents. Combinations of these predictors identified CSE with 84% sensitivity and 81% positive predictive value (PPV), CSE2 with 67% sensitivity and 89% PPV, and RCSE with 94% sensitivity and 85% PPV. Median time-to-treatment was 13 minutes for 1st line agents, 24 minutes for 2nd line, and 52 minutes for 3rd line. 60% of RCSE patients received a 3rd line agent within 60 minutes.
CONCLUSIONS: RCSE and its precursors can be identified automatically with high fidelity allowing automated calculation of time to treatment and the RCSE quality measure.
KEYWORDS: Epilepsy, Critical Care

111. Clinical Characteristics of Patients Admitted to Pediatric EMU and Correlation of Length of Stay with The Diagnostic Yield
Al Omari Mohammed (London, Ontario, Canada) Andrade Andrea, Prasad Asuri

OBJECTIVE: EEG is a standard diagnostic test for patients with epilepsy. The optimal duration for EEG recording varies between practitioners, and there is no consensus on the optimal duration for recording in pediatric age group. We retrospectively evaluated duration of EEG

recordings in our pediatric epilepsy unit to optimize the duration of the recording to maximize the diagnostic yield.
METHODS: This is a retrospective review of 199 patients admitted to pediatric EMU. Variables evaluated included; type and duration of epilepsy, etiology, and duration of EEG study. Results of first routine EEG were compared to prolonged recording in EMU.
RESULTS: There were 104 males, and 95 females under age 18 years. Focal-onset seizures found in 88 (44%) patients, followed by generalized-onset seizures (46 patients – 23%). Routine EEG (<30 min) was diagnostic in 51%, while prolonged EEG was diagnostic in 78.9% of the patients. The mean duration of EMU recording for non-diagnostic study was 32.4 hours, while for diagnostic recording was 43.23 hours, that was statistically significant (t=-2.49, P=0.014). The likelihood of a diagnostic study increased with longer duration of monitoring (73.3% (4-35 hours), 83.3% (36-52 hours), and 89.3% (> 52 hours)). EEG recording of >52 hours was diagnostic in 94.73% of focal epilepsy, and 100% of generalized epilepsy.
CONCLUSIONS: Length of EMU stay correlated positively with chances of obtaining a diagnostic test, especially for generalized-onset epilepsy. 36-52 hours EEG recording is likely to be diagnostic in 93.75% of focal epilepsy, longer duration of recording provides a higher yield for generalized epilepsy.
KEYWORDS: Epilepsy

112. Mosaic PCDH19 expression leads to aberrant neuronal migration and segregation in a transgenic mouse model
Ziobro Julie (Ann Arbor, MI, United States) Umemori Hisashi, Kalantry Sundeep, Parent Jack

OBJECTIVE: PCDH19 developmental and epileptic encephalopathy (PCDH19-DEE), an X-linked DEE that affects females, is posited to result from abnormal interactions between wild-type and mutant PCDH19-expressing cells during development. This “cellular interference” leads to varied phenotypes due to random X-inactivation. To explore this hypothesis, we used transgenic mice to examine the effects of mosaic PCDH19 expression.
METHODS: Female PCDH19$^{-/-}$ or PCDH19$^{+/+}$ mice were crossed with X-GFP male mice to obtain female offspring expressing GFP on the wild-type allele and no fluorescent marker on the X chromosome carrying the other PCDH19 null or wild-type allele. Brains from female offspring were harvested from E10-P60 for histological analysis. Prolonged EEG recordings were performed on P40-P50 mice to assess for spontaneous seizures. Mice then received an intraperitoneal injection of PTZ to examine seizure latency/severity.
RESULTS: Brains of PCDH19$^{+/-}$ offspring revealed a cell segregation pattern with segregated populations of GFP+ (PCDH19+) or GFP- (PCDH19-) cells, most notably in the cortex and hippocampal CA1 region. Cell segregation was observed at E10 (in progenitors) and persisted through adulthood. Prolonged EEG recordings failed to capture spontaneous seizures in adult mice. Seizure latency/severity with PTZ administration was not decreased vs. control mice.
CONCLUSIONS: Our mouse model supports the hypothesis that mosaic PCDH19 expression leads to aberrant neuronal migration and segregation between wild-type and knockout cell populations. Ongoing work is exploring molecular mechanisms underlying this early cell segregation and the physiologic implications at varying time points during development.
KEYWORDS: Epilepsy, Neuroscience, Rare Diseases

113. Pediatric Neurology Telemedicine Special Interest Group: Broad interest, New applications

Joshi Sucheta (Ann Arbor, MI, United States) Joshi Charuta, Fletcher Linda

OBJECTIVE: There is growing interest in telemedicine within the Child Neurology Society (CNS). To enrich this interest, a Telemedicine Special Interest Group (TM-SIG) was convened at the 48th annual CNS meeting, bringing together interested and committed individuals to assess current interest/practice, identify benchmarks for future applications and growth of telemedicine in pediatric neurology.
METHODS: TM-SIG attendees completed an IRB approved survey (table 1) and participated in guided discussion.

RESULTS: There were 34 participants. 27 surveys were returned. 21/27 attendees were from academic practices. 11/27 had < 2years in practice (trainees); 14 had >10 years (experienced practitioners). 7/11 (63%) trainees rated telemedicine as providing the same care as in-person visits versus 8/14 (57%) experienced practitioners. 70% (19/27) had not used telemedicine (10 trainees vs 6 experienced practitioners). 6 respondents currently used telemedicine for new patient evaluations, 20 more were willing to. Inability to do an examination was the primary reason for not seeing new patients (table 2). 76% respondents identified institution/administrative staff as appropriate in obtaining necessary licensures for telemedicine.
CONCLUSIONS: There is broad interest in using telemedicine in the practice of Pediatric Neurology, including among trainees. Trainees and experienced practitioners both regard telemedicine as delivering similar care to in-person visits. Whether a current non-user of telemedicine, or experienced practitioner there is willingness to incorporate telemedicine into practice, and broaden its scope (e.g evaluate new patients) Given the significant number of trainees who participated in the TM-SIG, telemedicine should be considered in the education and training of future cohorts of residents.
KEYWORDS: Epilepsy, Teaching of Child Neurology

114. Second Chance: Postoperative seizure outcome in children with intractable epileptic spasms who require repeat surgery.

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OBJECTIVE: We report the postoperative seizure outcome in children with intractable epileptic spasms who require repeat surgery.
METHODS: Medical records were reviewed of all consecutive children who had epilepsy surgery for intractable epileptic spasms at Cleveland Clinic between 2000 and 2018.
RESULTS: Of 70 children who had surgery (average age 16 months) for epileptic spasms, 35 (50%) had seizure recurrence after surgery and 12 had reoperation for seizure recurrence. Eleven had 2 surgeries and one required a third surgery; none had intracranial monitoring. In all but one child, the lesion visible on MRI had been completely removed or disconnected at initial surgery. Median time to seizure recurrence was 1 year. Mean time between the two surgeries was 35 months. The second surgeries were completion of hemispherectomy (n=5), extension of an anterior temporal resection to include more complete temporal lobectomy (n=2) or resection of parieto-occipital regions (n=4), or more posterior extension of frontal resection to include fronto-

parietal areas (n=1). At a mean follow-up 4.8 years after the last surgery, 6 children (50%) were seizure-free. All 6 seizure-free children had unilateral MRI abnormalities; 2 children with seizure recurrence had bilateral abnormalities on brain MRI. Hemispherectomy (4) and temporo-parieto-occipital resection (2) accounted for all 6 seizure-free cases.
CONCLUSIONS: In this cohort of children with epileptic spasms requiring repeat surgery, 50% were seizure-free, supporting similar results from other published surgical series. Hemispherectomy and temporo-parieto-occipital were more successful than lobar resections. Children with intractable spasms who failed initial epilepsy surgery should be carefully evaluated for candidacy for repeat surgery.
KEYWORDS: Epilepsy, Neuroimaging

115. Abnormal Pediatric Epilepsy Gene Panel Result is Predictive of Drug Resistant Epilepsy

Bonkowsky Josh (Salt Lake City, UT, United States) Porter Caleb, Olsen Jaxon, Wilkes Jacob, Doyle John, Scholl Erika, Newton Andrew, Sweney Matthew

OBJECTIVE: Our objective was to assess whether an epilepsy genetic panel test result was predictive of treatment failure (drug-resistant) versus seizure-free long-term outcome in pediatric epilepsy patients.
METHODS: This was a population-based study of all children evaluated for new-onset epilepsy in an integrated healthcare system at Primary Children's Hospital and the University of Utah. The study was IRB approved. Children were ages 6 months to 15 years at their initial presentation of epilepsy. The initial cohort was assembled over six years, with no less than eight years of follow-up. Patient outcome was determined at the conclusion of the study period and categorized according to their epilepsy control as seizure-free, treatment failure, or undetermined. Patients were randomly selected from the seizure-free or treatment failure outcome groups, contacted, consented, and tested by an epilepsy gene panel test (187 genes). 20 patients total were tested, 10 each from treatment failure and seizure-free groups.
RESULTS: In the seizure-free group, 1 patient had an abnormal (pathogenic variant) epilepsy gene panel. In the treatment failure group, 8 patients had an abnormal result. We assumed a 30% prevalence of treatment failure epilepsy. The positive predictive value of an abnormal result was 79% for long-term risk for treatment failure; the negative predictive value was 91% for long-term seizure-free with a normal panel result.
CONCLUSIONS: We found that results of an epilepsy gene panel test result is associated with long-term pediatric epilepsy outcomes. This suggests that early genetic testing in pediatric epilepsy patients may be important in guiding management.
KEYWORDS: Epilepsy, Genetics

116. Infraslow EEG Analysis Refines Epileptogenic Zone Localization and Simplifies Interpretation

Johnson Ervin (Boston, MA, United States) Hyde Damon, Bolton Jeffrey, Stone Scellig, Rotenberg Alexander

OBJECTIVE: Peri-ictal infraslow activity (ISA) is a poorly-understood intracranial EEG (iEEG) signal component that occurs over many-second timescales (<0.1Hz). ISA is present in most iEEG studies but is typically filtered out because its presence may confound conventional

visual iEEG tracing analysis. The current study employs modern visualization techniques to render the ISA signal into an easily-visualized format. This ISA analysis method simplifies data interpretation and may refine epileptogenic zone (EZ) localization.
METHODS: Seizures captured during stereotaxic iEEG recordings of 12 pediatric patients (6-18 years) were analyzed. ISA was extracted using a 10^{th} order lowpass Butterworth filter with 3dB attenuation at 0.1Hz, applied to sEEG data flanking ictal onsets. Two measures, averaged across all seizures per-patient, were examined: 1) instantaneous ISA at ictal onset and 2) ISA integrated from 0 to 10 seconds post-onset. Volumetric displays of ISA measures are being constructed using three-dimensional linear interpolation onto electrode positions segmented from post-surgical CT and co-registered to preoperative MRI.
RESULTS: In each subject for whom ISA analysis has been completed (5/12 patients), there is spatial concordance between the positive ISA field and the conventionally-identified ictal onset zone. Integrated ISA measures show greater concordance than instantaneous measures.
CONCLUSIONS: Peri-ictal ISA analysis renders ISA signal data into a format that is easily interpreted and can be used as an adjunct to refine EZ localization.
KEYWORDS: Epilepsy, Neuroscience

117. FHF1 DEVELOPMENTAL AND EPILEPTIC ENCEPHALOPATHY: recurrent p.Arg114His is cause of neonatal onset epilepsy

Trivisano Marina (Rome, Italy) Ferretti Alessandro, Bebin Elizabeth, Huh Linda, Lesca Gaetan, Carneiro Maryline, De Palma Luca, Takeshita Eri, Lagae Lieven, Minassan Berge, Vigevano Federico, Villard Laurent, Buyse Gunnar, Scheffer Ingrid, Specchio Nicola

OBJECTIVE: Fibroblast-growth-factor homologous factor (*FHF1*) gene variants have recently been associated with developmental and epileptic encephalopathy (DEE). *FHF1* encodes a cytosolic protein that modulates neuronal sodium channel gating. With this study, we aimed to refine the electro-clinical phenotypic spectrum of patients with pathogenic *FHF1* variants, analyze genotype-phenotype correlation and inform management and prognosis.
METHODS: Through an international collaboration, we retrospectively collected detailed clinical, genetic, neurophysiologic and neuroimaging data of 17 patients with *FHF1*-related epilepsy.
RESULTS: Sixteen patients had recurrent heterozygous *FHF1* missense variants: fourteen had c.341G>A (p.Arg114His) and two had c.334G>A (p.Gly112Ser). One patient carried a chromosomal microduplication involving *FHF1* gene. Twelve patients carried a *de novo* variant, while five patients (29.5%) inherited the variant from parents who had gonadic or somatic mosaicism. Patients with the p.Arg114His variant presented with neonatal onset DEE. Tonic seizures were the most frequent seizure type. The two patients with the p.Gly112Ser variant and the patient with the *FHF1* duplication had later epilepsy onset at median of 4 months (range 4-41 months). Drug-resistant epilepsy with frequent SE and cognitive and behavioral disturbances were common features. Brain MR was normal at epilepsy onset while mild cerebral and/or cerebellar atrophy appeared during follow-up in 8/14 (57.1%).
CONCLUSIONS: *FHF1*-DEE has an electro-clinical phenotypic spectrum characterized by drug-resistant epilepsy and cognitive and behavioral disability. The p.Arg114His variant is associated with an earlier epilepsy onset and more severe encephalopathy. Because of the high frequency of parental gonadic or somatic mosaicism, it is especially important to offer targeted reproductive counselling.

KEYWORDS: Epilepsy, Genetics, Rare Diseases

118. What outcomes should be measured to improve care for children with infantile spasms?

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OBJECTIVE: Learning healthcare systems improve outcomes through cycles of data collection from electronic health record systems (EHRs), followed by analysis, reporting, and practice change. The Pediatric Epilepsy Learning Healthcare System (PELHS) sought to identify outcomes for monitoring improvement in infantile spasms (IS) care with attention to the following criteria: (1) clinically important, (2) measurable in routine care, (3) commonly observed, (4) in need of improvement, and (5) unbiased by length of follow-up.
METHODS: A multi-stakeholder group (including clinicians, clinical researchers, and parents of children with epilepsy) generated a list of clinically important outcomes. We assessed each outcome with respect to our five criteria in a sample of children treated in 2016 for infantile spasms at 11 US academic medical centers. We estimate baseline rates of each outcome.
RESULTS: The stakeholders identified 17 candidate outcomes, abstracted from the EHRs of 58 children with confirmed IS diagnoses who received care at the participating hospitals (Table 1). Six outcomes met all available criteria (Table 2): need for a second anti-seizure medication (ASM) within 4 weeks of treatment initiation (baseline rate 55%), clinical spasms resolved by 4 weeks of treatment initiation (75%), recurrence of clinical spasms within 4 months of treatment initiation after an initial remission (20%), multifocal epileptiform discharges on the most recent EEG (28%), seizure-free for the past year (35%), and off ASMs for ≥1 month (24%).
CONCLUSIONS: EHRs should support automated extraction of these six outcomes for learning healthcare system initiatives. PELHS ongoing work to select outcomes will include field testing and additional multistakeholder review.
KEYWORDS: Epilepsy, Critical Care, Neuroscience

119. Functional motor and language mapping using surface tripolar EEG

Dhamne Sameer (Boston, MA, United States) Hall Joanne, Vincelli Jay, Besio Walt, Rotenberg Alexander

OBJECTIVE: Functional cortical mapping in children is necessary for various neurosurgical procedures but the current standard techniques, including fMRI, direct cortical stimulation, and Wada testing are impractical in young vulnerable patients who lack the capacity to cooperate with these protocols. Our goal is to develop an inexpensive, convenient, high resolution EEG scalp recording system and algorithms that can be used to localize and map cortical function. In this study, we tested the feasibility of novel tripolar EEG (tEEG) electrodes for noninvasive functional mapping and localization of language and motor regions in adult volunteers.
METHODS: Scalp EEG was recorded from both hemispheres with tEEG electrodes. For language mapping, participants performed overt (speaking aloud) and covert (silent speaking) picture naming tasks while motor mapping involved a hand contraction task of repeated opening and closing of the hand. Data were analyzed using a matlab script and EEGLab to generate event related potentials, head maps of the signals and assess changes in spectral power.

RESULTS: Preliminary results indicate dominant activations with a high degree of hemispheric lateralization for both motor and language tasks using tEEG. Further, language analysis revealed specific electrodes that were active in the temporo-posterior and anterior areas for language recognition and verbal expression tasks, respectively.
CONCLUSIONS: Functional localization and lateralization of motor and language is feasible by tEEG. This noninvasive functional cortical mapping technology can thus be potentially suitable for children and other vulnerable patient population, who cannot tolerate other functional mapping procedures.
KEYWORDS: Epilepsy

120. Clinical and MRI characteristics of vigabatrin-associated brain lesions in children with tuberous sclerosis complex.
Jóźwiak Sergiusz (Warsaw, Poland) Sadowski Krzysztof, Dębska Joanna, Pawliszak Piotr, Borkowska Julita, Ulatowska Agata, Chmielewski Dariusz, Jurkiewicz Elżbieta, Kotulska Katarzyna

OBJECTIVE: The frequency and significance of vigabatrin-associated brain abnormalities on MRI in pediatric population are not clear. The aim of this study was to analyze the risk, evolution, MRI characteristics and clinical symptoms of basal ganglia lesions in pediatric patients with TSC-associated epilepsy treated with vigabatrin.
METHODS: The clinical and MRI data of all TSC children receiving vigabatrin between 2010 and 2018 at The Children's Memorial Health Institute were reviewed. Eligibility criteria for the study included: definite TSC diagnosis, at least 4 weeks of full-dose vigabatrin treatment, availability of neurological data before and during vigabatrin treatment, as well as MRIs performed before and after at least 6 months after vigabatrin treatment onset. The control group consisted of 10 age-matched healthy children.
RESULTS: Out of 153 children receiving vigabatrin, 54 met the criteria for further analysis. Nine patients (17 %) demonstrated at least one focus of abnormal MRI signal in basal ganglia. The lesions were observed in thalami (88% of patients), midbrain (66%), tegmentum (88%), globi pallidi (66%), and dentate nuclei (22%). In all cases they were asymptomatic. The presence of basal ganglia lesions correlated with younger age of children, but not with sex, mutation, vigabatrin dosage, and treatment duration. Spontaneous resolution of MRI changes, despite continued vigabatrin, was observed in 8 out of 9 cases.
CONCLUSIONS: MRI abnormalities associated with treatment with vigabatrin are relatively common and clinically benign findings in children with TSC. In the vast majority of cases they resolve spontaneously.
KEYWORDS: Epilepsy, Neuroimaging

121. Efficacy and safety of antiepileptic treatment with rapamycin in pediatric patients with tuberous sclerosis complex.
Sadowski Krzysztof (Warsaw, Poland) Sijko Kamil, Domańska-Pakieła Dorota, Borkowska Julita, Chmielewski Dariusz, Ulatowska Agata, Jóźwiak Sergiusz, Kotulska Katarzyna

OBJECTIVE: Epilepsy develops in 70–90% of children with Tuberous Sclerosis Complex (TSC) and is often resistant to medication. Everolimus, an mTOR inhibitors has recently been approved as an adjunctive therapy in epilepsy associated with TSC but is not available in Poland.

The study evaluated the antiepileptic effect of another mTOR inhibitor, rapamycin, in children with TSC.
METHODS: This single center, open-label, prospective study evaluated safety and efficacy of one-year rapamycin treatment in 32 patients with drug-resistant epilepsy in TSC children aged from 11 months to 14 years.
RESULTS: At least 50% reduction in seizure frequency was achieved in 65.6% of patients in comparison to the year before rapamycin treatment ($p<0.05$). Concomitant treatment with vigabatrin ($p<0.05$), and to a lesser extent topiramate and levetiracetam, were additional good prognostic factors for better response to rapamycin. A linear relationship between the cumulative dose of rapamycin and its therapeutic effect was observed. The safety profile of the drug was acceptable in all age groups.
CONCLUSIONS: Long-term use of rapamycin in patients with TSC might be a beneficial therapeutic option in drug-resistant epilepsy. Concomitant vigabatrin enhances the antiepileptic effect of rapamycin.
KEYWORDS: Epilepsy, Rare Diseases

122. Clinical utility of next generation sequencing in childhood Epileptic Encephalopathies
Jha Ruchika (Pune, India) Kurup Arjun, Tiwari Sudhanshu, N Sangeetha, V Pooja, P Parvathi, Devgan Amit, Sondhi Vishal, Kohli Sarvesh

OBJECTIVE: To determine the diagnostic yield of Next Generation Sequencing (NGS) among children with Epileptic Encephalopathies (EE)
METHODS: All patients with EE (defined as intractable epilepsy, with global developmental delay and cognitive dysfunction) seen between January2018 and Jan2020 in a single tertiary care pediatric centre in India were included in this retrospective cohort study. All patients with EE, initially underwent clinical evaluation and neuroimaging. If no underlying etiology for EE could be discerned, then metabolic testing was performed. For the subset of patients, with no identifiably cause of EE or with clinical/ metabolic/ neuroimaging features suggestive of genetic etiology, targeted NGS was performed. All variants reported from NGS were annotated using the standard recommendations from mutation nomenclature.
RESULTS: Of 331 children with EE, 102 patients were suspected to have genetic EE; 91 patients underwent NGS and were included in this study. Pathogenic mutations were identified in 44 of 91 patients (48.4%); the mutations were classified as variant-of-unknown-significance in 24 (26.4%) and NGS was reported as normal in 23(25.3%). The identified pathogenic mutations included: sodium channelopathies (SCN1A=9, SCN2A=2, SCN9A=1), potassium channelopathies (KCNQ2=2, KCNT1=2), calcium channelopathies (CACNA1A=2), and mitochondrial encephalopathies (FBXL4=2, POLG=1, NUBPL=1, MT-RNR2=1, NARS2=1, PC=1). The impact of NGS result on clinical management included: changes in medication(n=26), medication discontinuation(n=19), reproductive planning(n=38), changes in disease monitoring strategies(n=9), assessment of asymptomatic sibling(n=6), investigation for systemic involvement(n=2).
CONCLUSIONS: The high diagnostic yield of 48% supports the use of NGS in childhood EE with undiagnosed etiologies. The definitive diagnosis may impact medical management, prognostication and reproductive planning
KEYWORDS: Epilepsy, Genetics

123. Abnormal Activity-Dependent Myelination in Absence Epilepsy

Knowles Juliet (Palo Alto, CA, United States) Frost Eleanor, Fraga Danielle, Tam Lydia, Xu Haojun, Ni Lijun, Saucedo Tristen, Huguenard John, Monje Michelle

OBJECTIVE: A recent discovery is that physiological neuronal activity promotes adaptive myelination *in vivo*, which is required for multiple forms of learning and memory. This process involves proliferation of oligodendrocyte precursor cells (OPCs) and their maturation (oligodendrogenesis), and myelination of neuronal axons by oligodendrocytes. We hypothesize that pathological neuronal activity in the form of seizures also induces changes in myelin structure, contributing to neuronal network dysfunction. The objective of this study was to determine whether abnormalities in oligodendrogenesis and myelination are present in rodent models of absence epilepsy.
METHODS: We assessed oligodendrogenesis using unbiased stereology and myelin structure by electron microscopy in Wag/Rij rats with seizures or control (Wistar) rats before and after seizure onset. In separate experiments, rats were treated with ethosuximide or vehicle to determine whether seizures are necessary to alter myelination. We also found increased oligodendrogenesis and myelin sheath thickness in a mouse model of absence epilepsy, *Scn8a*^{med} +/- mice.
RESULTS: 5-8 Hz spike wave discharge seizures in Wag/Rij rats were associated with increased OPCs and mature oligodendrocytes, and increased myelin sheath thickness in the corpus callosum, within a region interconnecting somatosensory cortices. Preventing seizures with ethosuximide prevented abnormal oligodendrogenesis.
CONCLUSIONS: Absence seizures lead to inappropriately increased myelination, which may alter network function, contributing to cognitive impairment and/or increased seizure frequency. Ongoing studies will assess the extent and functional impact of abnormal myelination in epilepsy. Maladaptive myelination may represent a novel disease mechanism in epilepsy and other neurological diseases.
KEYWORDS: Epilepsy

124. Gender differences in clinical demographics and psychosocial functioning in children with psychogenic non-epileptic seizures (PNES)

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OBJECTIVE: Psychogenic non-epileptic seizures (PNES) is over represented by females (F:M ratio up to 8:1). Understanding female predominance in PNES may provide a unique insight to approach and management of PNES. We investigated a sex difference in clinical demographics and psychosocial functioning in children with new onset PNES.
METHODS: Retrospective review of questionnaires of 42 consecutive patients who came to the PNES clinic at Children's Healthcare of Atlanta from July 2019 to January 2020. We assessed life adverse events, psychosocial functioning (Pediatric Symptom Checklist-17, PSC-17) and somatic symptoms (Children's Somatic Symptom Inventory-8, CSSI-8).
RESULTS: There were 33 females and 9 males (mean age =15 (± 2.6). The age of symptoms onset was 13.4 (± 2.8). Majority (33, 82%) had daily to weekly episodes. Twenty patients (53%) reported life-adverse events including sexual assaults (N=11, 29%). Sixteen patients (42%) had suicidal ideation or attempts. Of symptoms of CSSI-8, headache was the most common complaints, followed by dizziness and weakness. Female were more likely to have experienced

life adverse events (p= 0.03) while males were more likely to present with neurological disabilities such as autistic spectrum disorder, cerebral palsy and learning disability (p=0.04).
CONCLUSIONS: Female predominated in our PNES clinic (33:9 = 3.7:1). There were no significant difference in clinical demographics or psychosocial functioning between genders except for two predisposing factors: life-adverse events and neurological disabilities. Despite the broad clinical similarities between males and females, our data highlights gender-specific approaches and management may be needed.
KEYWORDS: Epilepsy, Cognitive/Behavioral Disorders (including Autism)

125. Clinical characteristics of infantile spasms from a tertiary care hospital in Bangladesh: analysis of 100 cases
Saha Narayan (Dhaka, Bangladesh) Hoque Sheikh Azimul, Islam Ariful, Chowdhury Yamin Shahriar, Harini Chellamani, Yuskaitis Christopher, Alam Md. Bardrul, Mohammad Quazi Deen, Mazumdar Maitreyi

OBJECTIVE: To describe the clinical and neurophysiological characteristics and short-term outcomes of infantile spasms.
METHODS: This observational study was undertaken the National Institute of Neuroscience & Hospital (NINS&H) in Dhaka, Bangladesh during March-December 2019. A total of 100 consecutive cases of infantile spasm were included. Data were obtained by standardized questionnaires and review of the medical record. Parents provided informed consent. The Human Research Committees at the NINS&H and Boston Children's Hospital approved this study.
RESULTS: Sixty-three percent of cases were male. The median age at onset of spasm was 4.9 months but the median age at time of presentation to NINS&H was 10.4 months. Typical hypsarrythmia was found in a quarter (26%) of children and modified hypsarrythmia in forty percent. Neuroimaging was available for 33 children and revealed HIE changes in 25 and cortical malformation in 8 cases. The main medication prescribed prior to presentation to NINS&H was phenobarbital (PB) (41%), followed by valproic acid (SVA) (37%). After evaluation at NINS&H, 59% of children received ACTH as monotherapy, 25% received a combination of ACTH and SVA, and 8% received a combination of ACTH and levetiracetam. Three percent of children received therapy that included Vigabatrin. Fifty percent achieved seizure freedom after 36 days, and this response rate was 74% after 6 weeks.
CONCLUSIONS: Among 100 children with infantile spasm in Bangladesh, we found a delay in receiving recommended treatment. Our series showed good short-term response to therapies containing ACTH therapy. Long-term follow-up and exploration of etiology are needed.
KEYWORDS: Epilepsy, Rare Diseases

126. Cathodal transcranial direct current stimulation (ctDCS) for children and adolescents with medically-refractory focal epilepsy
Kaye Harper (Boston, MA, United States) San-Juan Daniel, Salvador Ricardo, Damar Ugur, Pascual-Leone Alvaro, Ruffini Giulio, Shafi Moushin, Rotenberg Alexander

OBJECTIVE: Transcranial direct current stimulation (tDCS) is a noninvasive neuromodulation method where low-amplitude electrical current is conducted to the cortex via scalp electrodes. Cathodal tDCS (ctDCS) suppresses cortical excitability, and may suppress seizures in drug-

resistant epilepsy. Adults and children with intractable focal seizures were included in a recent 20-subject open-label ctDCS trial, where cathodal current was concentrated over a predetermined seizure focus, and the anodal components of the electrical field were distributed broadly over the scalp. We now report the outcome in the pediatric subgroup.
METHODS: Children (n=9; age range 9-18 years, a subgroup of the 20 enrolled subjects) with focal, intractable epilepsy, some with prior craniotomy (n=2) underwent 10-consecutive days of ctDCS. Per patient, a stimulation montage, comprised of ≤8 stimulation electrodes, delivering a total of 2 mA, was generated based upon cortical anatomy and seizure focus localization. Seizure frequency during 8-week-baseline and 8-weeks post-treatment was measured via diary. Adverse events were monitored continuously.
RESULTS: Median seizure frequency declined by 51% ($p<0.05$) at the 8-week follow-up after treatment. Mild-moderate adverse events included tingling sensation under the stimulation electrodes (n=9, 100%), and anxiety during stimulation (n=1, 11%). One participant reported a perceived increase in seizure frequency on day-3 of stimulation and thus exited from the study. Seizure suppression in this pediatric subgroup did not differ from the adult subgroup (n=11, n.s.).
CONCLUSIONS: Cathodal tDCS has potential to reduce seizure frequency, safely, in children with refractory focal epilepsy, including subjects who have failed prior epilepsy surgery.
KEYWORDS: Epilepsy, Translational/Experimental Therapeutics

127. Parenteral Knowledge, skills and Attitudes towards children with Epilepsy in Egypt.
Elsakka Elham (Alexandria, Egypt) Abd Elmaksoud Marwa, El said Huda, Ibrahim Eman

OBJECTIVE: To evaluate the knowledge, attitudes and skills toward epilepsy among parents of children with epilepsy in comparison to parents with children without epilepsy.
METHODS: Data collected through a structured questionnaire that was designed, translated into Arabic and analyzed statistically in a cross-sectional study in the period from January 2019 to June 2019 of a total of 683 Egyptian parents divided as two groups, group I (n=223) of parents who have a child with epilepsy recruited from Paediatric Neurology Outpatient Clinic of Alexandria University Children's Hospital and group II (n=460) of parents who do not have a child with epilepsy recruited from outpatient clinics, wards of AUCH, or from general population.
RESULTS: This study showed that poor knowledge was significant estimating 89.7% among parents who have a child with epilepsy and 77.2% among parents who do not have a child with epilepsy. As for the attitude, 69.5% of group I and 56.3% of group II have negative attitude. 66.8% of group I and 72.6% of group II have poor practice skills need for emergency management of an acute seizures. 41 % of parents of children with epilepsy feels like there is a discrimination against their children in our society, and there is not enough support from the community to their child's epilepsy.
CONCLUSIONS: Poor knowledge, negative attitudes and poor skills for management of acute seizures were found among both parents of children with epilepsy and children without epilepsy.
KEYWORDS: Epilepsy

128. Therapeutic Response in Pediatric Absence Epilepsy with Concomitant Focal Interictal Epileptiform Discharges
Rao Chethan (Jacksonville, FL, United States) Rappoport Adam, Sheth Raj

OBJECTIVE: Patients with absence epilepsies may additionally have focal interictal epileptiform discharges (FIEDs), for which the therapeutic consequences are not well understood. We, therefore, assessed the response to first-line treatment and number of anti-seizure medications (ASMs) required for childhood absence epilepsy (CAE) and juvenile absence epilepsy (JAE) patients with FIEDs.
METHODS: We performed a retrospective chart review of 48 patients ≤15 years of age seen between 2009 and 2015 with generalized spike-wave and FIEDs on routine EEG. Inclusion criteria were met for 16 patients with idiopathic primary generalized epilepsy (11 CAE and 5 JAE). Initial ASM response rates and mean number of ASMs required were calculated for both CAE and JAE. Independent-sample t-tests were conducted for mean comparisons.
RESULTS: The mean age was 10.1 years (SD=3.1). The overall response rate to initial ASM was 31.3%. The response rate among CAE was non-significantly higher (36.4%) compared with JAE (20.0%) (P-value=0.134). The average number of ASMs required for seizure freedom was 1.82 for CAE and 2.4 for JAE (P-value=0.342). The most frequent type of initial ASM used was ethosuximide (81.8% CAE, 60.0% JAE), which is in line with current treatment guidelines.
CONCLUSIONS: Our findings indicate a low response to initial ASM among both pediatric CAE and JAE patients with FIEDs compared with literature-reported initial response rates for CAE and JAE patients in general (53-59% and 70-90%, respectively). We observed a trend for a lower response rate and higher number of ASMs needed in JAE compared with CAE, but differences were not statistically significant.
KEYWORDS: Epilepsy

129. Eye-closure sensitivity in Sunflower Syndrome
Luo Yancheng (Boston, MA, United States) Sourbron Jo, Nagy Amanda, Thiele Elizabeth

OBJECTIVE: Sunflower syndrome (SS) is a rare, photosensitive epilepsy characterized by hand-waving (HW) associated with epileptiform discharges and an attraction to light. Eye-closure sensitivity (ECS) has been described in other idiopathic generalized epilepsies such as Juvenile Myoclonic Epilepsy and Jeavons syndrome[1]. The goal is to examine the eye closure abnormalities, which have not been previously defined in SS patients.
METHODS: The video-EEGs of 5 patients (A-E) with Sunflower syndrome were reviewed. All clinical episodes of hand-waving were reviewed. ECS is defined as epileptiform discharges occurring within 2 seconds after eye closure/rolling[2].
RESULTS: In total, 126 clinical events of handwaving were analyzed. 112 of the 126 events were associated with generalized epileptiform discharges. ECS was seen in 105 of the 112 events (94%). Please see graph 1.
CONCLUSIONS: Of all HW events captured in our SS patients, over 90% were preceded by eye closure, hence, eye-closure sensitivity. Eye-closure sensitivity has been described in other idiopathic generalized epilepsies with a female predominance and could be associated with worse seizure control[3,4]. The presence of ECS in SS might suggest a shared pathophysiology of these similar but also distinct epilepsy syndromes.
KEYWORDS: Epilepsy

130. Serum α-synuclein and IL-1β are increased and correlated with measures of disease severity in children with epilepsy: potential prognostic biomarkers?

Choi Jieun (Seoul, Republic of Korea) Kim Soo Yeon, Kim Hunmin, Lim Byung Chan, Hwang Hee, Chae Jong Hee, Kim Ki Joong, Oh Sohee, Shin Jeon-Soo

OBJECTIVE: To determine whether α-synuclein and cytokines are correlated with the degree of neuroinflammation and/or neurodegeneration in children with epilepsy and with acquired demyelinating disorders of CNS, as a prototype of autoimmune neuroinflammatory disorders.
METHODS: we analyzed serum and exosome levels of α-synuclein and serum proinflammatory and anti-inflammatory cytokines using single and multiplex ELISA kits among 115 children with epilepsy and 10 acquired demyelinating disorders of the CNS and compared to 146 controls. Patients were enrolled prospectively and blood was obtained from patients within 48 hours after acute afebrile seizure attacks or relapse of neurological symptoms. Acquired demyelinating disorders of the CNS include acute disseminated encephalomyelitis, multiple sclerosis, neuromyelitis optica spectrum disorders, and transverse myelitis.
RESULTS: Serum α-synuclein levels were significantly increased in patients with epilepsy and acquired demyelinating disorders of the CNS compared to controls (both, $p<0.05$) and showed correlation with measures of disease severity both in epilepsy ($p<0.05$, $r=0.2132$) and in acquired demyelinating disorders of the CNS ($p<0.05$, $r=0.5892$). Exosome α-synuclein showed a significant correlation with serum α-synuclein ($p<0.0001$, $r=0.5915$). Serum IL-1β levels were correlated only with the numbers of antiepileptic drug used in children with epilepsy ($p<0.001$, r=0.3428).
CONCLUSIONS: Serum α-synuclein levels were significantly increased in children with epilepsy and with acquired demyelinating disorders of the CNS and correlated with measures of disease severity. Serum IL-1β levels showed significant correlation only with drug resistance in children with epilepsy. Thus, these data support that serum levels of α-synuclein and IL-1β are potential prognostic biomarkers for disease severity in children with epilepsy.
KEYWORDS: Epilepsy, Infections/Neuroimmunology

131. Long-term epilepsy control, motor function, cognition, sleep and quality of life in a follow-up cohort of children with infantile spasms

Bhanudeep Singanamalla (Chandigarh, India) Madaan Priyanka, Sankhyan Naveen, Saini Lokesh, Malhi Prahbhjot, Suthar Renu, Gahlot Saini Arushi

OBJECTIVE: Considering the paucity of literature on long-term outcomes in infantile spasms (IS), the current study was designed to objectively assess epilepsy, motor function, cognition, sleep and quality of life outcome and their predictors in a follow-up cohort with IS at more than 5 years of age.
METHODS: A follow-up cohort of IS (diagnosed between 2002-2014; aged 5-14 years) was assessed (directly or telephonically) for epilepsy severity, functional status (gross motor and hand function), social quotient, behavioral comorbidities {Autism Spectrum Disorder(ASD) and Attention Deficit Hyperactivity Disorder (ADHD)}, sleep problems, and quality of life (QoL) using Early Childhood Epilepsy Severity Scale (E-Chess), Gross Motor Function Classification System (GMFCS), Manual Ability Classification System (MACS), Vineland Social Maturity Scale (VSMS), Diagnostic and Statistical manual of Mental disorders-5 (DSM-5) criteria, Children's Sleep Habits Questionnaire (CSHQ), and PedsQL-Epilepsy module respectively.
RESULTS: Among 402 children enrolled, one-third were seizure-free (for at least two years) at last follow-up while 60% evolved to Lennox-Gastaut syndrome (LGS). Comorbidities included

unfavorable motor status (130/402), moderate to profound intellectual disability (111/164), ASD (42/164), ADHD (18/164), poor sleep (135/164) and impaired quality of life (115/164). The predictors of long-term epilepsy control were etiology {Odds Ratio (OR)-3·83, p-<0·0001} and age at onset of spasms (OR-2·83, p-0·035). Etiology also predicted long-term sleep outcome (OR-3·21, p-0·006).
CONCLUSIONS: The etiology and age at onset of IS were significant predictors of long-term epilepsy control. Age at onset of spasms more than five months and probable genetic etiology were the predictors of early remission by five years of age.
KEYWORDS: Epilepsy, Cognitive/Behavioral Disorders (including Autism)

132. Comparing Quality of Life (QoL) among Adolescents with Epilepsy and/or Cerebral Palsy, and the General Population
Ronen Gabriel (Hamilton, Ontario, Canada) Boldyreva Uliana, Streiner David, Rosenbaum Peter

OBJECTIVE: To compare: (1) self- and proxy-reported quality of life (QoL) in adolescents with epilepsy, cerebral palsy (CP), both epilepsy and CP, and a representative general population sample; and (2) parental stress between parents of adolescents with epilepsy, CP, or both epilepsy and CP.
METHODS: This is a cross-sectional observational study with 496 adolescents with epilepsy, 699 with CP, 192 with both CP and epilepsy, and 15 396 from the general population, assessed with the KIDSCREEN-52 and Parenting Stress Index (PSI).
RESULTS: All KIDSCREEN-52 domains showed statistically significant differences across groups. The epilepsy population showed clinically better scores for 'school environment' than the general population (Cohen's d=0.62). Parents scored adolescents with CP lower than adolescents with epilepsy or general populations on 'physical health' (d=0.57, d=0.55) and 'social-support and peers' (d=0.82, d=0.91). Parents of adolescents with CP scored them lower than parents of the epilepsy group on 'autonomy' (d=0.62). Parents of adolescents with epilepsy scored them lower on 'mood and emotions' (d=0.52) and 'social acceptance' (d=0.66) than the general population. PSI scores were better for parents of adolescents with CP than for parents of adolescents with epilepsy (d=2.12, d=2.70, d=3.35, d=1.67).
CONCLUSIONS: Adolescents with epilepsy or CP self-report equal or better QoL than the general adolescent population, which should comfort families and allow clinicians to address parental concerns. Parental stress level was lower in parents of children with CP or both CP and epilepsy, than in those with only epilepsy.
KEYWORDS: Epilepsy

133. Neuronal Maturation can Change Excitatory/Inhibitory Synaptic Ratios in Epileptogenesis
Sarnat Harvey (Calgary, Alberta, Canada) Flores-Sarnat Laura

OBJECTIVE: The balance or ratio between excitatory (glutamatergic) and inhibitory (GABAergic) inputs into maturing individual cortical neurons influences their epileptic potential. Axodendritic synapses are mainly excitatory; axosomatic synapses are inhibitory. Pathological factors that alter either synaptic inputs can be demonstrated in tissue sections. Increased mitochondrial activity identifies excessively discharging neurons. Other factors of normal

neuronal maturation include sprouting of neurites, ATPase pump to maintain resting membrane potential/depolarization threshold, membrane receptors and ion channels, biosynthesis and axoplasmic transport of neurotransmitters and enzymes of degradation.
METHODS: Neuropathological study of surgical resections for epilepsy in 20 infants and children; and autopsy of 30 human fetuses of 13 to 38 weeks gestation were examined using immunocytochemical markers in all and electron microscopy in most surgical cases.
RESULTS: Factors influencing afferent synaptic ratios include: A) proteoglycan (keratan sulfate) binds to somatic membranes but not to dendritic spines, and may be focally diminished (cerebral atrophy; schizencephaly; lissencephaly) or augmented (holoprosencephaly); B) satellitosis of glial cells displaces axosomatic synapses; C) impaired development of dendritic spines causes decreased excitation (Down syndrome); D) synaptic short-circuitry of fused molecular zones of adjacent gyri (polymicrogyria); E) peri-neuronal inflammation (tuberous sclerosis) and heat-shock proteins.
CONCLUSIONS: Neuropathological examination of surgical and post-mortem brain tissue can demonstrate subcellular changes that help explain either epilepsy or lack of seizures at a cellular level in immature brains that compliments neuroimaging, EEG, genetic and clinical findings in individual patients. Excitatory/inhibitory synaptic ratios are altered by impaired neuroblast maturation in malformations and neonatal encephalopathies and influence neuronal epileptogenesis.
KEYWORDS: Epilepsy, Neonatal & Fetal Neurology, Neuroscience

134. In new onset epilepsy, does levetiracetam as the first anticonvulsant impact intractabiity?
Misra Sunita (Chicago, IL, United States) Tatachar Priyamvada

OBJECTIVE: A favorable response to the first anticonvulsant predicts a greater chance of seizure freedom. Intractability is defined as failure of two or more appropriate medications used at an adequate dose and duration. Currently, one third of patients with epilepsy are considered intractable. The goal of this study is to determine if patients who receive levetiracetam as the first anticonvulsant are more likely to become intractable and what clinical features may predict poor response to this medication.
METHODS: The study was approved by the Lurie Children's Hospital Institutional Review Board. A single site retrospective review of pediatric patients who received levetiracetam as the first medication for new onset epilepsy were identified. Data collected included epilepsy classification, anticonvulsant trials, reason for levetiracetam discontinuation, and surgical candidacy.
RESULTS: We reviewed 30 patients with levetiracetam prescribed as the first anticonvulsant. Twenty-two patients progressed to intractable epilepsy. Seventeen of the 22 intractable epilepsy patients had focal features and 11 are currently being evaluated for epilepsy surgery candidacy. Sixteen out of the 22 intractable patients discontinued levetiracetam due to inefficacy or side effects.
CONCLUSIONS: Many providers use levetiracetam as the first medication for all types of epilepsy, regardless of etiology. With levetiracetam there is a risk of inadequate seizure control combined with significant behavioral side effects that may lead to early treatment failure. Thus, a thoughtful approach to initiating medications on patients with new onset epilepsy is warranted to prevent intractability.

KEYWORDS: Epilepsy

135. Sleep characteristics among children with primary generalized epilepsy: A Polysomnography based study

Kaushik Jayashankar (Rohtak, India) Yadav Vikas, Bala Kiran, Nanda Sanjiv

OBJECTIVE: To describe the sleep profile in a cohort of children 5-15 years with idiopathic generalized epilepsy (IGE) using polysomnography (PSG) and Children's Sleep Habits Questionnaire (CSHQ) and Pittsburg Sleep Quality Index (PSQI)
METHODS: A case control study was performed among children aged 5-15 years with idiopathic generalized epilepsy (IGE) served as cases. The controls included age and gender matched healthy controls. The baseline demographic profile, clinical seizure characteristics were recorded. Sleep characteristics were recorded using CSHQ (5-10 years) and PSQI (11-15years). Overnight Polysomnography record was performed among all cases and controls.
RESULTS: A total of 30 cases of IGE [Juvenile absence epilepsy: 16 (53.3%); Juvenile myoclonic epilepsy: 11 (36.6%); Epilepsy with myoclonic absence: 2 (6.6%) and Doose syndrome: 1 (3.3%)] and 30 controls were enrolled in study. The global CSHQ score was significantly higher among children with IGE as compared to controls [58.81(10.85) vs 32.33(4.13); p<0.01]. All the sleep architecture parameters on PSG was comparable between cases and controls except percentage of REM sleep duration (in minutes) which was significantly lower among cases [6.18(5.45) vs 9.03(5.27); p=0.04]. Among the respiratory parameters AHI [4.94(6.52) vs 2.44(1.33); p=0.04], frequency of arousals [57.10(28.54) vs 31.46(13.68); p<0.01], percentage of oxygen desaturation >4% [31.93(41.73) vs 5.40(3.49); p<0.01], were significantly higher among children with IGE when compared to controls.
CONCLUSIONS: Children with idiopathic generalized epilepsy have significantly higher sleep disturbances when compared to healthy children. Hence sleep evaluation should be considered as a part of evaluation of children with primary generalized epilepsy.
KEYWORDS: Epilepsy

136. Clinical characteristics and risk factors of epilepsy associated with encephalomalacia in pediatric patients

Kong Juhyun (Yangsan, Democratic People's Republic of Korea) Nam Sang Ook, Lee Yun-Jin

OBJECTIVE: Encephalomalacia is characterized by localized softening of brain tissues due to inflammation or hemorrhage. There were few studies about encephalomalacia and its association with epilepsy. This study aimed to analyze the characteristics and risk factors of epilepsy in the patients with encephalomalacia.
METHODS: We reviewed 221 pediatric patients below 18 years old and visited Pusan National University Children's Hospital from November 2008 to March 2018. We included patients who had encephalomalacia on brain MRI, and follow up period more than 1 year after acute brain insult. Exclusion criteria were patients with hypoxic ischemic encephalopathy, neurodegenerative disease, mitochondrial disease, inborn errors of metabolism, and lesions confined only to white matter. We compared between the patients with (group A) or without epilepsy (group B).
RESULTS: There were 140 patients (73 Males, 67 Females, ratio 1:0.9) who met the criteria. There were 52 patients in group A (37%). The median age at acute insult was 0.11(IQR, 0-5.32)

years and the median age at diagnosis was 2.35 (IQR, 0.38-9.4) years. The duration between acute insult and diagnosis of epilepsy was 1.67±2.96 years. When compared with group B, seizure during acute insult (p=0.017), CNS infection as etiology (p=0.017), comorbidity of intellectual disability (P<0.001), and EEG abnormality with interictal epileptiform discharges and abnormal background activity (P<0.001) were significantly higher in group A.
CONCLUSIONS: Seizure during acute insult and intellectual disability after acute insult were risk factors of epilepsy. Abnormal EEG findings, especially abnormal background activity and interictal epileptiform discharges at the diagnosis of encephalomalcia were closely correlated with epilepsy.
KEYWORDS: Epilepsy, Neuroimaging, History of Child Neurology

137. Comparison of different methods to induce sleep in pediatric electroencephalogram recording
Holsakul Kornkamol (Bangkok, Thailand) Poonmaksatit Sathida, Tiumrakit Pariyapa, Veeravigrom Montida

OBJECTIVE: To compare the efficacy of melatonin versus melatonin and sleep deprivation versus chloral hydrate and sleep deprivation to induce sleep in pediatric EEG recording in Asians.
METHODS: A randomized single-blinded controlled trial of 45 patients aged 1-5 years and in-cooperative older patients, subjects were randomized into three groups; melatonin (group A), melatonin, and sleep deprivation (group B), and chloral hydrate and sleep deprivation (group C). The achievement of stage II sleep, sleep latency, and sleep duration was compared by the Kruskal-Wallis test, Mann-Whitney U test, and Pearson Correlation test.
RESULTS: From May 2019 to January 2020, 43 patients with a median age of 2.5 years (IQR = 1.7-3.8, range = 1.0-8.7 years) were included. There were 2 missing patients, EEG data loss, and undetermined sleep stages due to seizure. Stage II sleep was achieved in 92.8%, 100%, and 100% in groups A, B, and C, respectively. In groups A and B, patients needed ≥ 2 doses of melatonin 4/14 (28.6%) and 2/14 (14.3%), respectively. One patient (7.1%) in group A and B needed chloral hydrate. Sleep latency was not different statistically (p=0.06). Sleep duration was longer in group C as compared with groups A and B (p≤ *0.01*). Factors that affected sleep duration was younger age in group C (*p=0*.03). No side effect was observed in all groups.
CONCLUSIONS: Sleep latency was not different among the three groups. The use of melatonin or combined melatonin and sleep deprivation to induce sleep in routine EEG recording are safe and effective.
KEYWORDS: Epilepsy

138. The incidence and the risk factors of seizure after hematopoietic stem cell transplantation in children in South Korea
Moon Ja Un (Seoul, Republic of Korea) Lee In Goo

OBJECTIVE: Hematopoietic stem cell transplantation (HSCT) is associated with several nuerological complications including seizures. This study was designed to assess the seizure incidence, clinical manifestations and risk factors that can predict the occurrence of seizures after HSCT.

METHODS: The study group consisted of 36 patients (20 male, 16 female) who experienced seizure among 543 patinets (311 males, 232 females) who underwent HSCT at the Catholic University of Korea's Seoul St. Mary's Hospital.
RESULTS: The overall incidence of seizure after HSCT was 6.6%.
The onset of the seizure were most common after 100 days (52.7%). Among patients with seizures, 24 patients (66.6%) showed generalized seizure, 26 patients (75.0%) reported abnormal results in their electroencephalopgram, while 16 patients (61.5%) showed focal seizures and 30 patients (83.3%) reported abnormal results in their brain MRI. With regard to the possible risk factors of seizures, the type of HSCT and the grade of aGVHD were statistically significant. Patients with cord blood transplants had a 4.7-fold higher incidence of seizures compared to patients who underwent peripheral blood cell transplants or bone marrow transplants (P<0.001), and grade 2-4 of aGVHD had a 2.7-fold higher incidence of seizures (P=0.01).
CONCLUSIONS: Although the incidence of seizures in children with HSCT (6.6%) is much improved than the past (13.8%). Among the patients who underwent HSCT, using cord blood for transplanation and higher grade of aGVHD showed greater incidence of seizures occuring after HSCT. Overall, these findings provide a close observation and an intensive care are necessary for those high-risk patients.
KEYWORDS: Epilepsy

139. Epilepsy in Children with Tuberous Sclerosis Complex: A prospective observational study in Bangladesh.
Fatema Kanij (Dhaka, Bangladesh) Rahman Md Mizanur, Faruk Omar

OBJECTIVE: Epilepsy is an important neurologic feature of patients with Tuberous Sclerosis Complex (TSC). Most common seizure types are focal seizure and epileptic spasm. Seizure control often requires multiple antiepileptic drugs. This study has been done to evaluate the seizure types, EEG and neuroimaging features and drug treatment of epilepsy in TSC.
METHODS: This is a prospective observational study taken place in Bangabandhu Sheikh Mujib Medical University in 70 patients with TSC with epilepsy from 2011 to 2019.
RESULTS: Seventy patients with a mean (SD) age of 5.64+3.96 years were identified, 57.1% were female. Most common type of seizure was focal seizure (46%). Epileptic spasm occurred in 17% patients, all of them had seizure onset before 1 year. In 47% patients the EEG showed focal epileptic discharge; hypsarrhythmia was found in most of the patients with epileptic spasm. Majority of the patients needed more than one drug to control seizure. Only 34% patients were seizure free for at least 12 months, 22.8% patients had drug resistant epilepsy.
CONCLUSIONS: This study highlights the pattern of seizure, treatment pattern, response to drug and short time outcome of children with TSC with epilepsy in a developing country like Bangladesh.
KEYWORDS: Epilepsy

140. Intravenous Methylprednisolone with Oral Prednisolone versus Inj ACTH In infants with West Syndrome: A Randomized Controlled Trial
Fatema Kanij (Dhaka, Bangladesh) Rahman Md Mizanur, Akhter Shaheen

OBJECTIVE: West syndrome is an epileptic encephalopathy of infancy. According to guidelines Adrenocorticotrophic hormone (ACTH) is probably effective for short term

management of infantile spasm but there is little uniformity in treatment due to variable response. This study has been done to evaluate the efficacy of pulse methylprednisolone as compared to ACTH in children with west syndrome.
METHODS: Children between 3 months to 24 months with the diagnosis of west syndrome were included and ACTH and pulse methyprednisolone were given after randomization. In methyl prednisolone group oral prednisolone was given for 6 weeks
RESULTS: Total 87 children were enrolled; 12 patients lost in follow up. Finally 43 received ACTH and 32 received pulse methylprednisolone. After 6 weeks 42% of ACTH group showed 50-80% response, 25.5% showed 80-99 % response and only 3(7%) patients showed 100% response. In Pulse methylprednisolone group 31% showed 50-80% response, 25% showed 80-99 % response and 6 (19%) patients showed 100% response. This methylprednisolone treatment regimen did not cause significant or persistent adverse effects.
CONCLUSIONS: Pulse methylprednisolone followed by oral prednisolone for 6 weeks is as effective as ACTH for 6 weeks. Thus Methylprednisolone therapy can be an important alternative of ACTH.
KEYWORDS: Epilepsy

141. A study of disclosure practices of parents of children with epilepsy (CWE) in a tertiary care center.
Lachke Aishwarya (Mumbai, India) Desai Neelu, Udnai Vrajesh

OBJECTIVE: To study disclosure practices amongst parents of children with epilepsy (CWE), their attitudes about disclosure and relationship with demographic features. To identify enablers and barriers for disclosure and its impact.
METHODS: The study was undertaken over 7-month period in paediatric epilepsy clinic of a tertiary care hospital. It was a cross-sectional analytical, self-report survey about disclosure practices of parents of CWE with help of a semi-structured questionnaire validated after suggestions from experts.
RESULTS: 284 subjects were enrolled with male to female ratio of 1:1 for CWE whereas ratio of participating mothers to fathers was 3:2. 92.96% had disclosed their child's epilepsy to any two of the target groups and very few (7.04%) had kept it secret. Socio-economic status, type of family, epilepsy type, seizure frequency and timing did not influence disclosure. Almost all parents (99.29%) had revealed their child's epilepsy to extended family followed by friends, teachers, neighbours, peers of children and day care (wherever applicable). Type of seizure was the most common information (70.07%) disclosed followed by first aid and treatment regimens. Most common reason behind disclosure was better acceptance in society followed by increased assistance in emergency. Those with non-disclosure felt it was their private grief.
CONCLUSIONS: A significant change in the attitude of parents of CWE was noted regarding disclosure which enhances the chance of getting help from target groups and alleviates parental anxiety. However, some still consider epilepsy their private grief and maintain secrecy. Treating physicians should emphasize the importance of disclosure to parents of CWE.
KEYWORDS: Epilepsy

142. APPLICABILITY OF INTERNATIONAL LEAGUE OF EPILEPSY (ILAE) CLASSIFICATION OF EPILEPSY (1989,2010,2016) IN CHILDREN: AN OBSERVATIONAL STUDY IN A RESOURCE LIMITED SETTING

Anand Aakanksha (New Delhi, India)

OBJECTIVE: 1. To test the applicability of the 1989, 2010 and 2016 ILAE classification of epilepsy in a resource limited country in a hospital based population 2. To determine the electroclinical spectrum of pediatric epilepsy in a developing nation
METHODS: Children with epilepsy aged 1 month to 18 years presenting to the Epilepsy Clinic of a tertiary care centre in New Delhi, India were analyzed and classified by the 1989, 2010 and 2016 ILAE classification through parental interviews, review of medical records and available investigations (EEG, MRI, genetic/metabolic tests).
RESULTS: Seven hundred and twenty six children (436 males, mean age 6.4 years SD) were enrolled. Using the 1989 ILAE classification, we were able to classify 95.7%, and 82.6% children by the 2010 scheme. The 2017 ILAE classification could classify all 726 children at level I (seizure type), 664 (91.0 %) children at level II (epilepsy type) and an electroclinical syndrome could be identified in 409 (56.1%) of the children. An etiology could be identified in 75%, perinatal brain injury being the most frequent. West syndrome was the most common electroclinical syndrome identified in 22.7 % patients.
CONCLUSIONS: The 1989 ILAE classification systems was superior to the 2010 system (p=0.01) in epilepsy classification. There was no difference between the 1989 and 2017 schemes (p=0.31) or the 2010 and 2017 schemes (p=0.10). The 2017 ILAE classification, being multidimensional, allowed classification of children who could not undergo extensive evaluation due to economic constraints and also provided room for overlapping etiologies.
KEYWORDS: Epilepsy

143. Covariate Analysis Shows a Minor Role for Clobazam and Norclobazam in the Antiepileptic Efficacy of Co-administered Stiripentol

Koga Minako (Washington, DC, United States) Mekonnen Hana, Clarence-Smith Kathreen, Kazempour Kazem

OBJECTIVE: To assess the independent contribution of increased plasma concentrations of clobazam (CLB) and N-desmethylclobazam (NCLB) to the efficacy of stiripentol (STP).
METHODS: Two multicenter, randomized, double-blind, parallel group, placebo-controlled, 8 week-treatment trials in Dravet patients (STICLO France and STICLO Italy) were used for this study. A covariate adjusted analysis was performed based on using a logistic model where the dependent variable was treatment response (i.e., reduction by ≥ 50% of GTCS or GCS) and the independent variables were treatment group (i.e., STP or placebo), along with the change from baseline in CLB and NCLB plasma concentrations.
RESULTS: In both STICLO trials, STP was significantly more efficacious than placebo. Plasma concentrations of CLB and its metabolite NCLB at the end of treatment were higher in the STP group than the placebo group. Significant decrease in the frequency of GTCS and GCS in the STP group versus placebo was observed in all adjusted and unadjusted models. To evaluate if the covariates significantly contribute to the treatment effects, the covariates were added in the model. In the presence of STP treatment, neither increase in CLB nor NCLB plasma concentrations are significant contributors.
CONCLUSIONS: Results demonstrated that there is no statistically significant contribution of the increase in CLB and NCLB plasma concentrations on response to STP treatment. Thus, the effect of STP-associated increase in plasma concentrations of CLB and NCLB on treatment

response was marginal (if any); that is, the observed treatment effect is mainly from STP and not from an increase in CLB or NCLB.
KEYWORDS: Epilepsy, Rare Diseases

144. Ketogenic diet therapy for children with seizures secondary to neonatal hypoxic ischemic encephalopathy
Murray Ann (Rochester, MN, United States) Jagadish Spoorthi, Wong-Kisiel Lily, Nickels Katherine, Eckert Susan, Wirrell Elaine

OBJECTIVE: The ketogenic diet (KD) is an accepted treatment for refractory epilepsy, though limited evidence is available on impact of specific etiologies on efficacy. We evaluated children with epilepsy secondary to neonatal HIE treated with classic KD.
METHODS: Using a database of KD patients at the Mayo Clinic (2005-2017), data were abstracted specifically for children with epilepsy secondary to neonatal HIE. Children received classic KD, guided by the dietitian and epileptologist. Follow up data for efficacy and tolerability was obtained at 3, 6, 12, 24 months.
RESULTS: 16 children with seizures secondary to neonatal HIE were initiated on the KD. Median age at diet onset was 1.9 years, At time of diet initiation, patients were on a mean of 3 AEDs and had failed a mean of 4 medications. Retention rates on the diet were 94%, 88%, 75% and 56% at 3, 6, 12 and 24 months, with responder rates (>50% reduction in seizures) of 80%, 64%, 83% and 89% at the same time points. At final follow up, 7/16 had discontinued for: lack of efficacy (4), adverse effects (1, diarrhea), inability to achieve ketosis (1), and seizure freedom (1). Of those 9 that remained at 24 months, only 1 had side effect reported (malnutrition).
CONCLUSIONS: Among children with epilepsy secondary to HIE, the KD was effective and well tolerated. 8/16 were responders to the diet at 24 months. Diet was well tolerated by most, with only 1/16 discontinuing due to side effects.
KEYWORDS: Epilepsy, Neonatal & Fetal Neurology

145. A Community Health Worker (CHW) Approach to Improving Care for Children with Epilepsy in Zambia
Sham Lauren (Boston, MA, United States) Kalyelye Prisca, Chongo Harriet, Bell-Cross Sally, Sichilima Mukena, Mathew Manoj, Ciccone Ornella, Patel Archana

OBJECTIVE: Stigma surrounding epilepsy continues to play a significant role in the global treatment gap. Evidence suggests the most effective efforts for improved care incorporate community inclusion in addition to healthcare strengthening. This project demonstrates the impact of mobilizing community health workers (CHWs) at a first level clinic in Zambia, to promote improved care for children with epilepsy.
METHODS: 10 CHWs were trained on epilepsy education, medication compliance, and seizure first aid. First-level providers trained in a complimentary program on pediatric epilepsy referred families to the program (see Figure). Carers completed a pre-intervention questionnaire assessing baseline knowledge and attitudes toward their child's condition. Each CHW was assigned to visit 4 families, every 2 weeks for 10 months, with follow-up on changing knowledge and attitudes assessed routinely. Pre-intervention community focus groups were completed in the intervention site (Linda compound, Lusaka) and a control site without CHW intervention (Livingstone). Post-

intervention questionnaires will be completed at the end of the 10 month period by the carers, and post-intervention focus groups will be conducted in both the intervention and control sites.
RESULTS: 40 families were recruited. Interim analysis at 2 months has revealed issues around lack of consistent local medication supply and difficulty transporting non-ambulatory children to clinic, identifying avenues for potential intervention.
CONCLUSIONS: This study aims to assess the impact of a CHW program focused on epilepsy education and advocacy in a peri-urban community in Lusaka, Zambia, to address epilepsy stigma as well as act as a possible ongoing model of care in the community.
KEYWORDS: Epilepsy

146. Epilepsy and neurodevelopmental outcomes in a cohort with Tuberous Sclerosis with epileptic spasms- a developing country perspective
Saini Lokesh (Chandigarh, India) Mukherjee Swetlana, Sherawat Indar, Sankhyan Naveen, Madan Priyanka, De Dipankar

OBJECTIVE: To determine the epilepsy and neurodevelopmental outcomes in a cohort of Tuberous Sclerosis with epileptic spasms
METHODS: A prospective observational study and retrospective chart review involving children having Tuberous Sclerosis with epileptic spasms who were enrolled from January 2018 to July 2019. All children were subjected to DSM 5 criteria for Autism Spectrum Disorder (ASD), Attention Deficit Hyperactivity Disorder (ADHD) and Intellectual Deficit (ID).
RESULTS: Among the 30 children with Tuberous Sclerosis and epileptic spasms, median age of onset of spasms was 6 months (range-1 month to 12 months). However, median age at the time of enrolment was 5 years (range-1 year to 15 years). 73.3% (22) of these children fulfilled the criteria for West syndrome. At the time of enrolment, 76.6% (23) fulfilled the criteria for ID, 13.3% (4) had ASD and 16.6% (5) had ADHD. 4 children had ASD with ID whereas 3 had ID with ADHD. Median IQ/DQ score of 60.5 (range 20-105) was seen. 21 of these children (60%) had received Vigabatrin. Median duration of receiving Vigabatrin in these patients was 2 years (range 6 months to 3 years). 33.3% (10) children had drug refractory epilepsy at the time of enrolment. 3(10%) have evolved into EEG findings suggestive of Lennaux Gastaut syndrome. 8 (26.6%) have become seizure free out of which 3 were normal, 2 have ADHD and ID, 2 have ADHD and 1 has ID.
CONCLUSIONS: Children who require longer (more than 1 year) Vigabatrin therapy for epileptic spasm have poor long-term neurodevelopmental outcomes.
KEYWORDS: Epilepsy

147. Cathodal direct current stimulation induces drug-correctable potentiation of cortical excitability in TSC2 mouse in vitro
Sun Yan (Boston, MA, United States) Dhamne Sameer, Madsen Joseph, Stone Scelling, Sahin Mustafa, Rotenberg Alexander

OBJECTIVE: Cathodal direct current stimulation (cDCS) may suppress seizures, but its clinical efficacy is modest, and untested in genetic epilepsies. We tested, in vitro: a) whether cDCS can induce long-term depression (DCS-LTD) of cortical excitability in cortex derived from neuronal tuberous sclerosis complex 2 (TSC2) knockout mice (KOs) as it does in healthy mouse cortex; b)

whether novel drug-DCS pairing can facilitate cortical DCS-LTD to improve its antiepileptic capacity.
METHODS: cDCS effects on modulating neocortical field excitatory postsynaptic potential (fEPSP) were recorded by microelectrode array (MEA), and were plotted as an interpolated two-dimensional map. Given that TSC is characterized by an impaired mGluR5-mTOR pathway, we also tested the effects of a positive mGluR5 allosteric modulator (CDPPB) and an mTOR inhibitor (rapamycin) on the microanatomy of the cDCS modulatory pattern.
RESULTS: Our preliminary results showed that in TSC2 KO cortex (but not in control) long-term potentiation (DCS-LTP) of the fEPSP slopes, instead of cortical DCS-LTD was induced. The fraction of MEA channels expressing DCS-LTD under cathode was reduced from 56% in controls (n=5) to 28% in TSC2 KOs (n=7). We found that the fraction of MEA channels expressing DCS-LTD was increased to 60% (n=2) or 60% (n=3) by either CDPPB or rapamycin, respectively.
CONCLUSIONS: cDCS induces a large proportion of DCS-LTP of cortical excitability in epileptic cortex *in vitro*, which may explain the weakness of cDCS clinical efficacy. Moreover, our pharmacological results indicate a therapeutic potential of drug-DCS coupling to facilitate DCS-LTD in epilepsy treatment.
KEYWORDS: Epilepsy, Neuroscience, Translational/Experimental Therapeutics

148. Long-Term Safety and Efficacy of Cannabidiol (CBD) Treatment in Patients with Dravet Syndrome (DS): 3-Year Interim Results of an Open-Label Extension (OLE) Trial (GWPCARE5)

Shiloh-Malawky Yael (Chapel Hill, NC, United States) Halford Jonathan, Scheffer Ingrid, Nabbout Rima, Sanchez-Carpintero Rocio, Wong Matthew, Checketts Daniel, Dunayevich Eduardo

OBJECTIVE: DS is a developmental treatment-resistant epileptic encephalopathy, with onset by 15 months and a high mortality rate. This analysis assessed long-term safety and efficacy of add-on CBD treatment in patients with Dravet syndrome (DS) in the third analysis of the open-label extension (GWPCARE5 [NCT0224573]) of two randomized controlled trials (RCTs), GWPCARE1 (Phase 2/3) and GWPCARE2 (Phase 3).
METHODS: Patients initially received 20 mg/kg/day plant-derived highly purified CBD (Epidiolex®; 100 mg/mL oral solution); the dose could be decreased or increased to 30 mg/kg/day at the investigator's discretion. Primary endpoint: safety. Secondary efficacy endpoints: median percentage change from baseline in convulsive and total seizure frequency.
RESULTS: Of 330 patients who completed RCTs, 315 enrolled in GWPCARE5. At data cut-off, the OLE was ongoing and 43% of patients had withdrawn. Mean patient age was 10 years; 97% <18 years. Patients were taking a median of 3 concurrent antiepileptic drugs at baseline; during the OLE, 68% were taking clobazam, 67% valproate, and 38% stiripentol. Mean modal CBD dose was 22 mg/kg/day. Adverse events (AEs) and serious AEs occurred in 97% and 41% patients, respectively; 9% discontinued due to AEs. AEs of increased AST occurred in 12% of patients and increased ALT in 11% of patients. Four deaths occurred (considered nontreatment-related by the investigator). Median percentage reductions in seizure frequency overall (12-week windows over 156 weeks) was 45%-73% for convulsive and 49%–80% for total seizures.

CONCLUSIONS: Long-term treatment with add-on CBD in patients with DS produced sustained seizure reductions, with no new safety concerns.
Funding: GW Research Ltd
KEYWORDS: Epilepsy, Rare Diseases, Critical Care

149. Efficacy and tolerability of adjunctive lacosamide in the treatment of pediatric patients with primary generalized tonic-clonic seizures: subgroup analysis of a double-blind, randomized, placebo-controlled trial

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OBJECTIVE: To evaluate the efficacy and tolerability of lacosamide (up to 12 mg/kg/day or 400 mg/day) as adjunctive treatment for uncontrolled primary generalized tonic-clonic seizures (PGTCSs) in pediatric patients with idiopathic generalized epilepsy (IGE).
METHODS: SP0982 (NCT02408523) was a phase 3, double-blind, randomized, placebo-controlled trial of adjunctive lacosamide in patients (≥4 years) with IGE and uncontrolled PGTCSs taking 1-3 concomitant AEDs. The primary outcome was time to second PGTCS within 24 weeks of treatment. Data are presented for pediatric patients (≥4 to <18 years).
RESULTS: 49 pediatric patients were randomized and received ≥1 trial dose (lacosamide/placebo: n=24/n=25; Table 1). 23/24 (95.8%) patients on lacosamide and 23/25 (92.0%) on placebo completed the trial. Median treatment duration with lacosamide/placebo was 167/99 days. The risk of developing a second PGTCS during 24 weeks of treatment was numerically lower in patients on lacosamide than placebo (Kaplan-Meier survival estimates 61.03%/41.54%; hazard ratio 0.650 [95% CI 0.271-1.561]). The median time to second PGTCS was not estimable for lacosamide (>50% of patients did not experience a second PGTCS) and 132.0 days for placebo. Kaplan-Meier estimated freedom from PGTCSs at end-of-treatment for lacosamide/placebo was 20.0%/12.0%. More patients on lacosamide than placebo had ≥50% (70.8%/44.0%) or ≥75% (62.5%/36.0%) reduction from Baseline in PGTCS frequency/28 days, or were free from PGTCS during treatment (13.0%/8.3%). 22 (91.7%) patients on lacosamide and 15 (60.0%) on placebo had treatment-emergent adverse events (TEAEs) (Table 2).
CONCLUSIONS: Lacosamide was efficacious and generally well tolerated as adjunctive treatment for uncontrolled PGTCSs in pediatric patients with IGE.
KEYWORDS: Epilepsy

150. Safety and tolerability of intravenous lacosamide in children with epilepsy: an open-label trial

Farkas Viktor (Budapest, Hungary) Beller Cynthia, McClung Carrie, Yates Tanisia, Yuen Nancy, Roebling Robert

OBJECTIVE: To evaluate safety and tolerability of intravenous (IV) lacosamide infusion in pediatric patients (≥1 month to <17 years) with epilepsy.
METHODS: EP0060 (NCT02710890) was a Phase 2/3 open-label trial of lacosamide in pediatric patients (≥1 month to <17 years) with epilepsy. Patients received IV lacosamide (2-12 mg/kg/day or 100-600 mg/day; 15-60 minutes infusion) as replacement for oral treatment or initiated lacosamide as adjunctive IV treatment. Primary outcomes were adverse events reported

spontaneously by the patient and/or caregiver or observed by the investigator, and discontinuations due to adverse events.
RESULTS: 103 patients started and completed the trial; 55 patients in cohort 1 (≥8 to <17 years) and 48 patients in cohort 2 (≥1 month to <8 years) (Table 1). 79 (76.7%) patients had 1 infusion, 20 (19.4%) patients had 2 infusions, 1 (1.0%) patient had 3 infusions, and 3 (2.9%) patients had 10 infusions. Mean IV lacosamide exposure duration was 1.18 days (SD 0.71). Overall, 5 (4.9%) patients had a total of 7 treatment-emergent adverse events (TEAEs) following treatment with IV lacosamide (Table 2). The only TEAE reported in ≥2 patients was blood triglycerides increased. No patients reported serious TEAEs, severe TEAEs, or discontinued due to TEAEs; no TEAEs were considered drug-related by the investigator. No consistent or clinically relevant treatment-related changes from Baseline were observed for hematology, clinical chemistry parameters, vital signs, or 12-lead electrocardiograms.
CONCLUSIONS: IV lacosamide had an acceptable tolerability profile in pediatric patients (≥1 month to <17 years) with epilepsy, and no new safety concerns were identified.
KEYWORDS: Epilepsy

151. Quality Improvement Initiatives to Increase Administration of Folic Acid Supplementation for Adolescent Girls Prescribed Antiseizure Medication
Patel Namrata (Ann Arbor, MI, United States) Mackenzie Samuel, Hamade Maysa, Shellhaas Renée, McNamara Nancy, Fedak Romanowski Erin

OBJECTIVE: Antiseizure medications (ASMs) can reduce serum folic acid levels, which can lead to neural tube defects. Therefore, the AES and AAN recommend women of childbearing age who take ASMs receive daily folic acid supplementation (FAS). We aimed to improve rates of FAS prescription from 18.7% (averaged baseline) to 50% within one year with quality improvement (QI) interventions via Plan-Do-Study-Act cycles (Figure 1). We also aimed to identify barriers to prescribing FAS.
METHODS: Data were extracted via the DataDirect discovery tool from our outpatient pediatric neurology clinic visits between July 2016 and December 2019. Every three months, we compared rates of FAS among female patients aged ≥12 years prescribed ASMs. Our first intervention was a clinician education session combined with signage near provider work stations. The second intervention was a streamlined prescription process in the electronic medical record (EMR). We also surveyed our division clinicians to identify barriers to prescribing FAS.
RESULTS: There were 236±24 patients eligible for FAS within each three-month time interval. In the immediate post-intervention period, 21.8% received FAS. The proportion of FAS prescription remained ~20% thereafter (Figure 2). The most commonly identified barrier to prescribing FAS was the provider forgetting to discuss FAS during clinic visits.
CONCLUSIONS: Our first two QI interventions had only a marginal effect on increasing rates of FAS in the eligible population. Based on survey data regarding barriers to change, our next intervention will leverage the EMR for a Best Practice Advisory alert that will remind providers to prescribe FAS.
KEYWORDS: Epilepsy

152. STUDY OF BRAIN-TYPE NATRIURETIC PEPTIDE IN CHILDREN WITH EPILEPTIC SEIZURES

Bedair Hamdy (Alexandria, Egypt) Azouz Hanan, Elsakka Elham, Elbordini Magdy, Nour-Eldin Mohamed

OBJECTIVE: Elevated circulating amino-terminal of pro-brain natriuretic polypeptide (NT-proBNP) concentrations in childhood epilepsy and febrile convulsions, as well as in patients with brain ischemia and stroke have been reported suggesting a potential role of this prohormone in acute brain disorders. The potential use of the natriuretic peptides, as new biomarker for epileptic seizures was investigated
METHODS: The present study has been conducted in Alexandria University Children's Hospital on 30 epileptic children. Group I: (post-seizures group) comprised 20 postictal children were selected from those admitted to emergency room. This group was subdivided into: 10 children with partial motor epilepsy (PS) and 10 children with idiopathic generalized tonic clonic epilepsy (TCS). Group II: control group was randomly selected from those attending outpatient clinic after a seizure-free period at least for 2 month. For seizures group plasma concentration (NT-pro BNP) was measured within 4hrs after seizure onset and again 24–48 hours later. For control group NT-pro BNP was measured once.
RESULTS: NT-proBNP plasma concentrations within 4 hrs postictal were significantly higher among post-seizure group (285.83 ± 224.41 pg/ml; median: 219.00 pg/ml) compared to control group (mean:127.88 ± 16.44 pg/ml; median:119.80 pg/ml) P 0.02. Significant decrease of NT-proBNP levels in post-seizure group was observed after the 24–48 h follow-up (P 0.002). NT-proBNP plasma concentrations were significantly higher among TSC patients within 4 hrs postictal compared to both PS and controls (P 0.034)
CONCLUSIONS: The current study afford preliminary evidence that plasma NT-proBNP assay may be useful in recognition of epileptic seizures and the differential diagnosis between (TCS) and (PS).
KEYWORDS: Epilepsy, Critical Care

153. The clinical utility of initiating continuous video-EEG monitoring after midnight among hospitalized neonates and children

Buraniqi Ersida (Rochester, MN, United States) Nickels Katherine, Wong-Kisiel Lily, Wirrell Elaine, Payne Eric T.

OBJECTIVE: While continuous video-EEG monitoring (CEEG) has become standard of care at many tertiary pediatric hospitals, it remains resource intense with large institutional variability. We sought to determine the clinical utility of initiating CEEG after midnight among hospitalized neonatal and pediatric patients.
METHODS: This is a retrospective cohort descriptive study using our daily prospectively maintained inpatient CEEG database. At our institution, CEEG monitoring is available for hook-up 24/7 by registered EEG technicians who review, with epileptologist support, all EEG in real-time. We identified neonates and children who underwent clinically initiated CEEG on the ward or ICU between March 2015 - August 2019. We then abstracted detailed clinical and EEG characteristics for those patients hooked-up between 12-6 am, including the presence and duration of seizures or status epilepticus.
RESULTS: We identified 575 neonatal (age < 1 mos) and pediatric (1 mos – 18 yr) patients, among whom 105 (18%) had CEEG initiated between 12–6 am (*Figure 1*). The median age was 5 months (IQR range: 6.5 days – 4.5 years) and 54 % were females (*Table 1*). The majority

(64%) were admitted to our general pediatric ICU. Electrographic seizures with onset between 12–6 am were observed among 24/105 (23%) patients, and status epilepticus in 8/105 (8%). Subclinical only status epilepticus (all seizures lacked clinical correlate) occurred in 4/105 (4%). Among those with seizures, 50% were neonates.
CONCLUSIONS: Seizures are common among neonates and children evaluated with CEEG after midnight. CEEG is needed to identify status epilepticus in a small number of patients.
KEYWORDS: Epilepsy, Critical Care, Neuroscience

154. NEXT GENERATION WHOLE EXOME SEQUENCING IN THE GENETIC DIAGNOSIS OF EARLY ONSET EPILEPTIC ENCEPHALOPATHY
Hung Kun-Long (Taipei, Taiwan) Hsu Su-Jin, Wong Lee-Chin, Lu Jyh Feng

OBJECTIVE: Early-onset epileptic encephalopathy (EOEE) comprises a group of heterogeneous disorders in which development is impaired by recurrent clinical seizures during the early childhood period. The identification of causative mutations associated with EOEEs is useful for genetic counseling, and possibly for clinical management. The applications of next-generation DNA sequencing (NGS) technologies highlight the striking impact of these massive platforms on genetics and medicine.
METHODS: During recent years, we try to find the pathogenetic causes among cryptogenic epileptic encephalopathy patients through whole-exome sequencing (WES). Hereby we report the primary one-year data.
RESULTS: A series of 12 (6 males and 6 females) patients exhibiting EOEE with seizure onset within the first 2 years of life were collected and analyzed using WES. They aged 2 months to 23 years (average 5 years 11 months). Mutations were found in 8 (4 boys and 4 girls) probands; the overall mutation identification rate via WES was 66.7%. Two (25%) mutations involve ion channels, including each in GABRG2 and SCN2A. The other 6 (75%) mutations include each in CDKL5, KIDINS220, QARS1, SYNE2, TUBB2B, and IQSEC2. Seven (87.5%) of the identified mutations were confirmed to be de novo and one (12.5%) was parentally transmitted autosomal recessive inheritance. The majority (62.5%) of identified mutations were missense except for two nonsense mutations in CDKL5 and IQSEC2, as well as a frameshift mutation in KIDINS220.
CONCLUSIONS: Our data showed the genetic heterogeneity of EOEE. The clinical presentations were diverse with identified mutations. This study demonstrates the efficacy of WES in the genetic diagnosis of EOEE.
KEYWORDS: Epilepsy, Genetics

155. MODIFIED ATKINS DIET (MAD) VERSUS LOW GLYCEMIC INDEX TREATMENT (LGIT) IN DRUG-RESISTANT EPILEPSY IN CHILDREN: A RANDOMIZED CONTROLLED TRIAL
Kaushik Jayashankar (Rohtak, India) Gupta Surbhi, Dabla Surekha

OBJECTIVE: To compare the *efficacy and safety* of modified Atkins diet and low glycemic index diet (LGIT) among children with drug resistant epilepsy in terms of seizure reduction at 12 weeks and nature of adverse events.
METHODS: A randomized parallel arm, open labeled, controlled trial was conducted among sixty children aged 6 months to 14 years who had failed to respond to more than two anti-

epileptic-drugs. The trial was registered in CTRI (CTRI/2017/12/010898). Children were randomly assigned to receive MAD (n=30) or LGIT (n=30) as an add-on to the ongoing antiepileptic drugs.
RESULTS: Proportion of children with > 50% seizure reduction was significantly more in the LGIT group as compared to the mAD group (73.3% vs 43.3%, p < 0.02). The proportion of children with 90% seizure reduction (30% vs 13.3%, p = 0.21) and seizure freedom (16.6% vs 6.6%, p = 0.42) was comparable between the two groups at 12 weeks. Lethargy was the commonest side effect seen in mAD and LGIT group (53.3% vs 66.7%, *P*=0.43) followed by constipation and vomiting.
CONCLUSIONS: Low glycemic index treatment is an effective alternative to modified Atkins diet for treatment of children with drug resistant epilepsy considering its superior efficacy and comparable adverse effect profile
KEYWORDS: Epilepsy

156. Treatment of KCNT1-related epilepsy with similar clinical manifestations in two siblings with quinidine
Cheong Pou-Leng (Hsinchu, Taiwan) Fan Pi-Chuan

OBJECTIVE: To show the occurrence of KCNT1-related epilepsy with the same mutation and similar clinical manifestations in a family and the need of early use of quinidine and its efficacy.
METHODS: The medical records and electroencephalograms and epilepsy gene panel results of these two siblings were checked.
RESULTS: The elder brother has laryngomalacia, hypotonia, psychomotor retardation and progressive seizures since 6 months ago while the younger sibling has even earlier seizure onset since neonatal period with similar clinical manifestations. They have been given vigabatrin, carbamazepam, clobazam, phenobarbital and levetiracetam and even ketogenic diet and their seizure frequency was >10 times/day. Their EEG exam both showed multifocal epileptiform discharges. We used the gene panel and found them to have the same KCNT1 mutation (c.2719A>G; p.Thr907Ala). Then we added quinidine and their seizure frequency and duration decreased.
CONCLUSIONS: Though KCNT1-related epilepsy is inherited in an autosomal dominant manner, it is not reported to have a family with two siblings with the same genetic mutation and similar clinical manifestations. The use of quinidine is effective in stopping their seizures and its possible earlier use might result in a better neurodevelopmental outcome due to reduction of seizure frequency and duration.
KEYWORDS: Epilepsy, Genetics

157. Intractable Generalized Epilepsy and Autosomal Dominant Hypocalcemia: A Case Report
Rossi Gian (Memphis, TN, United States) Patterson Amy, McGregor Amy, Wheless James

OBJECTIVE: There is a heritable epilepsy linked to gain-of-function mutations of the calcium-sensing receptor (CaSR) gene, and independently to an endocrinopathy known as autosomal dominant hypocalcemia. Previously, there have been no reports of the two pathologies overlapping despite the purported single genetic cause. Our main purpose is to report an

exemplary case of a child meeting criteria for both intractable generalized epilepsy and autosomal dominant hypocalcemia due to a CaSR gene mutation.
METHODS: We detail our patient's clinical course to date and present the electrophysiological data, neuroimaging, neuropsychological and genetic testing. A literature review was performed concerning previously reported cases of genetic epilepsy associated with CaSR gene variants in humans with particular attention to serum calcium concentration abnormalities and related end-organ effects. Analysis is provided of the pertinent publications.
RESULTS: Our patient is a 16-year-old female with the unique presentation of intellectual impairment, behavior disorder, and intractable childhood-onset seizures, the latter of which include eyelid myoclonia with absences. Additionally, she has a chronic abnormality in calcium homeostasis presenting as hypocalcemia, hypercalciuria and central nervous system calcifications.
CONCLUSIONS: CaSR gain-of-function mutations may precipitate an intractable generalized epilepsy syndrome with a comorbid endocrinopathy. Epilepsy in these patients may be underdiagnosed, and further investigations are suggested in children with seizures presumed to be provoked by hypocalcemia.
KEYWORDS: Epilepsy, Genetics, Neurometabolic Disorders

158. Evaluation of adherence to pediatric status epilepticus management guidelines in Saudi Arabia
Tabarki Melaiki Brahim (Riyadh, Saudi Arabia) AlMohaimeed Bashayer, Bashiri Fahad, AlMohaimeed Suleiman, Hundallah Khaled

OBJECTIVE: To evaluate compliance with the 2017 Saudi pediatric status epilepticus management guidelines and to identify the main barriers to guideline adherence
METHODS: This was a cross sectional study conducted in September 2019, in which an electronic based survey using a case scenario to explore the usual management of a child with convulsive status epilepticus (CSE) was designed and sent to pediatric emergency physicians practicing in the Kingdom of Saudi Arabia. Adherence to the 2017 Saudi guidelines and to four algorithmic time-specific outlined goals was assessed.
RESULTS: 103 (70%) of 147 physicians working in Saudi Arabia and covering pediatric emergency departments responded to the survey. Of the respondents, 41% reported administering 2 or more doses of benzodiazepines, 6% administering non-benzodiazepine as first-line treatment, 23% administering suboptimal weight-based dosing, and 60% delaying the second-line management. In total, only 20% of the physicians reported full adherence to all four guideline components; 57% reported that they were not aware of the published guidelines.
CONCLUSIONS: Pediatric emergency physicians reported poor adherence to the 2017 published guidelines for the treatment of children with CSE in Saudi Arabia. The absence of awareness about the protocol was the main reported barrier to guideline adherence. Increasing awareness and training is, therefore critical for improving patient care.
KEYWORDS: Epilepsy

159. Evaluating the Efficacy of a Modified Atkins Diet Cooking Class to Improve Knowledge and Compliance: A Pilot Study
Briceno Lucia (Los Angeles, CA, United States) Klier Katie, Holder Deborah

OBJECTIVE: In an effort to improve understanding of the Modified Atkins Diet (MAD) in patients with epilepsy we started a monthly bilingual cooking class. Our goal was to provide additional education in a supportive group setting and to show families easy to prepare recipes in order to improve compliance and increase understanding of MAD.
METHODS: A ketogenic dietitian contacted MAD patients and invited them to a 2 hour group cooking class. A total of 17 families were contacted (7 English speaking and 10 Spanish speaking). The classes were held at Children's Hospital Los Angeles with food and supplies provided. The class was structured into 5 parts: Part 1: survey and pre-test, Part 2: presentation, Part 3: cooking time, Part 4: post-test, Part 5: discussion and networking.
RESULTS: Ten families participated, 5 in each class. One class was conducted in Spanish, one in English. Demographic characteristics for the participants were similar. Pre-test data indicated that the participating families, despite being on MAD for an average of 12-14 months scored a 2.9/5 on questions assessing their knowledge, compliance and comfort using MAD. Post-test data showed improvements to 4.1/5. Other benefits included learning new recipes and networking with new families with whom long term relationships were established.
CONCLUSIONS: Findings from this pilot study indicated that additional educational interventions are beneficial for patients on MAD for seizure control. A cooking class is an effective way to not only educate families but offer them a new support system that may improve long term success.
KEYWORDS: Epilepsy

160. Short-term Outcome of Infantile Spasms in Children Treated with Oral Prednisolone in Yangon Children Hospital, Myanmar
Hlaing Chaw Su (Yangon, Myanmar) Thair Cho, Min Aye Aye Mya, Ko Khine Mi Mi, Saan Aye Mu, Linn Kyaw, Thio Liu Lin, Mar Soe

OBJECTIVE: To compile and report the short-term treatment outcome of clinical infantile spasms (IS) on oral prednisolone. To determine factors associated with short term outcome of infantile spasms treatment
METHODS: A prospective cohort of 109 clinically diagnosed children with IS aged 1 month to 3 years were admitted to Yangon Children Hospital between August 2014 and October 2019. Mean age was 7.8 (2-36) months. Mean time lag to treatment was 2.4 (0-28) months. Prednisolone was administered according to United Kingdom Infantile Spasm Study (UKISS) protocol. EEG was performed on day 0 and 14 of oral steroid. All children were under intensive observation during treatment. Short-term seizure freedom was defined by an absence of clinical spasm for 48hrs on day 14.
RESULTS: On admission, the majority of the cohort had flexor spasms (87.2%). Hypsarrhythmia on initial EEG was found in 60 (55%). A majority (62.7%) had perinatal insult as presumed etiology. Clinical seizure freedom was noted in 82 (79.2%) at day 14 of prednisolone. Overall Improvement in EEG was seen in 96 (88.1%) on day 14, with hypsarrhythmia persisting in only 7 (6.4%) and non-hypsarrhythmia in 49 (45%).
CONCLUSIONS: The vast majority of this cohort was seizure free following 14 days of oral prednisolone. It was found that age of onset, time lag and etiology are not significantly associated with response to prednisolone. Only the presence of hypsarrhythmia on the first EEG shows a significant association with short-term seizure remission (see table).
KEYWORDS: Epilepsy

161. Effect of delayed treatment of seizures on neurodevelopmental outcome in children with KCNQ2 encephalopathy

Kamate Mahesh (Belagavi, India) Nalla Reddy Anuraag, Detroja Mayank

OBJECTIVE: To study the effect of delay in starting sodium channel blockers in treatment of seizures in KCNQ2 encephalopathy on the neurological and developmental outcome
METHODS: Children with genetically confirmed KCNQ2 mutations in the last 5 years were examined for neurological and developmental outcome. The final outcome was correlated with age at diagnosis of condition and use of sodium channel blockers
RESULTS: Five children had genetically confirmed KCNQ2 mutations. All had neonatal onset epileptic encephalopathy and normal neuroimaging findings. While 2 were treated with sodium channel blockers in the first 2 weeks of life, one was treated at 8 months of age, one at 12 months and one child was treated at 8 year of life with sodium channel blockers. While 2 who were treated in the first month of life were seizure free after a week and had normal development at 12 months and 2 years respectively, the two who continued to have seizures till 6-8 months of age because of non-use of sodium channel blockers, had speech delay with autistic spectrum disorders and the one where in the diagnosis was done at 8 years of age, had mixed (spastic and dyskinetic quadriparesis with contractures) and speech delay
CONCLUSIONS: Delayed diagnosis and delay in initiation of sodium channel blockers can lead to speech and behavioural problems in children with KNCQ2 mutations. If treatment delayed for years then there can be tone abnormalities like spasticity and dyskinesias along with speech and behavioural problems.
KEYWORDS: Epilepsy, Cognitive/Behavioral Disorders (including Autism), Genetics

162. Successful use of Brivaracetam in Super Refractory Status in FIRES (Febrile Infection Related Epilepsy Syndrome)

Ali Sikander (Leeds, United Kingdom) Taylor Michael, Pysden Karen, Hussain Shanawaz

OBJECTIVE: To describe the first use of brivaracetam in paediatric status.
METHODS: Retrospective review of patient notes, neurophysiological and pharmacological data.
RESULTS: A previously well 15 year old girl presented with new onset convulsive seizures in association with a non-specific febrile illness. She remained refractory to emergency status management and was admitted to PICU for management with midazolam and thiopentone but failed to achieve any control of clinical and subclinical seizures. She was trialled on Levetiracetam, Phenytoin, Phenobarbitone, Clobazam, Lacosamide and Carbamazepine. The ketogenic diet was employed early in the course but also failed to achieve adequate ketosis or seizure control. Extensive investigations looking at infective, structural and metabolic causes failed to find an etiology. Autoimmune encephalitis as well as treatment of a cytokine storm was considered and empirically treated with methylprednisolone, immunoglobulins, Anakinra and Tocilizumab. After remaining in refractory status for 6 weeks, a therapeutic trial of iv brivaracetam was commenced with a cessation of seizures within 24 hours.
The patient is now fully ambulant, breathing independently and attending hospital school. She has infrequent focal seizures which are managed by remaining on Brivaracetam with Clobazam and Valproate.

CONCLUSIONS: FIRES presents with catastrophic seizures in well children with a high mortality and cognitive morbidity. Our patient remained refractory until treatment with brivaracetam with a relatively good cognitive outcome. This is the first case, to our knowledge, where Brivaracetam has been used for pediatric status epilepticus successfully. It adds to the growing literature which supports the use of this medication in refractory status & FIRES.
KEYWORDS: Epilepsy, Infections/Neuroimmunology, Critical Care

163. Children with Dravet syndrome do continue to benefit from stiripentol along adulthood

Chiron Catherine (Paris, France) Helias Marie, Kaminska Anna, Laroche Cecile, de Toffol Bertrand, Dulac Olivier, Nabbout Rima, An Isabelle

OBJECTIVE: To evaluate continuing stiripentol treatment from childhood to adulthood in Dravet syndrome patients.
METHODS: Data from one center were retrospectively collected for the 40 patients in whom stiripentol was initiated during childhood or adolescence and continued in adulthood. Data were collected at all visits on stiripentol, from the last visit before 15 years (V_{15y}) to the last visit in adulthood (V_{adult}).
RESULTS: Generalized tonic-clinic seizures (GTCS) frequency and duration decreased (p=0.02 and p=0.008 respectively) from $V_{15y}$to V_{adult}.
At V_{adult}, even though most of the patients were still experiencing GTCS, 10 patients (25%) had had seizure-free period ≥ 1y during adulthood (up to 5y) and none experienced status epilepticus (vs. 3 at V_{15y}). Only one patient still had myoclonia. Early treated patients (from infancy to childhood) tended to present with better epilepsy and comorbidities outcome in adulthood than the lately treated patients (adolescence). No new stiripentol-related adverse events were reported and comedications were the same as in childhood (clobazam 40/40, valproate 39/40, topiramate 21/40). The mg/kg/day dose of stiripentol used in adults was lower than in children (typically 25-30 mg/kg/d vs 50 mg/kg/d).
CONCLUSIONS: The efficacy and safety of stiripentol started at pediatric age are maintained at very long term during adulthood. Prolonged stiripentol therapy tends to positively impact the late prognosis of epilepsy, especially when initiated before adolescence.
KEYWORDS: Epilepsy

164. Novel treatment approach to refractory nonconvulsive status epilepticus in a patient with Angelman syndrome utilizing intravenous methylprednisolone.

Karachunski Peter (Minneapolis, MN) Wang Sonya

OBJECTIVE: Nonconvulsive status epilepticus (NCSE) is a common complication in children with Angelman syndrome (AS). NCSE in AS is predominantly treated with i.v. and oral benzodiazepines and/or levetiracetam. We describe a patient with NCSE uniquely and successfully treated with i.v. administration of high dose of methylprednisolone.
METHODS: We conducted analysis of medical records. Electroencephalographic (EEG) studies were performed to confirm diagnosis of NCSE and response to treatment. EEG records were reviewed by two electroencephalographers independently utilizing qualitative and quantitative analysis.

RESULTS: A 7 yo male with AS presented with abrupt and severe behavioral deterioration which was diagnosed as NCSE. Initial treatment consisted of oral and then intravenous courses of benzodiazepines and levetiracetam without success. Patient was treated with daily 500 mg i.v. infusions of methylprednisolone for 5 days followed by slow oral prednisone taper. Initial, video EEG monitoring concurrent with behavioral change demonstrated significant burden of epileptic paroxysmal activity. Clinical improvement was achieved after 3 days of treatment. This correlated with resolution of electrographic seizures. Patient had a recurrence of NCSE in 6 months which was successfully treated utilizing the same novel approach.
CONCLUSIONS: This is the first report describing treatment of NCSE in the setting of AS with high dose of i.v. Methylprednisolone. This treatment was safe and effective and should be considered for AS patients presenting with refractory NCSE.
KEYWORDS: Epilepsy, Rare Diseases

165. Unsafe sleep practices are common among infants who require continuous video-EEG monitoring
Neville Kerri (Ann Arbor, MI, United States) Gaillard Jonathan, Shellhaas Renée

OBJECTIVE: Safe sleep practices can decrease the risk of Sudden Infant Death Syndrome (SIDS). American Academy of Pediatrics recommends: 1) supine positioning 2) room-sharing without bed-sharing 3) avoidance of soft bedding, pillows, or toys in the crib. The hospital setting provides an opportunity to re-enforce safe sleep practices for infants with complex medical conditions. To inform a quality improvement initiative, we obtained baseline data of sleep practices for infants who received continuous video EEG (cEEG) in a tertiary children's hospital.
METHODS: Infants aged 0-6 months who received cEEG between August and October 2019 and whose parents consented to research were included. Video recordings were reviewed for unsafe sleep practices.
RESULTS: Among 55 infants (total 150 cEEG days) 27% were neonates, 27% aged 1-3 months, 46% aged 4-6 months. cEEG occurred in the Emergency Department (N=13), general or moderate care floors (N=32) or Intensive Care Units (N=25; some had cEEG in >1 setting). Unsafe sleep was recorded for 50/55 infants (91%) with a median 2 unsafe sleep practices (IQR 1-2) per infant. Non-supine positioning occurred in 31/55 (56%) – 22 (39%) side-lying, 7 (12.5%) prone, and 4 (7.1%) other positions (i.e. in a stroller or swing). Co-sleeping was witnessed in 11/55 (20%) and soft bedding or extra items in the crib were seen in 42/55 (76%).
CONCLUSIONS: Among infants who require cEEG, unsafe infant sleep practices are ubiquitous. As this is a particularly vulnerable population at risk of SIDS and SUDEP, improvement in safe sleep while infants are admitted for cEEG should be a priority.
KEYWORDS: Epilepsy

166. Clinico-electroencephalographic features and outcome in pediatric convulsive status epilepticus: a longitudinal observational study
Chakrabarty Biswaroop (New Delhi, India) Tiwari Richa, Gulati Sheffali, Jauhari Prashant, Lodha Rakesh, Sankar Jhuma, Kumar Atin, Pandey RM, Sinha Rahul, Gupta Juhi, Zulfiqar M Luhar, Upadhyay Ashish, Kumar Suresh

OBJECTIVE: The objective of the current study is to prospectively describe clinical features, EEG and outcome in a pediatric convulsive status epilepticus (CSE) cohort and delineate outcome predictors.
METHODS: Children with CSE, aged 1 month to 14 years, presenting to a tertiary care teaching hospital in Northern India, from January 2017 to March 2019 were prospectively evaluated after ethical approval. The PCPS (Pediatric Cerebral Performance Scale) was used to determine in-hospital (timepoint A) and 3 months follow up (timepoint B) outcome. A drop in the PCPS scale from pre-status state by 2 or more levels was considered poor outcome.
RESULTS: Sixty one patients were analysed. The commonest etiology was structural (54.1%) and predominant semiology was generalised (62.3%).
An EEG done within 6 hours of presentation was abnormal in 85% . The predominant discharges were focal (41.2%) and multifocal (37.3%) arising from frontal regions (75%). One-fourth cases showed electrographic status.
Poor outcome at both timepoints (42.6% and 27.9% at A and B respectively) were significantly associated with benzodiazepine resistance, refractory SE, MODS and shock. Super-refractory SE at timepoint A, abnormal EEG background and generalised convulsive SE at timepoint B were also significantly associated with poor outcome. On multivariate analysis, benzodiazepine resistance at both timepoints and presence of MODS at time point B showed significant association.
CONCLUSIONS: Benzodiazepine resistance can be an early predictor of poor outcome in pediatric CSE. Multicentric prospective studies in larger population should be planned to identify risk factors and develop predictive models to prioritise therapy and aid prognostication.
KEYWORDS: Epilepsy, Critical Care

167. Discrepant expressive language localization by neuronavigated transcranial magnetic stimulation (nTMS) and functional magnetic resonance imaging (fMRI) in children and young adults with epilepsy

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OBJECTIVE: While fMRI is a widely-accepted method for pre-neurosurgical localization of eloquent cortical functions, neuronavigated transcranial magnetic stimulation (nTMS) has emerged as an important tool for noninvasive pre-surgical functional language mapping. Language maps resultant from fMRI and nTMS can yield discrepant results. This may relate to distinct physiologies measured by these techniques. fMRI measures the neurovascular response via the BOLD signal, while nTMS is reliant on induction of a virtual lesion. We test how often nTMS and fMRI provide discrepant expressive language mapping results.
METHODS: We compare lateralization of expressive language in cases where nTMS and fMRI results were discordant. We then compared these results to invasive mapping either by electrical cortical stimulation, Wada, or a decline in language abilities measured by Neuropsychology.
RESULTS: Successful expressive language mapping by nTMS and fMRI was achieved in 20 patients, where 9/20 (45%) of cases yielded discordant results. In 22% of these patients, fMRI revealed strictly unilateral expressive language (right n=2), while nTMS showed bilateral expressive language. In 44% of these patients, fMRI indicated bilateral cortical activation, while nTMS revealed unilateral expressive language function confined to the left hemisphere (n=4). In

the remaining patients with discrepant results (n=3) unilateral findings from the two modalities were such that fMRI showed right hemispheric expressive language, and nTMS showed contrasting left hemispheric lateralization.
CONCLUSIONS: In children and adolescents with focal epilepsy, presurgical language mapping by fMRI and nTMS may yield discordant results. In instances when fMRI indicates right frontal expressive language localization, nTMS may more accurately localize expressive language.
KEYWORDS: Epilepsy, Neuroimaging, Neuroscience

168. X-linked Familial Focal Epilepsy Associated with Xp22.31 Deletion
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OBJECTIVE: To describe the first genetic cause of X-linked familial focal epilepsy.
METHODS: We identified two families in our research database with X-linked focal epilepsy. Thorough epilepsy phenotyping was performed for all patients.
RESULTS: We identified three boys from two families, all of whom had X-linked ichthyosis and focal epilepsy. The two related boys were maternal cousins. Age of seizure onset ranged from 7 to 10 years, and all three patients had seizures that were relatively easily controlled. The epilepsy phenotype in all boys was consistent with self-limited focal epilepsy of childhood, most closely resembling childhood epilepsy with centrotemporal spikes (CECTS). Brain MRI was normal in two of the boys, with a third found to have a suspected focal cortical dysplasia. All three boys carried maternally-inherited hemizygous Xp22.31 deletions (estimated size 0.9 to 1.66 Mb), affecting 4 to 6 genes. Of the affected genes, only *STS* has clear clinical relevance; deletions and pathogenic variants in *STS* cause X-linked ichthyosis, though all patients described in this study had only minor skin findings.
CONCLUSIONS: The findings in these patients illustrate that X-linked familial focal epilepsy can occur, though is a rare entity. Although *STS* pathogenic variants are likely better categorized as an epilepsy risk factor, variants in this gene may partially explain the male predominance observed in specific epilepsy phenotypes, namely CECTS.
KEYWORDS: Epilepsy, Genetics, Rare Diseases

169. Use of Interleukin-6 Blockade with Tocilizumab in a Child with Febrile Infection-Related Epilepsy Syndrome (FIRES)
Stredney Coral (Boston, MA, United States) Case Siobhan, Sansevere Arnold, Son MaryBeth, Henderson Lauren, Gorman Mark

OBJECTIVE: Report tocilizumab as a novel treatment in children with FIRES. Tocilizumab was efficacious in a small series of adults with new onset refractory status epilepticus (NORSE)[1] and acutely in two children with FIRES-like presentations,[2] but efficacy and long-term outcomes in children are not well-established.
METHODS: Case report
RESULTS: A previously healthy six-year-old boy presented with focal seizures culminating in super-refractory status epilepticus one week after a febrile illness, meeting proposed diagnostic criteria for FIRES.[3] Initial brain MRI and CSF were unrevealing. EEG showed multi-focal seizures and extreme delta brush-like discharges.[4] Seizures were refractory to anti-seizure medications (ASMs), continuous midazolam, ketamine, and pentobarbital, and immunotherapy

(intravenous methylprednisolone, intravenous immunoglobulin, and anakinra). Ketogenic diet (KD) was initiated on day 14. On day 17, serum and CSF cytokine analysis revealed elevated IL-6 and 8 in the CSF only. Treatment with an IL-6 blocker, tocilizumab, was initiated on day 20. By day 23, seizure burden drastically decreased, allowing for weaning of continuous infusions. At one-year follow-up, he is seizure free outside of times of illness on five ASMs, attends kindergarten with an individualized education plan, and has acquired behavioral dysregulation and inattention. IQ subsets for processing speed, performance and verbal IQ are 60, 86 and 81, respectively.
CONCLUSIONS: This case highlights the use of KD and tocilizumab in a child with treatment-refractory FIRES with elevated CSF levels of IL-6 and 8. FIRES has high rates of morbidity and mortality not experienced by our patient.[5] Further controlled treatment trials are needed to understand the efficacy and safety profile.
KEYWORDS: Epilepsy, Infection/Neuroimmunology, Rare Diseases

170. Pulse methylprednisolone plus "low dose" prednisolone versus "low dose" prednisolone alone for treatment of children with West syndrome: An open-labeled randomized controlled trial
Kaushik Jayashankar (Rohtak, India) Kumari Nisha, Nanda Sanjiv, Bala Kiran

OBJECTIVE: To compare the efficacy and safety of intravenous pulse methylprednisolone followed by "low dose" prednisolone versus "low dose" prednisolone in management of children with infantile spasm.
METHODS: The study was an open-labeled, randomized controlled trial conducted among children aged two months to 30 months with a diagnosis of West syndrome. Children were randomly assigned to receive Pulse methylprednisolone (30 mg/kg for three days) followed by oral prednisolone (2 mg/kg) or oral prednisolone (2 mg/kg) alone.
RESULTS: A total of 24 participants received pulse methylprednisolone, and 26 participants received oral prednisolone. The efficacy of pulse methylprednisolone was comparable to oral prednisolone in terms of spasm cessation [11 (45.8%) Vs 7 (26.9%); P=0.24], more than 50% spasm reduction [16 (66.6%) Vs 11 (42.3%); p=0.09], more than 90% reduction [11 (42.8%) Vs 7 (26.9%); P=0.24], time to cessation of spasm [8 (6.3) days Vs 5.8 (2.5) days; P=0.41] and resolution of Hypsarrhythmia [5 (20.8%) Vs 2 (7.6%); P=0.21]. However, treatment failure was significantly less in the methylprednisolone group [9(37.5%)] when compared to the oral prednisolone group [17 (65.3%)] [P=0.04]. The adverse effect profile was comparable in the two groups.
CONCLUSIONS: Pulse methylprednisolone therapy followed by "low dose" prednisolone (2 mg/kg) was as effective as "low dose" prednisolone (2 mg/kg) therapy alone in achieving the cessation of spasm among West syndrome.
KEYWORDS: Epilepsy

171. First Time E-Cigarette Use Temporally Linked with Breakthrough Seizures in Two Adolescents with Epilepsy
Cook Robin (Ann Arbor, MI, United States) Leber Steven, Joshi Sucheta

OBJECTIVE: The neurological effects of e-cigarette use are poorly understood. Seizures temporally associated with e-cigarette use have been reported to the FDA. A minority of these

seizures occurred in people with a history of prior seizure. E-cigarette use may therefore pose particular risks in adolescents with epilepsy. Here we report two cases of breakthrough seizures in young people with epilepsy, temporally associated with first time e-cigarette use.
METHODS: We present two adolescents with epilepsy followed in the Pediatric Neurology Clinic at a tertiary care children's hospital who had breakthrough seizures within hours of first-time e-cigarette use. Written consent was obtained and electronic medical records were retrospectively reviewed.
RESULTS: The first (age 14) had focal epilepsy treated with levetiracetam monotherapy; in August 2017, she had a breakthrough seizure within an hour of first time e-cigarette use. The second (age 17) had catamenial generalized epilepsy treated with oral natural progesterone and levetiracetam; in October 2017, she had a breakthrough seizure within a few hours of vaping for the first time. Both patients were on levetiracetam and had experienced a single additional provoked breakthrough seizure in the 8 months prior to trying an e-cigarette, in the setting of non-adherence to medication or sleep deprivation.
CONCLUSIONS: E-cigarette use was temporally associated with breakthrough seizures in two adolescents with known, otherwise relatively well-controlled epilepsy. To help establish whether a causative relationship is present, providers should report breakthrough seizures which are temporally associated with e-cigarette use through the FDA's reporting website at http://www.safetyreporting.hhs.gov.
KEYWORDS: Epilepsy

172. Ketogenic Diet Therapy on Intractable Epilepsy and Neuro-inflammation in Infantile Alexander disease

Hamada Shu (Amagasaki, Japan) Kato Takeo, Sakakibara Takafumi, Kora Kengo, Okubo Tenshin, Kawaguchi Tatsuya, Tanaka Takayuki, Yoshida Tomokatsu, Shima Midori

OBJECTIVE: Infantile Alexander disease (iAxD) is a fatal progressive disorder and one of its serious symptoms is intractable epilepsy. In iAxD, mutations in the glial fibrillary acidic protein (*GFAP*) gene result in accumulations of protein aggregates in astrocytes, which causes astroglial inflammation. However, its influence on the pathophysiology is not elucidated. Also, ketogenic diet therapy (KDT) is established in many diseases, though its anticonvulsant effects in iAxD are not well known. We assessed the effect of KDT on the epilepsy and examined the correlations between neuro-inflammation, epilepsy and disease progression in iAxD.
METHODS: Three iAxD patients were enrolled; 14 and seven months old, diagnosed based on magnetic resonance imaging (MRI) and *GFAP* gene sequencing. They were suffering from drug-resistant seizures and their electroencephalogram (EEG) showed diffuse, frequent and high-amplitude poly-spike and waves. KDT was initiated at a low ratio of fats to carbohydrates and protein, and the ratio was increased until the seizures subsided. Astroglial chemokines and pro-inflammatory cytokines were analyzed before and after the initiation. The analyses were performed utilizing Bio-Plex Pro Human Cytokine Assay (Bio-Rad Laboratories, Inc. Hercules, CA, USA).
RESULTS: All the drug-resistant seizures and EEG abnormalities disappeared dramatically by KDT. Even after the favorable control, however, the brain MRI findings deteriorated. Also, the chemokines and cytokines levels in the cerebrospinal fluid declined but remained still high.

CONCLUSIONS: KDT is effective in controlling epilepsy in iAxD. Neuro-inflammation is likely involved in the pathophysiology of iAxD. Although KDT basically cannot restrain the disease progression, earlier initiation speculatively contributes to better prognosis.
KEYWORDS: Epilepsy

173. Clinical profile, EEG findings and response to treatment in patients with tuberous sclerosis from tertiary care centre of North India

Sinha Rahul (Delhi, India) Badal Sachendra, Anand Vaishakh, Singh Sonali, Jauhari Prashant, Chakrabarty Biswaroop, Yadav Sushila, Piwal Suresh, Piwal Suresh, Gulati Sheffali, Pandey RM

OBJECTIVE: To study the clinical profile, EEG findings and treatment response in patients with tuberous sclerosis
METHODS: Data of 38 pediatric patients of tuberous sclerosis with epilepsy from Dec 2017 to Dec 2019 were retrospectively analysed. The clinical details, EEG findings and treatment response to anti epileptic drugs were studied.
RESULTS: Thirty-eight subjects (26 males: 12 females) were identified with a mean age of 7.5 years. 15 (40%) patients had normal development at presentation. Delayed language and autistic features were noted in 18 patients (47%). All patients except 2 had ash leaf macules. Tonic seizures were found in 23 patients and spasms noted in 13. Twenty-three patients had seizure onset within 1 year of age. The EEG was normal in 12 patients (32%). Hypsarrythmia was the next commonest EEG finding. Most of the patients required multiple antiepileptic drugs and vigabatrin was tried in 15 patients and the response to seizure control was observed within 2 weeks of starting vigabatrin with electrographic resolution in 12 patients. Most common drug other than vigabatrin to which patients responded was levetiracetam. Dietary therapy was given to four children. Three patients received LGIT, one patient received modified Atkin's diet. One patient who received LGIT showed complete response and one patient on modified Atkins diet had 80% response.
CONCLUSIONS: Tonic seizures were commoner than infantile spasms in this population. Next to vigabatrin, levetiracetam was found to be most effective antiepileptic drug specially for tonic seizures.
KEYWORDS: Epilepsy

174. Treatment and Outcomes of Super Refractory Status Epilepticus in a Pediatric cohort from India

Bandi Ramya (Hyderabad, India) Mohan Ashwini, Aripirala Prasanthi, Lingappa Lokesh, Konanki Ramesh

OBJECTIVE: Although clinico-etiological profile of super refractory status epilepticus (SRSE) in children is known, data on optimal treatment protocol and outcomes is scarce.
METHODS: Prospective observational study -children (1 month to 18 years)
RESULTS: Eighteen children (11 male,7 female) with mean age 5.5 years (3 mo-12 yr) were included: 16 with typical development, one each with premorbid neuroregression and developmental delay; 11 children had fever at onset. Median hospital stay was 30 days (3-105). Etiology -3/18 were infective (Mycoplasma-two, scrub typhus-one), pyridoxine dependent epilepsy (PDE), craniphryngioma (post-operative), focal cortical dysplasia in one each, unknown

etiology in 12/18 children (NORSE). All children had normal CSF. MRI abnormal in 7/18 children. The median number of AEDs used were 8.5 (6-12).Midazolam was first line IV Anaesthetic drug (IVAD) which controlled clinical seizure (CS) in 16% (3/18) children, and electrographic seizures(EGS) in none. Of second line IVADs, Ketamine was effective in controlling both CS and EGS in 23% (4/17) and thiopentone in 25% (2/8). Isoflurane controlled both CS and EGS in 36% (4/11). Seven of 18 children required 3 and five children required 4 IVADs. Ketogenic diet was used in 12 children. A total of nine children died. At median follow-up of 14 months (2-30 months) one child was seizure free (PDE); mRS 1 in one child, 2 in 5 children, 3 in 2 children, and 5 in one child.
CONCLUSIONS: Isoflurane was the most effective anaesthetic in controlling both clinical and electrographic seizures in SRSE, and better than first-line IVADs. Despite aggressive treatment, mortality is high.
KEYWORDS: Epilepsy, Critical Care, Translational/Experimental Therapeutics

175. Clinical profile of a cohort of 47 children with absence epilepsies at a tertiary care hospital from North India attending Child Neurology Services over a period of 3 years
Gulati Sheffali (New Delhi, India) Badal Sachendra, Chakrabarty Biswaroop, Jauhari Prashant, Anand Vaisakh, Sirolia Vivek, Kaur Prabhjot, Luhar Zulfiqar, Singh Sonali, Sinha Rahul, Gupta Juhi, Kamila Gautam, Panda Prateek, NM Shruti, Madaan Priyanka

OBJECTIVE: Primary/Genetic generalized epilepsies in children have various types. Absence epilepsies include Childhood absence epilepsy (CAE), Juvenile absence epilepsy (JAE), Epilepsy with Myoclonic absences (Tassinari syndrome) and Eyelid myoclonia with Absences (Jeavon Syndrome)
METHODS: Clinical profile, electrographic findings and response to treatment of all the children attending Child Neurology Services were documented and followed up over three years.
RESULTS: Eighty nine children with Primary generalized epilepsies were diagnosed and seven had Juvenile Myoclonic epilepsy. Absence epilepsies were present in 47 children (53%), 27 boys(58%). CAE :15 children ,median age of onset 4.7 years(IQR : 2-8 years),6 boys (40%). JAE :18 children, median age of onset 9.2 years(IQR : 6-13 years) 11 boys (61%). Tassinari syndrome:8 children with median age of onset 7.2 years (IQR : 3-10 years) 5 boys (62%) Jeavon syndrome :6 children with median age of onset 4 years (IQR : 4 mths-10 years), 5 were boys (83%) . One child had GLUT1 Deficiency amongst all children who underwent CSF examination for absences onset before 4 years of age.
Response to Valproate was documented in <3 days in 20(42%), 3-30 days in 14 (30%),30-90 days in 3 (6%) Poor response in 10 children out of which one child with GLUT 1 responded to Ketogenic diet and 4 with Lamotrigine and 1 with Ethosuximide. Cognition was impaired in 3 children with Tassinari syndrome and two with Jeavon syndrome.
CONCLUSIONS: Jeavon syndrome and Tassinari syndrome are absences with special features and Valproate therapy had the best outcome as montherapy
KEYWORDS: Epilepsy, Genetics, Rare Diseases

176. Is newer ILAE classification of epilepsy better over the previous ones in children with cerebral palsy
K Archana (Chandigarh, India) Saini Lokesh, Sahu Jitendra, Singh Paramjeet, Sankhyan Naveen, Saini Arushi, Suthar Renu, Sharawat Indar, Yadav Jaivinder, Madaan Priyanka

OBJECTIVE: To classify epilepsy in children with cerebral palsy(CP) according to International League Against Epilepsy(ILAE) 1981 and 2017 classifications and determine the agreement between the two classifications.
METHODS: 300 consecutive children aged 1-12 years with CP were enrolled from January 2018-June 2019 in a tertiary center. Children having epilepsy were classified under ILAE 1981 and 2017 classification. E-Chess (Early Childhood Epilepsy Severity Scale) score was used to assess the severity of epilepsy.
RESULTS: The total number of CP cases was 300. Types of CP were classified as spastic type 256 (85.3%), mixed CP-25(8.3%) and dyskinetic-16(5.3%). Epilepsy was found to be in 79 (26%), out of which 89.9% of children had drug-responsive seizures and 10.1% had refractory seizures. When the seizures were compared under the 1981 and 2017 ILAE classification, it was noted that there was strong agreement between the two with kappa value being 0.875. 30.4% of children having spastic hemiplegia had seizures highest among other types of cerebral palsy, followed by spastic quadriplegia- 28.7%, spastic diplegia- 26.3%, mixed type- 24% and dyskinetic CP- 6.3%. GMFCS score of 5 had maximum seizures (52.9%) and mostly comprised of spastic quadriplegia, followed by a GMFCS score of 1 who mostly comprised of spastic hemiplegia. The association between epilepsy and GMFCS scores was statistically significant (*P* value=0.000).
CONCLUSIONS: In our study, epilepsy classification under 1981 and 2017 classification were in high agreement. Thus, we conclude that there is no advantage of classifying epilepsy under newer classification in children with cerebral palsy.
KEYWORDS: Epilepsy

177. Clinical Profile and Outcome of West Syndrome: Experience from Studies Done In a Tertiary Centre of Bangladesh
Akhter Shaheen (Dhaka, Bangladesh) Fatema Kanij, Kundu Gopen, Mannan Muzharul

OBJECTIVE: West Syndrome (WS) is the commonest epileptic encephalopathy in early childhood. Several studies reveal its clinical presentation, risk factors, management, side effects and long-term outcome. The aim of this article is to determine clinical profile and outcome of WS by reviewing studies done in one tertiary centre of Bangladesh.
METHODS: After reviewing eight prospective, retrospective and cross-sectional studies, clinical profile and outcome of west syndrome was determined and described.
RESULTS: Mean age was 15 months; 70% were males. History of perinatal asphyxia was found in 48% of cases. Almost 84% were found to be of symptomatic variety. On EEG, 92.8% had hypsarrhythmia and its variants. On neuroimaging, 93.5% had abnormal findings. No significant difference among ACTH, vigabatrin and oral prednisolone were found. One study concluded vigabatrin as the 1st line drug and another suggested high dose Methylprednisolone as an alternative to ACTH. Adverse effects of ACTH were found in most cases. These were hypertension (47%), irritability (41%), sleep disturbances (19%) and infection (12. 5%). After 4 years follow-up on average, 36% had cerebral palsy, 27.6% epilepsy, and 81% moderate to severe intellectual disability.
CONCLUSIONS: ACTH, oral prednisolone and vigabatrin showed effective response among patients and there was no significant difference in treatment response. Type of brain lesion makes a difference in seizure prognosis, which suggests the need to perform early neuroimaging

in every case of WS for choosing appropriate antiepileptic drug. Hypertension was the most common side effect, followed by irritability and sleep disturbances. Methylprednisolone therapy can be an important alternative to ACTH.
KEYWORDS: Epilepsy

178. Epilepsy phenotypes in children with Neurocutaneous Syndromes- a developing country perspective
Mukherjee Swetlana (Chandigarh, India) Saini Lokesh, Ahuja Chirag, Saini Arushi, Malhi Prahbhjot, Sherawat Indar, De Dipankar, Sankhyan Naveen, Suthar Jitendra, Padhy Susanta, Yadav Jaivinder

OBJECTIVE: To determine the proportion of epilepsy and its characteristics in children with neurocutaneous syndromes
METHODS: Prospective observational study in which 119 patients with neurocutaneous syndromes presenting to pediatric neurology clinics of a north Indian tertiary care centre aged between 1 and 15 years were recruited from January 2018 to July 2019. Epilepsy if present was classified using International League Against Epilepsy (ILAE) 2017 classification. Magnetic Resonance Imaging (MRI) and Electro-encephalogram (EEG) records if available were noted.
RESULTS: 94(79%) had epilepsy which included 38.1% of Neurofibromatosis 1(NF 1) patients, 95.8% (69/72) Tuberous Sclerosis (TS) patients, 87.5% (14/16) patients with Sturge Weber Syndrome (SWS) and 2 patients of Hypomelanosis Of Ito (HOI). Most common type of seizure observed in NF 1 was generalised motor tonic-clonic seizures (23.8%). Most common MRI finding in these children was Focal Areas of Altered Signal Intensity (FASI) in 68.7% children (11/16). In TS, most common type of seizure was generalised motor epileptic spasms (41.7%) followed by focal seizures (31.9%). Most common MRI findings in these children were subependymal nodules (SEN) with cortical tubers in 62.1% (41/66). Most common type of seizure in SWS was focal onset impaired awareness motor clonic seizure (58.3%). 30.8% (4/13) had leptomeningeal angiomatosis with cerebral hemiatrophy and dilated residual veins on MRI and 30.8% (4/13) had dilated residual veins as an isolated finding. Both children with HOI had GTCS.
CONCLUSIONS: In pediatric neurology services, epilepsy is over-represented than children with neurocutaneous syndrome in general.
KEYWORDS: Epilepsy

179. Mentoring Youth with Epilepsy: A Support Model for Transitioning Youth with Chronic Neurological Conditions
Niemann Madeline (Boston, MA, United States) Shamambo Luwi, Jonas Rinat, Camayd Cristina, Douglass Laurie

OBJECTIVE: Youth with epilepsy (YWE) must acquire transitioning skills to navigate the adult health-care system and achieve life goals. We piloted a mentorship program for YWE that encouraged greater independence around health management, created opportunities for healthy socialization, and was virtually accessible.
METHODS: Volunteers with undergraduate degrees were recruited to serve as year-long mentors to YWE. Mentors received initial training in epilepsy fundamentals, best-practices for mentorship, safety, and program goals. Epilepsy center providers identified YWE (14 years and

older) who were capable of developing greater independence and had some interest in mentorship. Parents completed a pre-match survey measuring their transition preparedness. YWE completed a transition readiness assessment (TRAQ 20). Mentors, mentees and families were trained in using secure video-calling and texting. Mentors/mentees were encouraged to meet at clinic visits, during hospitalizations, at Epilepsy Foundation events, and through video-call.
RESULTS: Eight mentees (5 F, 3 M) were gender-matched with mentors. Six mentees' parents completed the pre-match survey. 66% of parents reported understanding transition concepts, while 83% believed that their family was unprepared. 5 of 8 mentees completed TRAQ20 (average score = 43.5/100, with 100 indicating full transition readiness). Three months after their first meeting, 6 of 8 matches remained active. The 2 inactive mentees reported that transition readiness was not a priority for them and competing obligations interfered with participation.
CONCLUSIONS: YWE and parents often feel unprepared for transition. Mentorship may be useful in developing self-management skills for YWE. Reviewing the expectations of mentorship with mentees might improve youth engagement.
KEYWORDS: Epilepsy

180. Impact of a Pediatric Status Epilepticus Pathway: A Quality Improvement Project
Rashid Salman (Birmingham, AL, United States) Mamaeva Christina, Hayes Leslie

OBJECTIVE: This quality improvement project was geared to evaluate the clinical usefulness of a standard pediatric (non-neonatal) status epilepticus pathway, specifically in reference to the first-line medications (benzodiazepines).
METHODS: An institutional review board approval was obtained for this quality improvement project. After a thorough literature search and tabletop simulations, a group of healthcare providers (from Neurology, pediatric ICU, emergency room and pharmacy departments) developed a status epilepticus pathway at our hospital. The pathway was largely based on American Epilepsy Society 2016 guidelines for the management of status epilepticus. This pathway was made available (intervention) on 01/07/2018. We compared the in-hospital adherence with the first and second doses of the first-line medications {lorazepam 0.1 milligram/kilogram intravenous or midazolam (weight dependent intramuscular dose for patients who did not have an IV line)} among pre and post intervention groups. Both pre and post intervention arms included 25 patients each.
RESULTS: Please review the attached word file.
CONCLUSIONS: A pediatric status epilepticus pathway improved adherence with the standard recommendations for the doses of first-line abortive medication, and was also associated with a reduced need for the second dose. We are still working on other variables (for example, patient outcomes), and hope to present this data at the conference.
KEYWORDS: Epilepsy, Critical Care, Neuroscience

181. Getting Routine EEG in Emergency Department: Should It be A Routine or Case Specific?
Eksambe Padmavati (New Hyde, NY, United States) Shah Yash, Nath Manan, Theroux Liana, Amlicke Marie, Krief William, Steele Frances, Pavkovic Ivan, Kothare Sanjeev

OBJECTIVE: The need for routine electroencephalogram (rEEG) in the pediatric emergency department (ED) is unclear. Oftentimes, it is done for ruling out sub-clinical seizures or in the hope of detecting focal or generalized abnormalities, which may be best observed within the first 24 hours following a seizure. The purpose of this study was to evaluate the value of rEEG, its utility in determining the patient disposition and its impact on duration of stay in the ED in an urban tertiary care pediatric hospital.
METHODS: This is a retrospective cohort study of 328 patients over the duration of 6 months. The primary outcome was the duration of stay in the ED based on performing rEEG. Secondary outcomes were decision to discharge or admit to the PICU or floor based on rEEG findings
RESULTS: rEEG were obtained in 67 (20.4%) patients (See fig. 1 & table 1) Of the 9 patients with new onset seizures, 5 had interictal epileptiform activities suggestive of BECTS and 3 suggestive of absence epilepsy. rEEG was shown to prolong ED stay by 1.6 hours (7.4hrs vs 5.8hrs; $p<0.005$).
CONCLUSIONS: Our data shows that obtaining rEEG in ED prolongs hospital stay and although rEEG helps determine disposition in new patients, its utility in patients with established diagnosis of epilepsy is limited. Luxury of having rEEG is important, but it comes at the cost of the time and apparent triage is important on when to do rEEG.
KEYWORDS: Epilepsy

182. Imaging in pediatric patients with seizures in emergency department: Are we over-doing it?
Shah Yash (New Hyde, NY, United States) Eksambe Padmavati, Nath Manan, Varughese Robin, Amlicke Marie, Krief William, Steele Frances, Kothare Sanjeev

OBJECTIVE: Urgent neuroimaging in emergency department (ED) in children with seizures is warranted when examination is consistent with new focal deficits, prolonged altered mental status, and when electroencephalogram shows focal abnormalities. Though MRI-brain is preferred imaging modality for epilepsy patients, CT-head is often obtained first, due to its easy availability, shorter duration, non-requirement of anesthesia, and scenarios of possibly requiring emergent neurosurgical intervention. The aim of our study was to assess the use of imaging in patients presenting with seizure to the ED.
METHODS: This is a retrospective cohort study involving 328 patient records over the period of 6 months. The primary outcome was the duration of stay in the ED simultaneously noting the underlying rationale for ordering neuroimaging and correlations with patient's clinical condition.
RESULTS: Head-imaging was performed in 52 (15.8%) patients (Fig. 1). Reasons for obtaining neuroimaging included seizure associated with trauma (31.7%), healthcare provider witnessed events (24.4%), focal seizures (14.6 %) and miscellaneous causes (26.8 %). Obtaining any kind of imaging prolonged ED stay by 1.8hrs (7.7hrs vs 5.9hrs; $p<0.005$).
CONCLUSIONS: Obtaining emergent neuroimaging in the ED prolongs duration of stay in the ED. Physicians in ED should have a strong logical basis for obtaining these studies and must follow national guidelines. MRI, if required, could be performed with HASTE/SS-FSE single shot sequence, preferably with minimally invasive anesthesia.
KEYWORDS: Epilepsy. Neuroimaging

183. Outcome of children with seizures who presented to the emergency department over six months: A single center experience

Nath Manan (New Hyde, NY, United States) Eksambe Padmavati, Shah Yash, Amlicke Marie, Steele Frances, Krief William, Kothare Sanjeev

OBJECTIVE: Seizures form a significant number of children presenting for neurological evaluation to the emergency department (ED) with inadequate data on their outcome. The purpose of this study was to evaluate outcome of patients who presented to the ED with seizures, including revisits within 30 days
METHODS: This is a retrospective cohort study of children over a six month period with either new onset seizure or with breakthrough seizures. The primary outcome was the decision to discharge or admit and with secondary outcomes being office follow up and subsequent ED revisit.
RESULTS: Of the 328 children who presented to the ED with seizures, 183 (55.8%) were discharged home, 145 (44.2%) patients were admitted, of which 22 (18.7%) required PICU admission for status epilepticus or sedation related respiratory insufficiency (fig.1). A total of 218 (66.46%) patients were seen outpatient within 30 days after ED visit, while 18 (5.5%) had ED revisits. Patients who had outpatient follow up after ER visit had less ER revisits within 30 days as compared to those who did not have outpatient follow up ($p<0.001$).
CONCLUSIONS: Findings of our study indicated that patients who were followed closely in outpatient after ED visit had decreased ED visits within 30 days. Better paradigms need to be developed to prevent revisits to the ED and avoid respiratory insufficiency necessitating admission to the PICU
KEYWORDS: Epilepsy, Ethics

184. Presentation and Long-term Neurologic and Neurodevelopmental Profiles in Pediatric Patients with Febrile Infection-Related Epilepsy Syndrome (FIRES): A Single Institution Review

Fisher Kristen (Houston, TX, United States) Davis Kimberly, Martinez Monica, Shukla Nikita. Evankovich Karen

OBJECTIVE: We describe 8 patients from Texas Children's Hospital between 2017-2019 with diagnosis of FIRES, their acute neurologic presentation, treatments, and long term neurologic and neurodevelopmental outcomes.
METHODS: A retrospective chart review was performed on patients with diagnosis of FIRES. Demographic, clinical data, and neuropsychological evaluations were collected.
RESULTS: Mean age of presentation was 8.5 years (range 4-15 years). Mean seizure onset 3.6 days from febrile illness (range 1-6). All patients required anesthetics for seizure control in addition to antiepileptics. Immunotherapy included varying regimens of IVMP, IVIG, plasmapheresis, rituximab, and/or anakinra. The mean duration in burst suppression was 20.9 days (range 0-120). Mean hospital stay was 109 days (range 48-260). Neurocognitive function varied at discharge, with greater deficits seen in those with longer hospitalizations and duration of burst suppression. At last neurology follow up, 2 patients reported daily seizures, and remaining infrequent seizures on AED regimen (range 2-7 medications). 5 patients underwent neuropsychology evaluation (ranging 6.7 – 29.2 months from onset), with IQ ranging borderline to average. All patients showed impaired working memory and processing speed, and many with executive functioning problems. All currently require individualized education plan in school.

CONCLUSIONS: The neurologic and neurodevelopmental outcomes of this cohort of pediatric FIRES patients varied. All patients remain on AEDs for seizure control, some with continued daily seizures and others well controlled. All demonstrated decline in overall intellectual functioning with significant impairments in working memory, processing speed, and executive function. All continue to require additional supports in school setting, including those with normal IQ.
KEYWORDS: Epilepsy. Infections/Neuroimmunology, Neurorehabilitation

185. Dissecting the effects of the host genetic background in phenotypes of Dravet syndrome
Carney Paul (Chapel Hill, NC, United States) DeMarse Thomas, Xie Youmei, Zhao Junli, Anderson Christopher

OBJECTIVE: Mutations in SCN1A, encoding Nav1.1 cause Dravet syndrome (DS), a type of infant epilepsy that exhibits variable clinical severity including premature death. We utilized a heterozygous *Scn1a* knockout (*Scn1a*$^{+/-}$) mouse model of DS and a genetic reference population of Collaborative Cross (CC) mice with publicly available whole genome sequences to investigate the genetic basis for phenotype variability. The CC population is a genetically diverse recombinant panel derived from 8 fully inbred strains that has ~42 million segregating genetic variants.
METHODS: 215 mice from 6 CC lines and age-matched controls (*129/svj*) were phenotyped for susceptibility to seizures and SUDEP. Electrographic and behavioral seizures were scored by 3 independent researchers that were blinded to genotype. Male and female mice were used for experiments in equal genotypic ratios. All animal procedures were approved by the UNC IACUC.
RESULTS: The survival time varied significantly between specific CC lines.
Whereas *Scn1a*$^{+/-}$ mice bred with either C57BL/6J (F1.*Scn1a*$^{+/-}$) or CC 011 mice exhibit spontaneous seizures and high rates of premature death, *Scn1a*$^{+/-}$ mice bred with CC lines 024, 044, 079, and 081 have normal phenotype and lifespan (p-value <0.001) (Figs.1, 2). Whole genome sequences were established for each individual CC strain and controls.
CONCLUSIONS: *Gaba2* allele-specific expression is reduced in both C57BL/6J and CC 011 mice. However, only mice with C57BL/6J background exhibit spontaneous seizures and premature death. Our findings illustrate how differences in strain-and age-determine phenotype severity of the *Scn1a*$^{+/-}$ phenotype. The findings further emphasizes the contribution of host-specific genetic modifiers that influence expressivity of the DS phenotype.
KEYWORDS: Epilepsy, Genetics, Rare Diseases

186. Utilization of the Addis Clinic telemedicine platform for epilepsy care, past experience and future opportunities.
Varghese Sonia (Chapel Hill, NC, United States)

OBJECTIVE: Given the limited availability of specialty, sub-specialty, and physician care in areas around the world, The Addis Clinic was founded with the goal to connect volunteer physicians with local organizations providing frontline healthcare to vulnerable and underserved populations. The organization utilizes telemedicine to connect skilled physicians with underserved patients around the world by partnering with local organizations serving in resource

limited settings.
We reviewed prior years' epilepsy related consultations through the Addis Clinic's telemedicine platform. Assess utilization of the organization's services for support of community-based epilepsy care.
METHODS: Review of database of the Addis Clinic teleconsultations, and specific cases related to epilepsy. Demographics of patients, local providers and specific consultation questions. Neurology epilepsy specialists and Addis Clinic leadership discussed the results and reviewed future opportunities to expand and increase the impact of the service on epilepsy care.
RESULTS: Of total of 337 cases, and 563 teleconsultations conducted by the Addis Clinic in 2018 only 4 cases were related to epilepsy.
Discussion between epileptologists and the Addis Clinic leadership raised multiple opportunities for increased epilepsy consultation of the platform. Recruiting additional neurology and epilepsy specialists volunteers, connecting with new local healthcare organizations for partnerships, using the platform for education and training of local providers.
CONCLUSIONS: Telemedicine provides a platform that can provide epilepsy specialists consult in regions of low resources and limited specialist access. Utilization of the Addis Clinic services for epilepsy is low. Connecting with local organizations and increasing volunteer base may increase utilization for the benefit of epilepsy patients.
KEYWORDS: Epilepsy

187. Profile of Drug Resistant Epilepsy in Neonatal Hypoglycemic Brain Injury.
Shelke Madhavi (Aurangabad, India) Bhartiya Shirish, Vaidya Varsha, Saraf Sandeep, Muqueet Abdul

OBJECTIVE: Hypoglycemia in newborn is a leading cause of seizures, resulting into a typical pattern of brain injury on MRI with subsequent development of remote symptomatic epilepsy . We retrospectively studied the clinical profile of children with drug resistant epilepsy and MRIs showing neonatal hypoglycemic brain injury for identification of risk factors for drug resistance.
METHODS: A review was done of 43 children following up in neurology clinic with typical MRI features of neonatal hypoglycemic brain injury and drug resistant epilepsy .Children with history of HIE and congenital anomalies were excluded. Details of birth history ,onset and type of epilepsy, number of drugs used and duration of follow up were noted
RESULTS: Total 43 children(36boys and 7girls),3yr-16 years of age were reviewed .14/43(32%)were born by LSCS, 27/43(62%)were low birth weight and 22/43(51%) VLBW . 88% of children had history of neonatal seizure. Seizure onset was before 1 year in 23/43(53%) and later than 5 years in 5/43. First seizure type was epileptic spasms in 17/43(39%).Epileptic encephalopathy, west syndrome was seen in 18/43(41%)and evolved into LGS in 50%. Multiple seizure types were reported in 20/43(46%). 26/43(60%) had received more than 4 antiepileptic drug trials.Duration of follow up was from 2 years to 9 years.
CONCLUSIONS: Drug resistant epilepsy with neonatal hypoglycemic brain injury is associated with multiple drug usage and high incidence of long term drug trials .VLBW , onset within first year of life ,epileptic spasms as first seizure type and multiple seizure types were some of the risk factors predicting drug resistance.
KEYWORDS: Epilepsy

188. The Efficacy of Ketogenic Diet According to the Presence of mTOR Pathway Mutations

Ko Ara (Yangsan, Republic of Korea) Lee Joon Soo, Lee Jeong Ho, Kim Heung Dong, Kang Hoon-Chul

OBJECTIVE: One of numerous hypotheses suggested on mechanism of KD is via inhibition of mammalian target of rapamycin (mTOR) pathway by KD. With the assumption that KD demonstrates antiepileptic effect through mTOR pathway inhibition, this study aimed to assess the efficacy of KD in patients with pathologically confirmed focal cortical dysplasia (FCD) due to genetically identified mTOR pathway dysregulation.
METHODS: After prospectively constructing a cohort of patients with FCD who were screened for presence of somatic mTOR pathyway related mutations, we retrospectively evaluated the efficacy of KD according to presence of mTOR pathyway related mutations.
RESULTS: Of 25 patients, 12 patients (48.0%) had identified germline (1 patient, *DEPDC5*) or somatic (12 patients) mTOR pathway mutations (8 *MTOR*, 2 *TSC1*, 1 *TSC2*, and 1 *DEPDC5*). After 3 months of KD, a total of 12 (48.0%) patients showed response to KD (≥ 50% seizure reduction from baseline). When divided according to the presence of mTOR pathway mutations, 7 (58.3%) patients with mTOR pathway mutations were responders while 5 (38.5%) patients were responders to KD. However, the difference was not statistically significant ($p = 0.434$). Also, 4 (33.3%) patients with mTOR pathway mutations showed ≥ 90% seizure reduction from the baseline, while 2 (15.4%) patients without mTOR pathway mutations showed ≥ 90% seizure reduction. This difference was also not significant ($p = 0.378$).
CONCLUSIONS: The patients with mTORopathies did not show significant superior response to KD than those without mTORopathies, even though there was a trend toward the better response to KD.
KEYWORDS: Epilepsy

189. Epilepsy incidence among children attending the outpatient neurology clinic at Alexandria University Children's Hospital, Alexandria, Egypt.

Elsakka Elham (Alexandria, Egypt) Anwar Shimaa, Fahmy Shaimaa

OBJECTIVE: is to determine the incidence and describe different types of epilepsy among children with neurological disorders attending the Outpatient Neurology Clinic at Alexandria University Children's Hospital, Alexandria, Egypt.
METHODS: A total of 537, patients were included from 1/1/2018 till 31/12/2018. Patients' data were collected from record: detailed history, full examination, EEG results, etiology and type of epilepsy and the used antiepileptic drugs.
RESULTS: 537 patients enrolled in the study: 88 of them (16.4%) had epilepsy. 77% of cases had genetic epilepsy, 15.9% of cases had structural epilepsy, 3.4% of cases had infectious epilepsy, 2.3% of cases had metabolic epilepsy and 1.1% of cases had mixed epilepsy. 52% of cases had generalized tonic clonic seizures, 29.5% had focal seizures, 9.1% had focal to bilateral, 4.5% had absence seizures, 3.4% had atonic seizures and 1.1% had myoclonic seizures. 32.9% children with epilepsy were from 1 to 3 years, 60.2% aged more than 3 years to 10 years and 6.8% aged more than10 years. 45.5% of cases had positive family history of epilepsy. 75.5% of EEG done was abnormal. 27.2% of cases were on polytherapy while 60.2% of cases were on

monotherapy: 52.8% of them were on Na valproate, 53% on Carbamazpine, and 11.3% on Levetiracetam.
CONCLUSIONS: Epilepsy is a common disease between other neurological diseases. The most common type of seizures is generalized tonic clonic. The commonest etiology of epilepsy is genetic. Most of the cases show abnormality in the EEG. Many cases require monotherapy and the commonest used drug is valproate followed by carbamazepine.
KEYWORDS: Epilepsy

190. Generator replacement with cardiac based VNS device in children with drug-resistant epilepsy
Hadjinicolaou Aristides (Toronto, Ontario, Canada) Jain Puneet, Yau Ivanna, Whitney Robyn, Rutka James, Go Christina

OBJECTIVE: We aimed to study the proportion of patients with DRE and pre-existing VNS device, who show improvement of at least one class in McHugh seizure outcome classification at last follow up after generator replacement with cardiac based VNS device.
METHODS: We retrospectively reviewed children with DRE with the older VNS model (102) who underwent battery replacement with the AspireSR®, model 106 since September 2016 at our institution. We assessed the seizure outcomes since the first VNS device insertion till the last follow up after AspireSR® (with cardiac-based seizure detection) using McHugh seizure outcome classification.
RESULTS: The study population was comprised of 15 patients. The mean age at seizure onset was 2.7 years old, with mean age of initial VNS1 placement being 10.1 years and mean age of replacement with VNS2 being 14.9 years of age. The most common seizure types in our cohort were generalized tonic-clonic seizures (9/15), followed by generalized tonic seizures (7/15). Three of the fifteen patients had reported status epilepticus prior to initial VNS insertion, and none reported episodes following insertion. Two patients showed at least one class improvement in McHugh seizure outcomes at last follow up after VNS2.
CONCLUSIONS: Through our preliminary data at the present time, we note that the majority of our patients maintains their seizure control following replacement with VNS2 with a few showing improvement. Future plans include continuing to follow this cohort over time, as well as to obtain the data from our collaborator sites in order to draw stronger conclusions.
KEYWORDS: Epilepsy

191. Seroprevalence of Anti- N-methyl-D-aspartate (NMDA) receptor antibodies in children with seizures of unknown cause
Saadi Nebal (Baghdad, Iraq) Abdulameer Mohammed, Ghalib Batool

OBJECTIVE: immunological etiologies have been considered as causes of epilepsy by the International League Against Epilepsy (ILAE) in its last report of classification at 2017. The aim of this study was to determine the prevalence of anti-NMDA antibody in a group of patients presented with seizures of unknown cause.
METHODS: a prospective case-control study was conducted in two hospitals in Medical City Complex-Baghdad, in the period from Feb. 2019 to Oct. 2019. A group of children aged 2-18 years who manifested seizures solely without an identified causes were recruited, with additional

sex- and age-matched control group. Serum was tested in both groups for anti-NMDA receptor antibodies.
RESULTS: in the patients group, boys accounted for 65% (26/40) of the cases, the mean age was 6.6 years (range 2-14 years), and the mean duration since their seizures' onset was 2 months. Female patients manifested more focal seizures while most of the males presented with generalized seizures (57% versus 77% respectively). Only 5 patients (12.5%) were positive for Anti- NMDAR Ab, in contrast to no one in the control group (Corrected OR=12.5; 95% CI (0.6-216.7)). Significantly, most of seropositive patients were females (4, 80%) and showed focal types of seizures (4, 80%).
CONCLUSIONS: anti-NMDAR Ab was found to be prevalent in a relatively small proportion of children who presented with seizures of unknown causes. Demographic characteristics of the patients with variable testing status were found to be nearly comparable to the results from other related studies.
KEYWORDS: Epilepsy, Infections/Neuroimmunology

192. Atypical Phenotypic Expression of Non familial Sleep-Related Hypermotor Epilepsy
Tarhan Bedirhan (Gainesville, FL, United States) Seehra Grupreet, Gonik Renato, Lodolo Mauro

OBJECTIVE: Sleep-related hyper motor epilepsy (SHE) is focal epilepsy that primarily occurs during non-rem sleep and presents as asymmetric dystonic-tonic posturing and/or complex hyperkinetic automatisms. The diagnosis of SHE is primarily determined by clinical history and semiology. However, the disorder is likely to be under-diagnosed or in some cases misdiagnosed because of the absence of typical convulsive seizure and similar behavioral patterns to those observed in parasomnias. Prolonged video electroencephalogram (EEG) is the best way to assess seizure occurrence.
METHODS: Review clinical history, neurological examinations, prolonged video EEG, neuroimaging and treatment outcome.
RESULTS: A 7-year-old Caucasian female who presented to the neurology clinic for evaluation of clusters of mostly daytime spells manifesting as retropulsion of the head, turning her head to the left, irregular rocking movements associated with complex movements of kicking and cycling of limps, and facial expressions including smiling, with no auras or postictal state. These episodes lasted for 5 seconds and occurred 10-20 times a day. The patient had prolonged video EEG performed. The findings of EEG and seizure semiology were consistent with SHE, however, only during the waking time. Her seizure was initially well controlled with a combination of Valproic acid and Topamax however she is still experiencing intermittent seizures mostly during the daytime.
CONCLUSIONS: We present a case of SHE which expands the phenotypic expression of SHE. Understanding the features of SHE could lead to earlier recognition, diagnosis, and treatment, which will result in a less negative impact on cognitive functions and personal and social aspects of SHE.
KEYWORDS: Epilepsy, Rare Diseases

193. Long-term tolerability and retention of adjunctive brivaracetam in children with primary generalized or mixed seizure types: interim subgroup analysis of pooled data from two open-label trials

Patel Anup (Columbus, OH, United States) Gasalla Teresa, Nondonfaz Xavier, Elmoufti Sami, Elshoff Jan-Peer

OBJECTIVE: To assess tolerability and retention rate (effectiveness) of adjunctive brivaracetam in children with primary generalized seizures (PGS) or mixed seizure types.
METHODS: Pooled interim analysis (cut-off March 15, 2017) of children with PGS or mixed seizure types enrolled in N01263 (NCT00422422), an open-label trial of adjunctive brivaracetam in children (aged ≥1 month to <16 years) uncontrolled by 1–3 concomitant antiepileptic drugs, in which brivaracetam dose was up-titrated over 3 weeks (0.8 to 4 mg/kg/day), and open-label extension N01266 (NCT01364597), in which patients received flexible-dose brivaracetam (1 to 5 mg/kg/day [maximum 200 mg/day]; equivalent to 50–200 mg/day for patients weighing ≥50 kg).
RESULTS: Fifty-one children with PGS or mixed seizure types were enrolled (Table 1). Median brivaracetam exposure duration was 541 days; median modal dose was 4.0 mg/kg/day (equivalent to 200 mg/day for patients ≥50 kg). At cut-off, 20 (39.2%) patients were ongoing, 29 (56.9%) patients had discontinued (main reasons: adverse event [21.6%], lack of efficacy [17.6%], and caregiver choice [11.8%]). Forty-eight (94.1%) patients experienced ≥1 treatment-emergent adverse event (Table 2). Two (3.9%) patients died (acute respiratory failure/aspiration/circulatory collapse and pneumonia); neither death was considered brivaracetam-related. Kaplan-Meier estimated 12- and 24-month retention rates were 56.9% (95% confidence interval 42.2–69.1) and 47.1% (33.0–59.9).
CONCLUSIONS: Long-term adjunctive brivaracetam was generally well tolerated in children with PGS or mixed seizure types with a safety profile consistent with that reported in children with focal seizures only. Two-year retention rate (~50%) suggests potential treatment benefit in this pediatric population. Additional studies are needed. Funding: UCB Pharma-sponsored
KEYWORDS: Epilepsy

194. Intrathecal dexamethasone for febrile infection-related epilepsy syndrome
Horino Asako (Tokyo, Japan) Kuki Ichiro, Inoue Takeshi, Nukui Megumi, Okazaki Shin, Kawawaki Hisashi, Togawa Masao, Amo Kiyoko, Ishikawa Junichi, Ujiro Atsushi, Shiomi Masashi, Sakuma Hiroshi

OBJECTIVE: Increasing report suggest a role for immunological mechanisms in febrile infection-related epilepsy syndrome (FIRES). The objective of this study was to elucidate the efficacy and safety of intrathecal dexamethasone therapy (IT-DEX).
METHODS: We assessed six pediatric patients with FIRES who were administered add-on IT-DEX in the acute (n=5) and chronic (n=1) phases. We
evaluated clinical course using the original severity scale score representing the degree of seizure control, electroencephalography (EEG) findings, and prognosis.
We measured cytokines/chemokines in cerebrospinal fluid (CSF) from FIRES patients at several points, including pre- and post-IT-DEX, and compared them with control patients with chronic epilepsy (N=12, for cytokines/chemokines) or with non-inflammatory neurological disease (NIND, N=13, for neopterin).
RESULTS: Anesthesia was weaned after a median 5.5 days from IT-DEX initiation (n=6). Severity scale scores decreased over 2 points in five patients after IT-DEX. No patient experienced severe adverse events. Seizure spreading and background activities on EEG were improved after IT-DEX in all patients. The levels of CXCL10, CXCL9,

IFN-γ, and neopterin at pre-IT-DEX was significantly elevated compared to levels in epilepsy controls, and CXCL10 and neopterin were significantly decreased at post-IT-DEX, but were still higher compared to patients with chronic epilepsy. IL-6, IL-8, and IL-1β was significantly elevated before IT-DEX compared to epilepsy controls, though
there was no significant decrease post-treatment.
CONCLUSIONS: IT-DEX represents a therapeutic option for patients with FIRES that could shorten the duration of the critical stage of the disease. The effect of IT-DEX on FIRES might include cytokine-independent mechanisms.
KEYWORDS: Epilepsy, Critical Care, Infections/Neuroimmunology

195. Time to Onset of Cannabidiol (CBD) Treatment Effect and Resolution of Adverse Events in Patients with Dravet Syndrome: Pooled Analysis of Two Randomized Controlled Trials

Madan Cohen Jennifer (Hartford, CT, United States) Checketts Daniel, Dunayevich Eduardo, Gunning Boudewijn, Hyslop Ann, Madhavan Deepak, Villanueva Vicente, Zolnowska Marta, Zuberi Sameer

OBJECTIVE: We conducted a post-hoc pooled analysis of 2 phase 3, randomized, placebo-controlled trials (GWPCARE1/NCT02091375; GWPCARE2/NCT02224703) in order to estimate time to onset of CBD treatment effect in Dravet syndrome.
METHODS: Patients received highly purified CBD (Epidiolex®; 100 mg/mL oral solution) at 10 mg/kg/day (CBD10; GWPCARE2) or 20 mg/kg/day (CBD20; both trials), or placebo for 14 weeks. CBD treatment started at 2.5 mg/kg/day, reaching 10 mg/kg/day on Day 7 and 20 mg/kg/day on Day 11. Percent reduction in convulsive seizure frequency by cumulative treatment day (including previous days) and timing of adverse events (AEs) were assessed.
RESULTS: 194 patients were randomized to CBD and 124 to placebo. Percent reductions in convulsive seizure frequency were significantly greater for CBD than placebo in GWPCARE1 (CBD20 39% vs placebo 13%, p=0.0123) and GWPCARE2 (CBD10 49%, CBD20 46% vs placebo 27%, p=0.0095 and p=0.0299). Differences between CBD and placebo emerged during titration (nominal $p<0.05$ by Day 13 for CBD10 and Day 12 for CBD20) and were maintained throughout the trial. In patients with AEs, onset occurred during titration in 60%. AEs resolved within 4 weeks in 40% of patients and by end of trial in 60%. Increases in ALT/AST (>3× upper limit of normal) occurred in 3 (5%) patients for CBD10, 25 (19%) for CBD20, and 1 (1%) for placebo; all on concomitant valproate. All elevations resolved.
CONCLUSIONS: CBD treatment effect (seizure reductions and AEs) may occur as early as the titration period. The majority of AEs resolved during the trial.
Funding: GW Research Ltd
KEYWORDS: Epilepsy, Rare Diseases, Critical Care

196. Seasonal distribution of febrile seizure and the relationship with respiratory and enteric viruses in Korean children based on nationwide registry data

Chae Soo Ahn (Seoul, Republic of Korea) Han Do Hoon, Kim Su Yeong, Lee Na MI, Yi Dae Yong, Yun Sin Weon, Lim In Seok

OBJECTIVE: The seasonal distribution patterns of febrile seizures and of respiratory and enteric viral pathogens are similar. In this study, we analyzed trends in febrile seizures and viral

infection in Korean children, using big data from the Korean Health Insurance Review and Assessment Service (HIRA).
METHODS: We analyzed children younger than 6 years who visited the hospital and were diagnosed with febrile seizures from 2009 to 2016, using medical records in the HIRA database. A total of 666,136 medical records of children with a main or subdiagnosis of febrile seizure from 2008 to 2016 were included. Of these records, patients younger than 1 month and records before 2009 were excluded. Finally, 558,130 records were extracted.
RESULTS: The medical records included 315,774 male children and 242,356 (43.4%) female children, with a mean age of 2.31 ± 1.31 years. The annual incidence of febrile seizure was 25.4 per 1000 person-years (27.9 for boys and 22.7 for girls). The ratio of male to female children was 1.30: 1, and records of 1-year-old children comprised the highest proportion (n = 210,400, 33.70%). The total monthly number of patients was highest in May (n = 64,969, 11.6%), and peaks were formed from April to July. The fewest patients were seen in October (n = 34,424, 6.17%). The most common viral pathogens were influenza in April and enterovirus during May-July.
CONCLUSIONS: The seasonal distribution of febrile seizures was high from late spring to summer, and influenza virus and enterovirus were most frequently associated.
KEYWORDS: Epilepsy, Infections/Neuroimmunology

197. IMPACT OF ANTI-EPILEPTIC DRUGS ON BLOOD CARNITINE AND ACYLCARNITINE LEVELS IN CHILDREN - A STUDY USING TANDEM MASS SPECTROMETRY
Neelam Harsha (Chandigarh, India) Attri Savita, Saini Arushi, Sahu Jitendra

OBJECTIVE: Prolonged anti-epileptic therapy is often associated with multiple adverse effects which include metabolic disturbances. Our study aimed to study the effect of antiepileptic drugs on free carnitine and acylcarnitine levels in epileptic patients.
METHODS: This prospective cohort study was conducted between January 2018 to June 2019 in epileptic patients (2-12 years), over a period of 6 months, through tandem mass spectrometer, giving an advantage of better technology over other studies which used enzymatic or radiochemical assays.
RESULTS: We screened and enrolled 125 children from Pediatric Neurology OPD, who were started on antiepileptics, out of which 98 i.e., 52 (53%) on Valproate, 29 (30%) on Carbamazepine, 17 (17%) on Phenytoin, could be followed up for 6 months. Our study showed a significant decrease in carnitine levels in the Valproate cases i.e., from median value of 25.46µM (IQR =10) to19.5 µM (IQR = 10.6) at the end of 6 months. The acylcarnitine profile showed increase in the short and medium chain acylcarnitine which include Malonylcarnitine (C3DC), Butyrylcarnitine (C4), Succinyl/methylmalonylcarnitine (C4DC), (C5:1) Tigly carnitine, Glutarylcarnitine (C5DC), Hexanoylcarnitine (C6) and C8:1-Carnitine, whereas the long chain acylcarnitines (derivatives of C12, C14, C16, C18) showed a decreasing trend in the children on Valproate monotherapy.
CONCLUSIONS: The salient findings include decrease in Carnitine levels in the children on Valproate which was significant, increase in acylcarnitine profile in the short and medium chain in children on Valproate, and a decreasing trend in long chain in the children on Valproate or carbamazepine or phenytoin monotherapy.
KEYWORDS: Epilepsy

198. Comparison of serum Magnesium level among children with febrile seizure and control group: a systematic review and metanalysis

Panda Prateek (Rishikesh, India) Lourembam Radhapyari, Sharawat Indar

OBJECTIVE: To compare serum Magnesium levels among children with febrile seizure and control group.
METHODS: Electronic databases like Pubmed, Scopus and Google scholar were searched in January 2020, using MeSH terms "yoga'', ''children'' and ''attention deficit hyperactivity disorder''. All articles were reviewed independently by two reviewers. Newcastle-Ottawa Scale(NOS) for nonrandomized studies and CONSORT criteria and Cochrane risk-of-bias tool for randomized trials were used for quality assessment. The review was registered in PROSPERO.
RESULTS: Total 21 relevant articles were identified out of 67 search items, after reviewing the contents and excluding duplicate results. Total 14 (12 case-control, 2 uncontrolled) studies were found among these articles. Out of these, 10/14 studies were found to be of high quality (NOS score ≥7) and included in the final metanalysis, describing a total of 785 febrile seizure cases and 685 control with febrile illness. Serum Magnesium level was found to be significantly lower in children with febrile seizure (1.96±0.53 mg/dl) as compared to controls (2.09±0.47 mg/dl) (p=0.001). Only one study each compared serum Magnesium level between complex and simple febrile seizure & CSF Magnesium level between febrile seizure and controls (no significant difference). Follow up serum Magnesium level was available only for one study, which demonstrated serum Magnesium level rises to normal level two weeks after febrile seizure.
CONCLUSIONS: Serum Magnesium level among children with febrile seizure is significantly less than febrile controls and may be a contributing factor in its neuropathogenesis. RCTs are required to evaluate the effect of Magnesium supplementation in prevention of recurrence of febrile seizure.
KEYWORDS: Epilepsy, Infections/Neuroimmunology

199. Predictor of recurrence after a first unprovoked seizure in childhood: A prospective study

Ruby Naznin (Dhaka, Bangladesh) Rahman Muhammad, Akhter Shaheen

OBJECTIVE: Revised definition of epilepsy by ILAE at 2014, second part of definition allows a condition to be considered epilepsy after one seizure if there is a high risk of having another seizure, if the risk factors is not precisely be known we have to wait for another seizure, this definition allows to search for a probable risk factors, so this study aimed to assess the recurrence rate and associated risk factors for recurrences after a first unprovoked seizure
METHODS: This prospective observational study was conducted at BSMMU during period of June 2016 to December 2018. Among 137 children finally 120 children aged between1 month to 14 years after a first seizure were followed up for 2 years. Diagnosis of seizure was confirmed on the basis of diagnostic criteria and none of the children was treated by any antiepileptic drugs after first episode.
RESULTS: Overall recurrence rate within 2 years of follow up was 38%. Majority of recurrence (65%) observed within 6-10 months of initial seizure. Significant risk factors were an abnormal EEG Findings (p=<0.001), focal seizure (p=<0.001), seizure at sleep (p=0.001) and initial

presentation with status epilepticus (p=0.001). Abnormal neuroimage findings were also associated with seizure recurrence but the finding was not statistically significant.
CONCLUSIONS: A great percentage of first seizure didn't show recurrence but there are so many factors can determine the possibilities of recurrence, early identification of risk factors specially the focal pattern of seizure, seizure in sleep, status epilepticus and abnormal electrophysiology are the best predictive factors of recurrence.
KEYWORDS: Epilepsy

200. Early differentiation of acute encephalopathy with biphasic seizures and late reduced diffusion from febrile status epileptics using phase lag index
Oguri Masayoshi (Tkamatsu, Japan) Okanishi Toru, Nishiyama Masashi, Kuki Ichiro, Nakamura Yuko, Ogo Kaoru, Himoto Tkashi, Maegaki Yoshihiro

OBJECTIVE: To differentiate between acute encephalopathy with biphasic seizures and late reduced diffusion (AESD) and febrile status epilepticus (FS) using phase lag analysis of electroencephalography (EEG) data.
METHODS: We retrospectively collected data from 34 children who had status epilepticus and from whom EEGs were recorded within 24 hours. These included patients with a final diagnosis of AESD (n=17) and FS (n=17). We performed phase lag analysis to calculate the phase lag index (PLI) of EEG signals between two electrodes. The electrodes were placed according to the international 10–20 system using 12 channels (Fp1, Fp2, F3, F4, C3, C4, P3, P4, O1, O2, T3 and T4) and intra and interhemispheric PLI was analyzed. Artifact-free 60-second epochs were selected from each record and both average and max PLI were calculated between each pair of electrodes from a single patient.
RESULTS: Of all pairs in all band EEG frequencies, the AESD group showed higher max PLI in the theta band than the FS group (p=0.005). The alpha, beta, and gamma PLIs of these groups were not significantly different. In the interhemispheric results, the PLIs of the AESD group were also significantly higher at Fp1-Fp2 in the delta band and at C3-C4 and P3-P4 in the theta band than those of the FS patients. There were no significant findings regarding the intrahemispheric PLIs.
CONCLUSIONS: The results suggested that interhemispheric connectivity in slow-wave oscillations in AESD is enhanced in the acute phase and may be useful to discriminate AESD and FS within 24 hours.
KEYWORDS: Epilepsy, Teaching of Child Neurology, Neuroscience

201. Utilization of the Addis Clinic telemedicine platform for epilepsy care, past experience and future opportunities
Varghese Sonia (Chapel Hill, NC, United States) Wabulya Angela, Shiloh Malawsky Yael

OBJECTIVE: Given the limited availability of specialty, sub-specialty, and physician care in areas around the world, The Addis Clinic was founded with the goal to connect volunteer physicians with local organizations providing frontline healthcare to vulnerable and underserved populations. We reviewed prior years' epilepsy related consultations through the Addis Clinic's telemedicine platform. Assess utilization of the organization's services for support of community-based epilepsy care.

METHODS: Review of database of the Addis Clinic teleconsultations, and specific cases related to epilepsy. Demographics of patients, local providers and specific consultation questions. Neurology epilepsy specialists and Addis Clinic leadership discussed the results and reviewed future opportunities to expand and increase the impact of the service on epilepsy care.
RESULTS: Of total of 337 cases, and 563 teleconsultations conducted by the Addis Clinic in 2018, only 4 cases were related to epilepsy. In 2019 the total number of consultation doubled, however, only 4 cases focus was seizures or epilepsy. Discussion between epileptologists and the Addis Clinic leadership raised multiple opportunities for increased epilepsy consultation of the platform. Recruiting additional neurology and epilepsy specialists volunteers, connecting with new local healthcare organizations for partnerships, using the platform for education and training of local providers.
CONCLUSIONS: Telemedicine provides a platform that can provide epilepsy specialists consult in regions of low resources and limited specialist access. Utilization of the Addis Clinic services for epilepsy is low. Connecting with local organizations and increasing volunteer base may increase utilization for the benefit of epilepsy patients.
KEYWORDS: Epilepsy

202. Pattern of medical treatment in children who underwent epilepsy surgery for lesional epileptic spasms.
Erdemir Gozde (Cleveland, OH, United States) Moosa Ahsan, Wyllie Elaine, Gupta Ajay, Kotagal Prakash, Lachhwani Deepak, Pestana-Knight Elia

OBJECTIVE: To describe treatments that children with lesional epileptic spasms failed prior to epilepsy surgery.
METHODS: Medical records were reviewed of all consecutive children who had epilepsy surgery for intractable epileptic spasms at Cleveland Clinic between 2000 and 2018. Demographic data and weight were recorded. Treatment was classified as standard to include ACTH, oral corticosteroids (OC), and vigabatrin (VGB), and conventional to refer to anti-seizure medications (ASM). The data describes the combination of therapies tried but not the order.
RESULTS: Seventy children had surgery during this period. Mean age at surgery was 22 months. Average weight at surgery was 12.6 kg and 96% of the children were operated by the same surgeon. Twenty-four children (34.2%) received ASM alone, and forty-five children (64.3%) received hormonal therapy or vigabatrin or both prior to surgery. Of the latter group, treatment combinations included: 23 children (33%) failed all standard and conventional treatments; 12 (17%) failed ACTH and or oral corticosteroids and ASM; 7 (10%) failed VGB and ASM, 2 (2.9%) failed ACTH alone and 1 patient (1.5%) failed oral corticosteroids and VGB. One child (1.5%) received surgery without prior medical treatment for epileptic spasms.
CONCLUSIONS: Prior to epilepsy surgery for lesional epileptic spasms, the children received a variety of medical treatments with a significant number never receiving standard of care treatment and only 1/3 of the patients exhausting all class of treatment modalities prior to surgery. Availability of standard of care drug during the studied period may explain the results.
KEYWORDS: Epilepsy, Rare Diseases

203. Efficacy of Modified Atkins Diet (MAD) as Treatment for Intractable Epilepsy in Children - A Randomized Controlled Trial.

Haque Nazmul (Dhaka, Bangladesh) Chowdhury Yamin, Debnath Bithi, Hoque SK Azimul, Islam Ariful

OBJECTIVE: To determine the efficacy ,adverse effects and tolerability of MAD in intractable epilepsy of children
METHODS: This was a randomized controlled trial done from July 2016 to December 2017. This study was carried out in Paediatric Neurology, NINS Dhaka, BSMMU, Dhaka, Dhaka Shishu Hospital. At each of the study sites intractable epilepsy cases aged 3 to 18 years having at least 3 seizures per week who intended to be enrolled were randomized either as in study group (MAD treatment group) and control group (getting normal family diet).
Children were evaluated thereafter through detail history and clinical examination ,lab test were obtained. Subsequently cases were randomized by lottery method . After one month observation period MAD was given to the study group and 3 follow up visit at an interval of one month was made. Parents checked urine ketones by reagent test sticks daily throughout 3 month.
RESULTS: Age and sex of both the group is comparable.Phenytoin,valproate,Carbamazepine were the common AED for study group whereas valproate,levitiracetum,carbamazepine and phenobarbitone were the common AED for the control group to treat intractable epilepsy child. The primary outcome of this study at the endpoint of 3rd follow-up, 71 % children had at least 50% or more seizure reduction and 25.7 % children had a ≥ 90% seizure reduction
CONCLUSIONS: Results of the study documented that MAD was found to be effective in reducing seizure burden in children with refractory epilepsy, well tolerated in the studied children and only few adverse effects were observed during study period.
KEYWORDS: Epilepsy

204. Long-term Safety and Efficacy of Cannabidiol (CBD) for the Treatment of Seizures in Patients with Tuberous Sclerosis Complex (TSC) in an Open-Label Extension (OLE) Trial (GWPCARE6)

Wheless James (Memphis, TN, United States) Bebin E, Sparagana Steven, Filloux Francis, Jansen Floor, Kwan Patrick, Loftus Rachael, Sahebkar Farhad, Thiele Elizabeth

OBJECTIVE: To evaluate long-term safety and efficacy of add-on cannabidiol (CBD) for treatment of seizures in patients with TSC in an interim analysis of an OLE trial (GWPCARE6; NCT02544750).
METHODS: Patients who participated in a 16-week, double-blind, randomized controlled trial (RCT) could enroll to receive highly purified CBD (Epidiolex®; 100 mg/mL oral solution) in the OLE (starting dose 25 mg/kg/day, titration up to 50 mg/kg/day). Primary endpoint: safety. Secondary endpoints: percentage reduction in seizures (countable focal or generalized) and total seizures, responder rates, Subject/Caregiver Global Impression of Change (S/CGIC).
RESULTS: Overall, 99% (199/201) eligible patients entered the OLE. Baseline median seizure frequency/28 days: 57 seizures. OLE median treatment time: 267 days (range, 18–910). Mean modal dose: 27 mg/kg/day; 39 patients (20%) withdrew. Adverse event (AE) incidence: 93%; serious AE incidence: 15%; 6% discontinued due to AEs. There was 1 death deemed unrelated to treatment by the investigator. Most common AEs (≥20%): diarrhea (42%), seizure (22%), decreased appetite (20%). Elevated ALT/AST >3× ULN were reported in 17 (8.5%) patients; 12 on concomitant valproate. Median percentage reductions in seizures (12-week windows over 48 weeks): 54–68%. Seizure responder rates (≥50%, ≥75%, and 100% reduction) were maintained

up to 48 weeks, ranging from 53–61%, 29–45%, and 6–11% across visit windows. Improvement in S/CGIC was reported by 87% of patients/caregivers at Week 26.
CONCLUSIONS: Long-term add-on CBD treatment in patients with TSC had an AE profile similar to that observed previously. Reductions in seizures were maintained through 48 weeks.
Funding: GW Research Ltd
KEYWORDS: Epilepsy, Rare Diseases, Critical Care

205. Yield & spectrum of findings of neuroimaging & EEG studies obtained in healthy children presenting with their first unprovoked seizure, a single tertiary center experience
Khair Abdulhafeez (Wilmington, DE, United States) Hussain Sumair, Salvucci Alana

OBJECTIVE: The first unprovoked seizure continues to be a cause of major patient and family anxiety as well as medical diagnosis and management challenge. There is still a debate with regard to the acuity or specifications of these neuroimaging or neurophysiological studies.
METHODS: Trying to streamline and standardize the high volume of children patients presenting with first seizure, we decided to review our own data and practice. We believe our initial testing results showed several actionable findings. Full data results will be analyzed in light of current available evidence-based literature from other scientific bodies and major institutions.
RESULTS: We reviewed all children between the ages of 1-month-old up to 18 years who presented with first clinical seizure in 2018. We reviewed 282 patients, from them 100 presented with first unprovoked seizures, out of them 35 fulfilled inclusion & exclusion criteria. Neuroimaging studies were abnormal in 13 out of the 35 patients (37%) and 14 patients (40%) had abnormal initial EEG. One year follow up was completed and date regarding seizure control and anti-seizure medications are under active review and analysis.
CONCLUSIONS: By reviewing our tertiary center experience over the course of one year, we hope to learn more about our patients' demographics, clinical presentations, and evaluation process. Looking at the preliminary results, we have identified a higher percentage of neuroimaging and EEG abnormalities in our patient cohort than previously reported in medical literature. We are hopeful that via the study will be able to formulate an institutional guidelines eventually.
KEYWORDS: Epilepsy, Neuroimaging

206. INTUBATION IN PATIENTS PRESENTING WITH SEIZURES TO A PEDIATRIC EMERGENCY DEPARTMENT
Mohanty Mugdha (Worcester, MA, United States) Torres Alcy, Zahoor Hovra, Rosman N. Paul

OBJECTIVE: Patients seen for uncontrolled seizures in a Pediatric Emergency Department (ED) often require tracheal intubation (TI). We compared patients requiring TI with those who did not.
METHODS: In this single-center retrospective study, we analyzed 56 consecutive seizing patients who presented to a Pediatric ED. Twenty-six/ 56 (46%) required TI.
RESULTS: Intubated group: 16/26 were male, ages birth to 21 years (mean: 6.9 years). Seizure duration ranged from > 5 to 30 minutes most frequently (13/21). Most seizures were complex febrile convulsions (8/26). Seizures were controlled with benzodiazepines alone (3/26) or with benzodiazepines plus fosphenytoin and/or levetiracetam (17/26). TI was necessitated by

respiratory failure (11/25) or for airway protection (14/25). TI was needed for less than 2 days in 18/25. Abnormalities were found in: 4/18 EEGs, 6/15 CT scans, and 3/9 MRIs. Non-intubated group: 17/30 were male, ages birth to 20 years (mean 6.3 years). Seizure duration was less than 5 minutes most frequently (10/29). Most seizures were "break-through," in patients with epilepsy (13/30); next were complex febrile seizures (5/30). Seizures were controlled with benzodiazepines alone (12/30) or with benzodiazepines plus fosphenytoin or levetiracetam (6/30). Abnormalities were found in: 4/8 EEGs, 3/13 CT scans and 1/4 MRIs.
CONCLUSIONS: In patients presenting to an ED with uncontrolled seizures, those seizures requiring tracheal intubation were most frequently complex febrile convulsions, were longer in duration, and poly-drug therapy was usually needed to achieve seizure control.
KEYWORDS: Epilepsy, Critical Care

207. Epileptic Encephalopathy and Progressive MRI Abnormalities in a Patient with Pathogenic SCN2A Variant
Nagy Amanda (Boston, MA, United States) Luo Yancheng, Krishnamoorthy Kalpathy

OBJECTIVE: *SCN2A* encodes the alpha subunit of voltage-gated sodium channels and is involved in action potential propagation in excitatory neurons during development. Mutations in *SCN2A* have been associated with a range of phenotypes including infantile epileptic encephalopathy, benign familial infantile epilepsy, and autism spectrum disorder.
METHODS: We present case history, MRI and spectroscopy, EEG findings, and whole exome sequencing (WES) of a patient presenting with poor feeding and hypotonia due to epileptic encephalopathy.
RESULTS: Our patient was born at 34 weeks and presented to our institution on day of life 18 with encephalopathy, hypotonia, poor feeding and one episode of clonic arm movements. EEG showed migrating focal seizures which were refractory to numerous antiepileptic and anesthetic agents but were eventually controlled on Dilantin. Despite refractory electrographic seizures, she did not have clear clinical seizures. Serial MRIs revealed a progressive central pattern of injury as well as symmetric T2 signal hyperintensity in the frontal, temporal, and subinsular white matter and the basis pontis. Spectroscopy demonstrated an elevated glycine peak, although serum and CSF amino acid studies were unremarkable. WES revealed a de novo pathogenic missense mutation in SCN2A (c.2501G>A p.(Ser834Asn)).
CONCLUSIONS: Pathogenic *SCN2A* variants have been reported in patients with a range of neurologic presentations. Here we report a neonate with a pathogenic missense mutation in SCN2A presenting with migratory epilepsy. Intriguingly, this patient never developed clear clinical seizures. In addition, this patient exhibited profound, progressive neurologic injury on MRI, which is atypical for most channelopathies but may be related to the significant seizure burden.
KEYWORDS: Epilepsy, Neonatal & Fetal Neurology

208. DESCRIPTIVE EPIDEMIOLOGY OF "CONTINUOUS SPIKE AND SLOW WAVE IN SLEEP (CSWS)" EPILEPSY AT A TERTIARY CARE CENTRE IN INDIA
Batra Sakshi (Delhi, India) Sharma Suvasini

OBJECTIVE: This study describes the electro clinical spectrum and treatment modalities in children with CSWS attending the Epilepsy clinic of a tertiary care centre in North India.

METHODS: Retrospective analysis of the clinical and electroencephalographic characteristics, treatment and prognosis was performed in 20 children diagnosed with CSWS.
RESULTS: All boys aged between 10 months and 12 years (mean age: 3.58 years) were affected. They had variable seizure types mostly comprising of generalized tonic clonic and atonic seizures. The majority children had an unknown etiology. Perinatal events causing CSWS were seen in 2 cases and postnatal meningitis was seen in 1 child. The epilepsy was pharmacoresistant in most cases requiring steroids and multiple antiepileptic drugs. Hyperactivity and behavioural abnormalities were common comorbidities along with cognitive and language regression. One child had clinical characteristics of rolandic epilepsy with EEG suggestive of CSWS.
CONCLUSIONS: Fall during seizures is an important characteristic that could be used for early clinical diagnosis of CSWS. For the patients those with multiple forms of epilepsy and stagnation or retrogression in intelligent and physical development, monitoring EEG should be performed in order to avoid misdiagnosis. Steroids combined with antiepileptic drugs had good effect on the treatment and the prognosis of CSWS.
KEYWORDS: Epilepsy

209. Benign Childhood Epilepsy Syndromes
Rizk Tamer (Saint John, New Brunswick, Canada)

OBJECTIVE: International League Against Epilepsy (ILAE)'s definition of a benign epilepsy syndrome is "a syndrome characterized by epileptic seizures that are easily treated, or require no treatment and remit without sequelae". Many children who have epilepsy syndromes that are not usually considered benign, nevertheless, have a good outcome. Many children with congenital hemiplegia who develop focal seizures have only a few seizures, respond well to medication, and eventually successfully discontinue treatment [1]. [2
METHODS: Benign epilepsy syndromes have been classified according to age of onset into three types: benign neonatal epilepsy syndromes with onset during early neonatal period; benign infantile epilepsy syndromes with onset outside the neonatal period and before first birthday; and benign childhood epilepsy syndromes with its sub-classification; these usually occur in children older than 1 year.
RESULTS: Benign focal epilepsies of childhood do not follow simple Mendelian inheritance, which has strong concordance for idiopathic generalized epilepsies in monozygotic twins, but not for rolandic epilepsy. Autosomal dominant genetic linkage has been reported to 15q14 for BECTS.
Researchers found that EEG traits characterizing these disorders may surprisingly show Mendelian inheritance even if the seizure phenotype did not; this is still an area of debate and needs further studies. Vadlamudi found strong concordance for idiopathic generalized epilepsies in 26 mono- zygotic twins, but no concordance for Rolandic epilepsy in six monozygotic twins.
CONCLUSIONS: Mendelian inheritance in individual families with forms of benign focal epilepsy has been established. EEG trait characterizing these disorders may show Mendelian inheritance, even if the seizure phenotype does not.
KEYWORDS: Epilepsy

210. Switch from enzyme-inducing antiepileptic drugs to new antiepileptic drugs in patients with epilepsy

Ichiyama Takashi (Shunan, Japan) Kohno Fumitaka, Matsufuji Hironori, Isumi Hiroshi, Sugio Yoshitsugu

OBJECTIVE: The enzyme-inducing antiepileptic drugs (carbamazepine, phenytoin, and phenobarbital) have many metabolic side effects, such as osteoporosis, hyperlipidemia, hypothyroidism, cardiovascular disorders, and hyponatremia. To avoid the metabolic risks, we have switched from the enzyme-inducing antiepileptic drugs to new antiepileptic drugs in 28 patients with epilepsy.
METHODS: Twenty-eight patients with epilepsy whose medicines were switched from the enzyme-inducing antiepileptic drugs to the new antiepileptic drugs (20 males and 8 females, aged from 6 to 51 years; median, 20.5 years) were enrolled this study from April 2015 to October 2019. Clinical records of the patients were retrospectively analyzed.
RESULTS: Carbamazepine (CBZ) taken by 14 patients, phenytoin (PHT) by 8, and phenobarbital (PB) by 7 were switched to the new antiepileptic drugs at first. Eleven patients took levetiracetam (LEV), 11 lacosamide (LCM), 4 lamotrigine (LTG), and 2 perampanel (PER) as the new antiepileptic drugs at first. The new antiepileptic drugs taken finally were LEV in 20 patients, LCM in 12, LTG in 5, and PER in 3. The epileptic seizures of 5 patients (18%) were worsened transiently during the switch. The comparisons of epileptic condition of the patients before and after the switch were improvement in 4 patients, no change in 23, and a change for the worse in 1.
CONCLUSIONS: The epileptic seizures of 18% of the patients were worsened transiently during the switch similar to the previous reports. Taking various metabolic side effects of the enzyme-inducing antiepileptic drugs, the switch to new antiepileptic drugs should be considered.
KEYWORDS: Epilepsy

211. Identifying the Significance of Consanguinity for Epilepsy Patients at King Abdulaziz University Hospital in Jeddah, Saudi Arabia

Bamaga Ahmed (Jeddah, Saudi Arabia) Eslhoubaki Abdulraheem, Banjar Akram, Al-Ahmadi Faisal M, Alahdal Saud, Subyani Abdulaziz

OBJECTIVE: Epilepsy in children is the most common neurological disorder leading to disability. A large percentage of epilepsy is idiopathic. It is defined as two or more unprovoked or reflex seizures occurring more than 24 hours apart. There are 724,500 individuals living with epilepsy in the Arab world. Prevalence in Saudi Arabia is approximately 6.5/1,000. Around the world, cultures play a role in consanguineous marriages. Consanguinity means the involvement or union of two individuals who share a common family member. Consanguineous marriages are socially preferred and account for 20-50% of all marriages worldwide. Moreover, around 50% of Arab marriages are consanguineous. In Saudi Arabia, the overall consanguinity is 42.1% to 66.77%. The goal of this study was to assess if there is a significant association between consanguinity and epilepsy.
METHODS: This unicentric, retrospective cross-sectional study of all patients who were admitted to the pediatric inpatient department at King Abdulaziz University Hospital between 2016 and 2018, and who were in the pediatric age group. Data were collected by telephone interviews with the patients' parents after taking verbal consent.
RESULTS: A total of 247 participants were phone interview, out of which 137 were included in the result. The overall percentage of epilepsy was 47.4%, and 65 (76.5%) of children were

products of consanguineous marriages and diagnosed with idiopathic epilepsy. However, a proportion of 23.5% did not have consanguineous parents.
CONCLUSIONS: We found that there is an statistically insignificant association between consanguinity and epilepsy, which may suggest that consanguinity is not a major risk factor for epilepsy.
KEYWORDS: Epilepsy

212. Impact of intracranial monitoring technique on rates of surgical treatment and outcome in children with medically refractory epilepsy
Starnes Keith (Rochester, MN, United States) Brinkmann Benjamin, Britton Jeffrey, Burkholder David, Wirrell Elaine, Payne Eric, Nickels Katherine, Van Gompel Jamie, Wong-Kisiel Lily

OBJECTIVE: We compared rates of surgical treatment and seizure outcomes following intracranial monitoring between eras - when only subdural grids (SDG) were available and when both SDG and stereoelectroencephalography (sEEG) could be chosen.
METHODS: This is a single-center retrospective review of patients <18 years who underwent intracranial monitoring from 2011-2014 (SDG-only era) and 2015-2018. Patient characteristics, subsequent surgical treatment, and good outcome (ILAE classification 1 or 2) were compared. Implantations were retrospectively labeled as “deep” based upon electrode placement.
RESULTS: Seventy-seven patients (38 female, 0.5–18 years) underwent intracranial monitoring, 52 with SDG (32 during SDG-only era) and 25 sEEG. sEEG patients were older (12.7 ± 3.8 vs 10.1 ± 4.3 years; p=0.01), and more likely to undergo bilateral implantation (32.0% vs 3.8%; p=0.001) and have "deep" hypothesis (72.0% vs 44.2%; p<0.05). There was no difference in lesional MRI.
Surgical treatment was more likely during SDG-only era (81.3% vs 60.0%; p<0.05). Surgical treatment followed 39/52 SDG and 14/25 sEEG implants. Good outcomes occurred in 56.4% of SDG and 57.1% of sEEG. Good outcome was associated with single, focal pre-implantation hypothesis in SDG (20/31 vs 2/8; p<0.05).
CONCLUSIONS: The higher rate of surgical intervention after SDG may result from more conservative patient selection, as risks are higher vs sEEG. Bilateral implantation and older age in sEEG is probably related to technical limitations in SDG and selection bias. Patient selection should rely on consideration of noninvasive evaluations to support the modality most able to evaluate a well-formed pre-implantation hypothesis.
KEYWORDS: Epilepsy

213. Clinical features of cryptogenic febrile infection-related epilepsy syndrome (FIRES) in two distinct cohorts
Sakuma Hiroshi (Tokyo, Japan) Horino Asako, Kuki Ichiro, Mizuguchi Masashi

OBJECTIVE: Febrile infection-related epilepsy syndrome (FIRES) is a severe epileptic encephalopathy with febrile illness prior to onset and is defined as a subcategory of new-onset refractory status epilepticus (NORSE). While NORSE does not exclude viral or autoimmune etiologies, the term ‘cryptogenic’ is used when the cause remains unknown after extensive workup. Despite the lack of diagnostic biomarkers, previous reports on FIRES have identified its distinctive clinical features and provided support for the idea that cryptogenic FIRES is not a

clinical presentation, but a specific clinical entity. To clarify and to compare clinical features and trends in the treatment of FIRES in two distinct cohorts from Japan based on nationwide survey.
METHODS: Twenty pediatric patients who developed FIRES between 2014 and 2018 were enrolled. Their clinical, laboratory, and neuroradiological features were compared to those in our historical cohort (26 patients between 2010 and 2014).
RESULTS: Clinical hallmarks included male predominance (73% vs 75%), median onset at early school-age, and predominant focal seizures involving face. Additional features included minimal cerebrospinal pleocytosis (76% vs 71%), periodic discharges on electroencephalography, and occasional involvement of hippocampi (37% vs 29%), basal ganglia, or claustrum/insular cortex on MRI. Most cases were treated by combination of anesthetic agents, antiepileptic drugs, and immunodulators. There was no difference in the duration of barbitutrate treatment between two cohorts.
CONCLUSIONS: Highly reproducible results obtained from two different cohorts suggest that cryptogenic FIRES represents a single clinical entity. There was no change in its therapy, which was still dependent on barbiturate coma.
KEYWORDS: Epilepsy, Critical Care, Infections/Neuroimmunology

214. Two years outcome of status epilepticus in children with encephalitis
Chou Cheng Che (New Taipei City, Taiwan) Wang Huei Shyong, Chen Tien Hsing

OBJECTIVE: Status epilepticus (SE) is a condition known as continuous seizure activity lasting more than 5 minutes or repetitive seizures without regaining full consciousness. Encephalitis is the most common cause of status epilepticus in children. Our study aimed to analyze the two years outcome of SE in children with encephalitis.
METHODS: Chang Gung research database which comprises medical records from seven institutes of Chang Gung Memorial Hospital (CGMH) since 2000 to 2018 was retrospectively reviewed to recruit the children, younger than 18 years of age, diagnosed with both SE and encephalitis. SE was identified by patients with hospitalization discharge claimed for ICD-9 in the "345.3" series. The Encephalitis was identified with ICD-9 in the "320 – 326" series. The primary outcome was analyzed by readmission rate. The secondary outcome was analyzed by rate of intractable epilepsy 2 years after discharge.
RESULTS: Totally, 672 (male : female = 1.33, mean age: 5.2) children were diagnosed to have status epilepticus from 2001 to 2018 at CGMH. And 197 (29.3%) of them, including 128 males (65%) and 69 females (35%) SE patients were diagnosed to have encephalitis. The average age of SE with encephalitis was 5.6-year-old. 55 (11.6%) patients were intubated and average ventilation duration was 11.2 days. 104 patients (52.8%) were readmission within 2 years after discharge and 46 patients (23.3%) developed intractable epilepsy at 2 years after discharge.
CONCLUSIONS: Encephalitis as the etiology of status epilepticus had worse 2 years outcome as higher readmission rate and intractable epilepsy rate than SE children without encephalitis.
KEYWORDS: Epilepsy, Critical Care

215. SURGERY FOR EARLY ONSET EPILEPSY, EXPERIENCE OF AN EPILEPSY SURGERY WORKING GROUP IN COLOMBIA.
Perez-Poveda Juan (Bogotá, D.C., Colombia) Zorro-Guio Oscar, Guio-Mahecha Laura, Nariño-Gonzalez Daniel, Naranjo-Florez Andres, Martinez-Martinez Adriana

OBJECTIVES: To describe the clinical outcomes of patients undergoing epilepsy surgery before age 3 years and had seizures onset before the first year of life.
METHODS: We studied all children whose seizures began during the first year of life and were operated before age 3 years in two Hospitals in Bogota, Colombia between 2011 and 2019. We included children who had a clinical follow-up at least two years and eight months after the procedure. The long term results of those interventions were analyzed in a retrospective observational descriptive cross sectional study.
RESULTS: Fourteen patients underwent epilepsy surgery (7/14 were females). The most common procedure was hemispherectomy (50%) and the main etiology for epilepsy was cortical malformation (43%). Seizure outcome was ILAE Class 1 in seven of the patients (50%), Class 3 in three of the patients (21.4%), Class 4 in one patient (7.2%) and Class five in three of the patients (21.4%). Three children had complications derived from the surgical procedure but there was not mortality. Third-teen children had neurocognitive deficits prior to surgery and this remained unchanged after surgery, but one patient had improved functions as the result of seizure control.
CONCLUSIONS: This study documents our experience with pediatric epilepsy surgery in the first years of life in two hospitals from Bogota, Colombia. Even though the number of patients is limited, our results suggest that employment of epilepsy surgery brings promising and safe outcomes in children with early onset epilepsy.
KEYWORDS: Epilepsy

216. Characterizing the Phenotype of Epilepsy in Children with Past Hematological Malignancies
Abushanab Elham (Cleveland Heights, OH, United States) Pestana Knight Elia, Naduvil Valappil Ahsan Moosa

OBJECTIVE: Describe the profile of refractory epilepsy in children with a history of hematological malignancies.
METHODS: 226 patients with history of malignancy and epilepsy were identified of whom 34 had hematologic malignancies. Of those, 10 patients had refractory epilepsy. Electronic medical records were reviewed for details of cancer and its treatment, seizure history, specific epilepsy syndrome, treatments for seizures, and seizure outcome. Primary statistical methods used were descriptive.
RESULTS: 60% of patients were found to have an epileptic encephalopathy, with the rest being focal epilepsy. 3 of 4 patients with focal epilepsy had temporal lobe epilepsy. 2 of 6 patients with epileptic encephalopathy had structural abnormalities, unclear if causative. 3 with focal epilepsy had structural abnormalities, all in the temporal lobe. 3 of the epileptic encephalopathy underwent corpus callosotomy with resolution of all seizures in one, resolution of drop attacks in another, and no change in the third. 2 of the patients with temporal lobe epilepsy had a temporal lobectomy with subsequent seizure freedom. Seizures were poorly controlled despite multiple AED's and other treatments in the epileptic encephalopathy group. Outcomes were more favorable in focal epilepsy.
CONCLUSIONS: Childhood leukemia or its treatment pose a risk factor for developing refractory epilepsy. In most cases a structural etiology was not identified, leaving the underlying mechanism unclear.
KEYWORDS: Epilepsy, Brain Tumors/Oncology

217. Ketogenic Diet Training for Caregivers: Taking Advantage of Current Popular Media
Knight Vinita (New Haven, CT, United States) Nussbaum Ilisa, Shabanova Veronika

OBJECTIVE: The ketogenic diet (KD), which is a low-carbohydrate, restricted protein, high-fat diet, has been shown to significantly reduce seizure frequency. One of the common barriers to success in KD is compliance. In an effort to improve knowledge about and comfort with KD among our patient families, we developed and pilot-tested educational videos, focusing on preliminary estimates of effects.
METHODS: We produced a video series for creating meals for families with children diagnosed with refractory epilepsy. A 5-question knowledge and 6-question comfort questionnaires, and 2 open-ended questions were used to evaluate these two constructs. Face and content validity of questionnaires were performed using KD experts. The questionnaires were administered upon KD initiation hospital discharge (Time A), 2 weeks later (Time B), and after caregivers viewed the videos 2 to 4 weeks later (Time C). This was a within-person, pre-post design pilot study, using a convenience sample of pediatric patients in ketogenic diet clinic.
RESULTS: Among 9 patient families, with median child age of 9 years (range: 1.4 - 16.5 years), knowledge at Time B (median 3.5) was significantly lower than both Time A (median=4.0, p=0.05) and Time C (median=5.0, p=0.03). Median comfort scores significantly increased across time points from 27 to 28.5 to 30.
CONCLUSIONS: In this pilot study, we found that most parents leave the hospital comfortable with KD, but their knowledge of KD decreased over time. Our educational intervention mitigated this and improved comfort level with KD. A larger study is warranted given the promising findings thus far.
KEYWORDS: Epilepsy

218. Sexual and reproductive healthcare for adolescent and young adult women with epilepsy: a qualitative study of pediatric neurologists and epileptologists
Kirkpatrick Laura (Pittsburgh, PA, United States) Collins Amy, Sogawa Yoshimi, Kazmerski Traci

OBJECTIVE: Adolescent women with epilepsy (WWE) have unique sexual and reproductive health (SRH) needs, including counseling on teratogenesis, folic acid, and interactions between contraception and antiseizure medications. There are no prior studies regarding SRH practices of pediatric neurologists. In this study, we explore attitudes and practices of pediatric neurologists regarding SRH for adolescent WWE.
METHODS: Interviews were conducted with pediatric neurologists regarding their attitudes and practices with SRH for adolescent WWE. Interviews were audio-recorded and transcribed. Thematic analysis was conducted.
RESULTS: Sixteen neurologists (44% male) participated. Major themes included: (1) SRH is important for AYA women with epilepsy and should be co-managed with pediatricians and/or obstetrician-gynecologists. (2) There is little standardization in practice with variability in content, frequency, and quality of SRH. Important subthemes included parent education and decision-making based on perceived patient risk factors. (3) SRH provision differed substantially for women with intellectual disabilities. (4) Barriers to SRH provision included limited time; provider, patient or family discomfort; and lack of knowledge or expertise. (5) Facilitators to

SRH included strategies for standardization of patient education, transition programs, partnerships with pediatricians and/or obstetrician-gynecologists, and provider training on SRH.
CONCLUSIONS: This is the first study to assess attitudes and practices of pediatric neurologists regarding SRH for AYA women with epilepsy. Our findings suggest there is a need for improved systems for SRH delivery and co-management for AYA women with epilepsy. Providers identified barriers and facilitators that might serve as the basis for interventions to improve care.
KEYWORDS: Epilepsy

219. Understanding the relationship between time of day and seizure severity
Cuddapah Vishnu (Philadelphia, PA, United States) Sehgal Amita

OBJECTIVE: Parents of children with refractory epilepsy report that the unpredictability of seizures can be as distressing as seizure frequency and severity. Emerging data suggest that the likelihood of having a seizure in people with epilepsy may related to the time of day.
METHODS: Using *Drosophila melanogaster*, the common fruit fly, we sought to understand the relationship between seizure severity and time of day. We used 3 fly models that experience seizures after mechanical stimulation: *tko, bss,* and *eas* mutant flies, as well as 2 fly models that experience seizures at elevated temperatures: GEFS+ and Dravet Syndrome (DS) fly knock-in models. At six timepoints through the day, we quantified the number of flies having seizures and duration of various seizure components.
RESULTS: In *tko* flies we find the likelihood of having a seizure peaks in the late day with a trough early in the night. This trend was also noted in *bss* flies and *eas* flies. In addition, *tko* flies had a longer tonic/clonic phase in the early morning timepoint. At elevated temperatures, GEFS+ flies had a decreased latency to seizure activity at night. Similarly, DS flies had a prolonged latency to recovery at night.
CONCLUSIONS: Here we find a correlation between time of day and seizure severity in fly models. This could be secondary to behavioral state (e.g. awake versus asleep), direct circadian influences, or other environmental factors (e.g. changes in light exposure). Further studies will be necessary to understand which of these underlying mechanisms contribute to seizure likelihood.
KEYWORDS: Epilepsy, Neuroscience, Genetics

220. Time to treatment of pediatric status epilepticus in patients with and without intellectual disability / developmental delay
Amengual-Gual Marta (Boston, MA, United States) Sánchez Fernández Iván, Loddenkemper Tobias, on behalf of pSERG

OBJECTIVE: Evaluate whether time to treatment of pediatric refractory status epilepticus (rSE) is longer in patients with developmental delay / intellectual disability (DD/ID) compared to patients without DD/ID.
METHODS: This is a retrospective analysis of a prospectively collected cohort of pediatric patients (1 month to 21 years of age) with rSE from June 2011 to November 2019. We developed a multivariable Cox proportional hazards model using purposeful selection, as proposed by Hosmer and Lemeshow [1], to evaluate the effect of DD/ID on time to treatment.

RESULTS: We included 324 patients (56% male) with a median (p_{25}-p_{75}) age of 3.8 (1.2-8.9) years (Table 1). There was no difference in the time to first benzodiazepine with or without DD/ID in univariable [15 (5-48) versus 20 (5-42) minutes, p=0.94] or multivariable [HR: 0.95 (95% CI: 0.73-1.24), p=0.72] analysis (Table 2). There was no difference in the time to first non-benzodiazepine anti-seizure medication in univariable [69 (41-155) versus 65 (30-128) minutes, p=0.17] or multivariable [HR: 0.96 (95% CI: 0.75-1.24), p=0.73] analysis (Table 2). Among the 147 patients with at least one continuous anesthetic infusion, there was no difference in time to first continuous infusion in univariable [180 (122-525) versus 157 (85-589) minutes, p=0.95] or multivariable [HR: 0.95 (95% CI: 0.73-1.24), p=0.72] analysis (Table 2).
CONCLUSIONS: Our data did not identify different time to treatment for rSE in children with and without DD/ID.
KEYWORDS: Epilepsy

221. Quantifying "Clinically Meaningful Changes" in Seizure Frequency – Data From Three Phase 3 Studies of ZX008 (Fenfluramine Hydrochloride Oral Solution) in Dravet Syndrome: Do Expectations and Views Change Over Time?
Gammaitoni Arnold (Emeryville, CA, United States) Sullivan Joseph, Dlugos Dennis, Farfel Gail, Galer Bradley, Morrison Glenn, Haney Douglas, Nabbout Rima

OBJECTIVE: We used an anchor-based method to calculate percentage seizure frequency reduction associated with "clinically meaningful change" in caregiver and investigator Clinical Global Impression of Improvement (CGI-I) ratings ("Much improved" or "Very much improved"). Data were from randomized controlled trials (RCTs) of fenfluramine for treating Dravet syndrome.
METHODS: This analysis used data from two 14-15-week phase 3 RCTs (n=206) and a long-term open-label extension (OLE) study (n=330; median treatment duration, 63.5 weeks; range, 1.0-128.4). Patients in the phase 3 studies received placebo or add-on fenfluramine (0.2-0.7 mg/kg/day). Receiver operating characteristic (ROC) analysis compared change in monthly convulsive seizure frequency (MCSF) with binary versions of investigator and caregiver CGI-I Likert scale ratings. The cutpoint for a clinically meaningful change equaled the change in MCSF at which sensitivity≈specificity.
RESULTS: In both RCTs, a positive association emerged between MCSF reduction and caregiver/investigator CGI-I scores emerged. In the RCTs, ROC analysis identified cutpoints of ≥44% and ≥37.5% reductions in MCSF being associated with CGI-I ratings of "Much Improved" or "Very Much Improved." In the OLE a different pattern emerged: these same CGI-I ratings corresponded to ≥78%-80% cutpoints (Table 1).
CONCLUSIONS: Major differences were found in the cutpoints between the two RCTs and the OLE. These unexpected results suggest that both caregiver and investigator views regarding MCSF reduction and rating a patient "Much improved" or "Very much improved" may change over long periods of time, possibly related to changing expectations of drug effect. Other factors may include non-seizure effects, tolerability, and OLE vs RCT study design.
KEYWORDS: Epilepsy

222. A Phase 1 Healthy Volunteer Trial Investigating the Dose-Ranging Effects of Cannabidiol (CBD) on the Pharmacokinetics (PK) of Clobazam and N-desmethylclobazam
Morrison Gilmour (Cambridge, United Kingdom) Critchley David, Crockett Julie, Tayo Bola

OBJECTIVE: CBD is approved for treatment of seizures associated with Lennox-Gastaut or Dravet syndromes in patients ≥2 years. In previous studies, CBD increased exposure to *N*-desmethylclobazam (N-CLB), clobazam's (CLB) active metabolite. This trial investigated effects of steady-state CBD (1–20 mg/kg/day) on safety and PK of CLB and N-CLB.
METHODS: Arms 1–5 enrolled 12 subjects each. On Day 1, all subjects received 10 mg CLB; Arms 1–4 also received CBD-matched placebo. Arm 1 received 0.5 mg/kg CBD (Epidiolex®; 100 mg/mL) twice daily (BID; Days 11–35) and 10 mg CLB (Day 25). Arms 2–4 titrated to 2.5, 5, or 10 mg/kg CBD BID (Days 11–21), received target dose (Days 22–46), and 10 mg CLB (Day 36). Arm 5 received 400 mg fluconazole (potent CYP2C19/3A4 inhibitor; Day 11), 200 mg fluconazole (Days 12–35), and 10 mg CLB (Day 25). CBD, CLB, and metabolite concentrations were determined.
RESULTS: CLB exposure was unaffected by CBD dose. CBD (1–20 mg/kg/day) dose-dependently but non-linearly increased N-CLB exposure (C_{max}: 1.2–2.2-fold; AUC_{0-t}: 1.3–2.6-fold), tending towards saturation at therapeutic doses (10–20 mg/kg/day). Metabolite-to-parent ratios (N-CLB:CLB) were similar between 10–20 mg/kg/day CBD. Fluconazole increased CLB $AUC_{0-\infty}$ 3.85-fold. Most adverse events were mild; somnolence was most common (20% subjects).
CONCLUSIONS: Co-administration of CBD with CLB increased N-CLB exposure in a dose-dependent manner, but the effect is saturable. CLB dose reductions may be required when combined with CBD. Co-administration of CBD with CLB was generally well tolerated.
Funding: GW Research Ltd.
KEYWORDS: Epilepsy, Rare Diseases, Critical Care

223. Long-term Efficacy and Safety of Add-On Cannabidiol (CBD) in Patients with Treatment-Resistant Epilepsies (TRE): 4-year Results from the Expanded Access Program (EAP)

Patel Anup (Columbus, OH, United States) Devinsky Orrin, Lopez Merrick, Park Yong, Pichon Zentil Pilar, Szaflarski Jerzy, Thiele Elizabeth, Wechsler Robert, Checketts Daniel, Sahebkar Farhad

OBJECTIVE: To evaluate efficacy and safety of CBD in patients with TRE through 192 weeks of treatment in the EAP.
METHODS: Patients received oral CBD (Epidiolex®) increasing from 2–10 mg/kg/d to tolerance or maximum 25–50 mg/kg/d dose. Efficacy endpoints: percent change from baseline in convulsive seizures and responder rates across visit windows.
RESULTS: Of 892 patients in safety analysis set, 322 (36%) withdrew, lack of efficacy (19%) and AEs (7%) being the most common reasons. Median (range) age: 11.8 years (0–74.5); median (range) baseline AEDs: 3 (0–10); most common baseline AEDs: clobazam (48%), levetiracetam (34%), and valproate (28%). Median (IQR) top CBD dose: 25 mg/kg/d (24–30); median (range) exposure duration: 694 days (10–1793). Baseline median (IQR) monthly convulsive seizure frequency for efficacy analysis set: 40 (12–112). Median percent reduction in convulsive seizures (12-week windows through 192 weeks) was 50%–67%. At least 50%, 75%, and 100% reductions in convulsive seizures were maintained through 192 weeks, ranging from 51%–59%, 33%–42%, and 11%–19% of patients across visit windows, respectively. AEs were reported by 88% of patients and serious AEs by 41%; 8% withdrew due to an AE. There were 20 deaths,

deemed unrelated to treatment by the investigator. Most common AEs (≥20% of patients): diarrhea (33%), convulsion (24%), and somnolence (23%). Liver-related AEs in >1% of patients: abnormal LFT (4%) and increased ALT (3%) and AST (3%).
CONCLUSIONS: Add-on CBD produced sustained seizure reduction for up to 192 weeks with an acceptable safety profile. FUNDING: GW Research Ltd.
KEYWORDS: Epilepsy, Rare Diseases, Critical Care

224. A Pilot Study: Electrical Source Imaging in the Evaluation of Children with Epilepsy
Freibauer Alexander (Hamilton, Ontario, Canada) Jones Kevin

OBJECTIVE: To evaluate the effectiveness of low density Electrical Source Imaging (ESI) as a secondary imaging modality for epilepsy surgery work up at a level 3 comprehensive epilepsy centre.
METHODS: We performed a retrospective review of 20 patients who underwent epilepsy surgical evaluation. Initial potential epileptogenic zone was based on seizure semiology, scalp EEG and brain MRI. 8 were potential surgical candidates, and 7 had functional data useful for ESI analysis. Their EEGs were extracted, and interictal and ictal spikes marked. Brain MRIs and marked EEGs were uploaded into Curry ESI software, which generated head models using the boundary element method, representative single equivalent dipoles for spike peaks, moving dipoles of the spike rising phase and sLORETA reconstructions to represent irritative zones. Moving dipoles or fixed independent component analysis dipoles were used to analyze ictal onset zones. Potential epileptogenic zones were re-evaluated with ESI data and compared to the initially determined location.
RESULTS: In comparison of the epileptogenic zones determined with and without ESI, data was concordant in all cases. ESI provided more specific localization of the potential epileptogenic zone in 5 cases. Dipole orientation, and progression of the moving dipole supported the localization hypothesis in 5 cases. We show that ESI produces images of the irritative zone and interictal zones congruent with estimations made by analysis of EEG, MRI and seizure semiology.
CONCLUSIONS: We infer that ESI would have been a valuable secondary imaging modality in epilepsy surgery work up by being a fast and accurate tool in defining the potential epileptogenic zone.
KEYWORDS: Epilepsy, Neuroimaging

225. Development of XEN496, a Pediatric Immediate-Release Formulation of the Potassium Channel Opener Ezogabine
Cadieux Jay (Burnaby, British Columbia, Canada) Tandy Matthew, Namdari Rostam, Aycardi Ernesto

OBJECTIVE: To develop a pediatric-friendly granular formulation of ezogabine to allow for flexible weight-based dosing without requiring extemporaneous compounding in the KCNQ2-related developmental and epileptic encephalopathy (KCNQ2-DEE) population.
METHODS: A modified quality-by-design approach was implemented in the formulation development of this Biopharmaceutical Classification System Class 2 (low water solubility, high permeability) drug. Tiered assessments included excipient compatibility, dissolution profiles, processability by dry granulation, chemical stability, particle sizing and binding to common

plastics. The candidate formulation was then advanced to rat pharmacokinetic (PK) studies in order to confirm its biopharmaceutical performance *in vivo* and placed on long-term stability studies.
RESULTS: The lead formulation (XEN496) showed *in vitro* dissolution profiles (both pre- and post-granulation) consistent with an immediate-release product (*e.g.*, 91.2 ± 1.2% released after 10 minutes, 99.1 ± 1.0% released after 45 minutes). Optimal dissolution performance was observed with a 20% w/w ezogabine load. Granulation parameters were optimized to provide a suitable particle size distribution. Spike-recovery experiments conducted with several common plastics showed no more than 6% relative loss of ezogabine. Stability studies are ongoing and have shown no significant physical or chemical degradation or trends. The suitable PK profile of this lead formulation were confirmed through rat PK studies.
CONCLUSIONS: A pediatric formulation of ezogabine (granules suitable for dispersal in breast milk, infant formula or soft foods, packaged in sprinkle capsules of varying fill weights) was identified and progressed into GMP drug product manufacturing and clinical development. This formulation is presently the focus of a Phase I PK study in adult healthy volunteers.
KEYWORDS: Epilepsy, Translational/Experimental Therapeutics, Rare Diseases

226. Safety of Valtoco® (NRL-1; Diazepam Nasal Spray) in Children With Epilepsy: Updated Interim Subgroup Results From a Phase 3, Open-Label, Repeat Dose Safety Study

Wheless James (Memphis, TN, United States) Segal Eric, Tarquinio Daniel, Miller Ian, Dlugos Dennis, Desaig Jay, Mauney Weldon, Ayala Ricardo, Cascino Gregory, Biton Victor, Carrazana Enrique, Rabinowicz Adrian

OBJECTIVE: To evaluate the safety/tolerability of long-term treatment with diazepam nasal spray (Valtoco®, NRL-1) for seizure clusters in a subgroup of patients aged 6-11 years.
METHODS: The study enrolled patients aged 6-65 years with frequent seizure clusters (ie, acute repetitive seizures). Age- and weight-based doses of 5, 10, 15, or 20 mg of diazepam nasal spray were administered; second doses were permitted 4-12 hours later if needed. Safety assessments included treatment-emergent adverse events (TEAEs) and assessment of nasal irritation.
RESULTS: Of 177 enrolled patients, 54 (30.2%) were aged 6-11 years (56.1% female, 87.8% white). In this pediatric safety analysis (n=41), exposure duration was ≥12 months in 27 (65.9%) patients, 6 to <12 months in 9 (22.0%), and <6 months in 5 (12.2%). Twenty-two (53.7%) patients averaged ≥2 doses/month, with a total number of doses (range) of 1-188 at day 365. Overall, 33 (80.5%) pediatric patients had a TEAE (Table). Fifteen (36.6%) had a serious TEAE, none considered treatment-related. No patients discontinued because of a TEAE. Two (4.9%) treatment-related TEAEs occurred (eye irritation, epistaxis), both were mild and transient. Mild nasal irritation, (Grade 1A: focal), was noted in 2 patients at baseline but was lower at all subsequent timepoints, including day 365 (n=1). Four patients discontinued for other reasons.
CONCLUSIONS: In this interim, long-term safety analysis in a pediatric subgroup with seizure clusters, repeated doses of diazepam nasal spray were well tolerated, with a safety profile consistent with diazepam, and no discontinuations due to TEAEs. The retention rate was high.
For the DIAZ.001.05 Study Group
KEYWORDS: Epilepsy

227. A Standardized Protocol to Improve Management of Acute Seizures in the Pediatric Epilepsy Monitoring Unit

Pavitt Sara (Palo Alto, CA, United States) Carley Alison, Porter Brenda, Knowles Juliet

OBJECTIVE: Systematic studies to improve pediatric patient safety during Phase 1 epilepsy monitoring unit admissions, particularly with regard to acute seizure management, are lacking. We found only 42% of seizures during Phase 1 admissions at our hospital were managed with complete standard safety measures (referred to as "seizure first aid"). Our goals were to increase consistency and speed of seizure first aid delivery in acutely seizing patients.
METHODS: Following a root cause analysis, major factors contributing to seizure management variation were identified. Key drivers necessary for improved acute seizure management were identified as (1) standardization of bedside seizure care, (2) "buy in" and competency of team members, (3) incorporation of the protocol into daily work. Targeted interventions, jointly developed by physicians and nurses, were implemented through quality improvement methodology.
RESULTS: Complete seizure first aid increased from 42% to 90% post intervention (p=0.03). Pre-intervention, 17% of seizures were associated with a complete focused neurological assessment, which increased to 90% after intervention (p=0.003). On average it took 3 min to begin to obtain vital signs and 3.3 min to begin neurologic assessment which decreased to 1.2 min (p=0.02) and 1.6 min (p=0.03) respectively. Nursing perceived care effectiveness increased from 29% to 51%.
CONCLUSIONS: A collaborative effort between physicians and nurses led to wide adherence to a standardized seizure management protocol and significantly improved management of acute seizures. These relatively simple interventions could be adapted in other institutions' epilepsy monitoring units to improve quality of patient care.
KEYWORDS: Epilepsy

228. Implementation of a Standardized Method to Measure Seizure Outcomes in a Clinical Practice Setting.

Paudel Sita (Hershey, PA, United States) Kandel Prakash, Mainali Gayatra, Kumar Ashutosh, Byler Debra, Michael Elizabeth, Miller Stacey, Kothari Saira, Farrell Kathleen, Fureman Brandy, Harding Christina, Buchhalter Jeffrey, Trescher William

OBJECTIVE: Outcomes measurement at the practice level is critical to improve the quality of medical care. The Epilepsy Learning Healthcare System (ELHS) is a multicenter network to improve epilepsy outcomes. The aim of this effort was to use ELHS measures at one practice site and identify challenges to using a standardized approach to record epilepsy outcomes.
METHODS: We used Quality Improvement (QI) methodology to evaluate recording of standardized outcomes at follow up visits for patients at one ELHS site. A Pediatric Epilepsy Quality Care Form developed by the ELHS was converted to a paper Epilepsy Outcomes Form (EOF), which captured the date of the last seizure, frequency of seizures, effects of the seizures and medications on daily activities, Emergency Department visits, and hospitalizations. Through Plan-Do-Study-Act (PDSA) cycles, we assessed the completion rate of the EOF at follow up visits for patients with epilepsy. All data were entered into a REDCap database approved by the IRB for QI.

RESULTS: Initially, clinicians completed the EOF in 29% of patient visits (Figure). Through PDSA cycles, we achieved an EOF completion rate of 90%. Analysis of 849 follow-up visits for epilepsy care, revealed challenges to completion of individual items. Missing data or uncertainty on data elements combined ranged from 20% to 50%, with the highest rates for the effects of seizures and medications on daily activities.
CONCLUSIONS: Utilizing QI methodology, we achieved an overall 90% rate of EOF completion to measure epilepsy outcomes, but individual items pose challenges to full completion of the form.
KEYWORDS: Epilepsy

229. Effectiveness of Corticosteroids Versus Adrenocorticotropic Hormone for Infantile Spasms: A Systematic Review and Meta-analysis
Kuo Yung-Ting (Taipei, Taiwan) Chang Yin-His, Chen Chiehfeng, Chen Shu-Huey

OBJECTIVE: To compare the therapeutic effectiveness of oral corticosteroids with that of adrenocorticotrophic hormone for infantile spasms.
METHODS: Embase, Scopus, and the Cochrane library were searched to retrieve studies published before December 2018 to identify pediatric patients with a diagnosis of infantile spasms. The interventions of oral corticosteroids and adrenocorticotrophic hormone were compared. We included only randomized controlled trials that reported the cessation of spasms as treatment response. The primary outcome was clinical spasm cessation on day 13 or 14. The secondary outcomes were the resolution of hypsarrhythmia, side effects, continued spasm control, spasm relapse rate, and subsequent epilepsy rate. Following the Preferred Reporting Items for Systematic Reviews and Meta-Analyses, the study-level quality assessment was conducted using the Cochrane risk-of-bias tool.
RESULTS: After extensive review, 39 articles were included for meticulous evaluation. Five randomized controlled trials with a total of 239 individuals were eligible for further analysis. No significant difference was detected between the corticosteroids and adrenocorticotrophic hormone in the cessation of clinical spasms (odds ratio [OR]: 0.54; 95% confidence interval [CI]: 0.16 to 1.81; $p = 0.32$). The subgroups of high-dose prednisolone versus adrenocorticotrophic hormone and low-dose prednisone versus adrenocorticotrophic hormone also exhibited no significant difference. Furthermore, the two subgroups did not differ in terms of hypsarrhythmia resolution, side effects, relapse rate, or subsequent epilepsy rate.
CONCLUSIONS: This meta-analysis suggests that high-dose prednisolone is not inferior to adrenocorticotrophic hormone and that it be considered a safe and effective alternative treatment.
KEYWORDS: Epilepsy

230. 'A video tells a thousand words.' A review of videos used in acute Pediatric Neurology referrals at a regional children's hospital in the UK
Parida Amitav (Birmingham, United Kingdom) Wassmer Evangeline

OBJECTIVE: Paroxysmal events are the most common acute neurological presentations in children. During the coronavirus pandemic remote review of children has become a necessity. We aimed to review the diagnostic utility of videos sent by referrers from local hospitals to a regional Pediatric Neuroscience centre.
METHODS: A retrospective review of all acute referrals over a 4-month period.

RESULTS: 343 referrals were identified. 6% (N=19; Male=6, Female=13) were accompanied by videos. Age range was 1 month-15 years. Mean age was 3 years. 10 (52%) children were less than 12 months of age. 89% (N=17) of videos were created on parental smartphones and 11% (N=2) were recorded by medical videography services. All videos were reviewed by an Attending (Consultant) Pediatric Neurologist. A likely clinical diagnosis was made in 15/19 (79%) cases. All videos were of adequate quality. The most common diagnosis was an epileptic seizure in 8/19 (42%) children with Epileptic Spasms present in 4 of these cases. An alternative diagnosis of a non-epileptic seizure (N=1), self-gratification (N=1), motor stereotypy (n=1), dystonic movements (N=1) and motor tic (N=1) was made where the referrer had suspected an epileptic event. 2 cases of opsoclonus were also identified with one child subsequently found to have a neuroblastoma.
CONCLUSIONS: Videos are a vital tool in a remote neurology consult. We should encourage referrers to send videos to help identify important diagnoses, avoid unnecessary investigations and reduce the need for face-to-face consults. A robust system of consent and information governance is necessary to facilitate transfer of patient videos between institutions.
KEYWORDS: Epilepsy, Movement Disorders (including Cerebral Palsy)

231. Met813Lys ATP1A2 mutation causes a severe epileptic encephalopathy distinct from but sharing some features with Alternating Hemiplegia of Childhood
Elliott Courtney (Chapel Hill, NC, United States) Hunanyan Arsen, Keough Karen, Mikati Mohamad

OBJECTIVE: Describe two patients with epileptic encephalopathy with c.2438T>A, Met813Lys variant and the knock-in mouse demonstrating pathogenicity of that variant.
METHODS: Retrospective review of the two cases. Generation of the knock-in mouse using CRISPR/Cas9 with pronuclear injection of single guide RNA, cas9 mRNA and a repair oligo into fertilized mouse embryos.
RESULTS: Patient 1 is a ten-year-old with refractory multifocal seizures, with concurrently and independently occurring hemiplegias, since the age of 15 months. He also manifested recurrent episodes of status epilepticus leading to hospitalizations and severe developmental regression. Patient 2 is a three-year-old who manifested monthly episodes of right hemiplegias as of one years of age. At two years of age, he developed an episode of left hemiplegia with concurrent focal status epilepticus and right cerebral edema. Six months later, he presented with a similar but right sided episode. Both had a de novo ATP1A2 (c.2438T>A, Met813Lys) variant interpreted as possibly pathogenic. All generated mice (four) with the point mutation (Sanger sequencing), were very weak, ataxic and ¾ died before weaning. The survivor took 343 seconds to complete the balance beam test. His normal littermates (six) took 14.7±7.97seconds with a 95% confidence interval of (0.17-41.17). It lasted 0 seconds on the rotarod while normal littermates lasted 46.7±60.13 seconds with a 95% confidence interval of (-5.6-120.6). After this test, this mutant died too.
CONCLUSIONS: The Met813Lys ATP1A2 is a recurrent disease-causing mutation that causes a severe epileptic encephalopathy distinct from, but sharing some features with Alternating Hemiplegia of Childhood.
KEYWORDS: Epilepsy, Rare Diseases

232. Importance of Seizure Time of Day in Children With Epilepsy Treated With Valtoco® (Diazepam Nasal Spray): Interim Subgroup Results From a Phase 3, Open-Label, Repeat Dose Safety Study

Segal Eric (Hackensack, NJ, United States) Tarquinio Daniel, Miller Ian, Dlugos Dennis, Wheless James, Desai Jay, Mauney Weldon, Ayala Ricardo, Cascino Gregory, Biton Victor, Rabinowicz Adrian, Carrazana Enrique

OBJECTIVE: Diurnal seizure patterns may provide important information for improving aspects of patient care ranging from seizure control and quality of life to SUDEP. Seizures in children have been reported to occur in specific circadian patterns and sleep/wake distributions depending on seizure type and onset location. However, there are few time-of-day data for seizure clusters (acute repetitive seizures) in pediatric patients. Therefore, a hypothesis-generating time-of-day analysis of seizure-cluster onset was conducted in the 6-11 year-old subgroup of a long-term, repeat-dose study of diazepam nasal spray (Valtoco®, NRL-1).
METHODS: The study enrolled patients aged 6-65 years with seizure clusters despite antiseizure drugs. Age- and weight-based doses of 5, 10, 15, or 20 mg of diazepam nasal spray were administered. Clock time of onset of each cluster was assessed.
RESULTS: Of 177 enrolled patients, 54 were aged 6-11 years (safety population, n=41). Exposure was ≥12 months in 27 (65.9%) patients, 6 to <12 months in 9 (22.0%), and <6 months in 5 (12.2%); 22 (53.7%) averaged ≥2 doses/month. Among 666 treated clusters, seizure onset was generally highest during mornings and late evenings and lowest in the afternoon (Table).
CONCLUSIONS: These preliminary results support the view that circadian rhythms influence time of day when monitoring children with seizure clusters may need stressing in daily practice. In this study of diazepam nasal spray, dose groups corresponded to patient weight and age; however, small numbers limit interpretation in higher-dose groups. Further analysis by seizure type and other factors is warranted upon study completion. For the DIAZ 001.05 Study Group
KEYWORDS: Epilepsy

233. Epilepsy Outcomes Measured by a Standardized Method in a Clinical Practice Setting.

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OBJECTIVE: The Epilepsy Leaning Healthcare System (ELHS) is a multicenter network focused on improving epilepsy outcomes. The aim of this report is to evaluate and describe standardized epilepsy outcomes at one practice site of the ELHS.
METHODS: With an ELHS designed measure, we recorded outcomes at a single follow up visit over 8 months for 849 unique patients. A Pediatric Epilepsy Quality Care Form developed by the ELHS was converted to a paper Epilepsy Outcomes Form (EOF). Clinicians completed an EOF at each patient visit. The data were entered into an IRB-approved REDCap database.
RESULTS: We achieved an overall 90% rate of EOF completion to measure epilepsy outcomes at each patient visit. When the most recent seizure occurred and the frequency of seizures in relationship to the clinic visit are described in the Table (A. Timing, B. Frequency). As reported by the patient/caregiver, seizures were better in 49.1%, the same for 39.6%, and worse for 7.3% of patients, with missing data for 4.0%. Treatment side effects were reported in only 13.3% of patients, no side effects in 73.0%, uncertain or unknown in 7.9%, with missing data in 5.8%.

Emergency Department visits occurred for 11.7% of all patients and hospitalizations for 6.1% of all patients.
CONCLUSIONS: Through the ELHS network, we have begun to measure epilepsy outcomes in a standardized manner in clinical practice. This effort is being performed within a Quality Improvement Science framework with limitations present. Targeted interventions will be necessary to improve our ability to measure epilepsy outcomes.
KEYWORDS: Epilepsy

234. Evaluation of outpatient administration of Repository Corticotropin Injection (RCI, Acthar Gel) for the treatment of Infantile Spasms (IS): Pilot Study
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OBJECTIVE: Most U.S. practitioners initiate repository corticotropin injection (RCI, Acthar Gel) inpatient due to training program's convention. Joshi et al. '06 reported 76% of responding CNS providers "always admitted," whereas only 6% "admitted less than 25%." 90% admitted simply for "education for injection." We compared financial data, adverse events (AE), and perceived nursing education success between inpatient (IP) and outpatient (OP) RCI initiation for Infantile Spasms (IS) to assess if the OP model we developed was less expensive and equally successful.
METHODS: Consecutive, newly-diagnosed, untreated IS patients (<2yo) initiating RCI IP or OP by established treatment protocols were verified via EPIC chart query after RCI treatment. Data included: (1) retrospective, EPIC chart review for demographics, comorbidities, financial data, efficacy, AE; (2) caregiver telephone survey regarding nursing education for RCI and injections. Descriptive statistics, risk difference, and confidence intervals were utilized.
RESULTS: 20 IP and 13 OP were studied. Median age was 8.6 months (IP) and 10.9 months (OP). There was a large difference between total charges (median IP: $8071; OP: $1097; see Figure 1). Minor AE occurred in 19/20 of IP and 11/12 of OP. No serious AE occurred in either group. Nursing education for RCI indication and risk/benefit was considered adequate for 14/17 of IP and 8/8 of OP respondents (see Table 1 Q1).
CONCLUSIONS: OP RCI initiation is much less expensive, with similar observed AE and successful nursing education rates. Small sample sizes limited ability to draw conclusions about differences between IP/OP for AE, efficacy, and successful nursing education.
KEYWORDS: Epilepsy

235. Efficacy of combining Ketogenic diet and Vagus Nerve Stimulation in children with epilepsy
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OBJECTIVE: Studying the efficacy of combined Ketogenic diet (KD) and Vagus Nerve Stimulation (VNS) in children with Drug Resistant Epilepsy (DRE)
METHODS: Retrospective review of 33 patients (1-17 years) with DRE treated with VNS and KD. Efficacy data were aggregated across all patient visits determining seizure reduction rates at Baseline, 3, 6, 12 and 24 months after adding the second non-pharmacological therapy.

RESULTS: At one month, 10% showed no change in seizure frequency, 40% had < 50% improvement, and 50% had > 50% improvement. At 3 months, 10% no change, 35% had < 50% improvement, 50% had > 50% improvement and 5% seizure free. At 6 months, 4.6% showed no change, 31.8% had < 50% improvement, 59.1% had > 50% improvement and 45.6% seizure free. At 9 months, 27.8% showed no change, 16.7% had < 50% improvement and 55.6% had > 50% improvement. At 12 months, 6.3% showed no change, 12.5% had < 50% improvement, 75% had > 50% improvement and 6.3% seizure free. At 15 months, 8.3% showed no change, 25% had < 50% improvement, 58.3% showed > 50% improvement and 8.3% were seizure free. At 18 months, 33.3% showed < 50% improvement, 50% showed > 50% improvement and 16.7% seizure free. At 24 months, 33.3% showed < 50% improvement, 44.4% showed > 50% improvement and 22.2% seizure free. At 24 months, 16.7% showed < 50% improvement, 66.7% showed > 50% improvement and 16.7% seizure free.
CONCLUSIONS: Combining KD and VNS therapy is more effective than either therapy alone in children with DRE.
KEYWORDS: Epilepsy

236. Diagnostic yield of biochemical CSF neurotransmitter testing in infants
Patel Amisha (Philadelphia, PA, United States) Fung France, Kessler Sudha

OBJECTIVE: Biochemical analysis of cerebral spinal fluid (CSF) for diagnosis of neurotransmitter (NT) disorders is labor intensive, costly, and requires an invasive procedure (lumbar puncture). Recent advances in genetic testing may obviate the need for CSF analysis. We conducted a retrospective cohort study to evaluate the diagnostic yield of CSF neurotransmitter testing in infants with new onset epilepsy.
METHODS: Infants ages 0-12 months who underwent CSF NT testing between January 2008 and December 2017 at Children's Hospital of Philadelphia were identified by an electronic medical record query of laboratory orders. Charts were manually reviewed to evaluate clinical characteristics of tested infants, as well as the percentage of CSF NT tests yielding a diagnosis among all tested infants, and in the subset with epilepsy.
RESULTS: CSF NT testing was performed in 186 infants. In this work in progress, the first 65 consecutive charts were reviewed. Presenting features included seizures in 16 patients (85%). The remainder presented with abnormal limb or eye movements, motor impairment, or developmental delays. CSF NT revealed a diagnosis in no patients. Genetic testing (including SNP microarray, epilepsy gene panel or whole exome sequencing) revealed a diagnosis in 16 patients (25%). Four patients (6%) were found to have cortical malformations on brain MRI not seen on initial evaluation.
CONCLUSIONS: CSF NT testing is a low yield diagnostic study in infants presenting with seizures and/or abnormal movements. Routine use prior to higher yield testing including high quality imaging and genetic testing should be reconsidered.
KEYWORDS: Epilepsy, Neurometabolic Disorders, Genetics

237. Evaluating the effect of sedation on obtaining an informative magnetoencephalography (MEG) in pediatric epilepsy patients
Dale Brianna (Memphis, TN, United States) Williard Theresa, Freeman Haley, Brooks Lai, Benefield Lauren, Gienapp Andrew, Rezai Roozbeh, Babajani-Feremi Abbas, Wheless James

OBJECTIVE: To understand the effects of standard magnetoencephalography (MEG) sedation in pediatrics.
METHODS: We completed retrospective chart review of 167 patients who underwent sedated MEG (January 2015–August 2019). Data collected included medications, and maintenance and induction doses (propofol, dexmedetomidine). We noted if language and sensory mapping were tested, and if they were successful (i.e., was an informative study obtained).
RESULTS: We reviewed 166 patients (55.4% male), aged 0–16 years (mean, 5.4; median, 5); 24, 1, and 139 received propofol, dexmedetomidine, or combination for maintenance anesthesia, respectively; 30, 9, and 125 received propofol, dexmedetomidine, or combination for induction, respectively. Successful sensory responses were obtained in 18/144 (12.5%)—2 with propofol, 1 with dexmedetomidine, and 15 with combination doses. Propofol doses ranged 190–820 mg (median, 400 mg; mean, 440.06 mg) vs. 6–50 mcg with dexmedetomidine (median, 16.5 mcg; mean, 18.3 mcg). Successful language responses were obtained in 45/145 (31.0%)—2 with propofol, 1 with dexmedetomidine, and 15 with combination doses. Total propofol doses ranged 132–860 mg (median, 324 mg; mean, 371.1 mg) vs. 6–60 mcg with dexmedetomidine (median, 13 mcg; mean, 17.4 mcg).
CONCLUSIONS: High dose propofol is needed to prevent patient arousal during MEG; however, propofol use results in few informative MEG studies. Dexmedetomidine is a milder sedative and allows more informative MEG studies. Together, low dose propofol and optimized dexmedetomidine administration is sufficient to prevent patient arousal and allows for an informative MEG study. We plan future studies to evaluate dexmedetomidine monotherapy efficacy.
KEYWORDS: Epilepsy

238. Anxiety and Depression in Adolescents with Epilepsy at Philippine Children's Medical Center

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OBJECTIVE: Epilepsy is a chronic neurologic disorder complicated by neurobehavioral comorbidities, including affective disorders, which adversely affect quality of life. The study determined the prevalence of anxiety and/or depression in adolescents with epilepsy and the association of these disorders with sociodemographic variables and seizure-related factors such as age of onset, duration of epilepsy, seizure frequency, electroencephalogram/neuroimaging abnormalities, type of epilepsy including epilepsy syndromes and drug treatment in a tertiary center in the Philippines.
METHODS: This is an analytical, cross sectional study. All adolescent patients with epilepsy who fulfilled the inclusion and exclusion criteria were screened using the Hospital Anxiety and Depression Scale (HADS)/ Hospital Anxiety and Depression Scale-Pilipino (HADS-P). Epilepsy-related and sociodemographic variables in association with anxiety and depression were determined and analyzed.
RESULTS: A total of 145 adolescent patients were included in the study. There was a 17.4% prevalence of anxiety and 3.4% prevalence of depression in this study population according to the screening tool. However, a confirmatory diagnosis was not done in some patients. There was no significant factor associated with occurrence of anxiety. Factors that were highly associated with depression were a psychiatric illness in the first degree relative, frequent seizures at onset,

no anti-epileptic drug use and monotherapy at the time of study. Presence of anxiety also increased the odds of having depression.
CONCLUSIONS: Affective disorders are common in adolescents with epilepsy and factors related to their occurrence must be anticipated. Hence, the need to screen the patients for psychiatric symptoms early and regularly.
KEYWORDS: Epilepsy, Cognitive/Behavioral Disorders (including Autism)

239. The effect of weekends and holidays on time to treatment in pediatric convulsive status epilepticus
Barcia Aguilar Cristina (Brookline, MA, United States) Sanchez Fernandez Ivan, Loddenkemper Tobias, on behalf of pSERG

OBJECTIVE: Evaluate the impact of weekends and holidays on time-to-treatment of pediatric convulsive status epilepticus (SE).
METHODS: Retrospective analysis of prospectively collected observational data from June 2011 to May 2019 of pediatric patients (1 month to 21 years of age) with SE, defined as convulsive seizures that required administration of at least two anti-seizure medications (ASMs), including at least one non-benzodiazepine ASM (non-BZD ASM). We compared time to treatment during weekdays and weekends/federal holidays with multivariate analysis by cox proportional-hazard regression, adjusting for potential confounders.
RESULTS: We included 446 patients (57% males) with a median (p25-p75) age of 4.1 (1.4-9.4) years. Of these, 319 (72%) had SE onset during a weekday, and 127 (29%) during a weekend/holiday. The median (p25-p75) time to the first BZD administration was shorter on weekends/holidays than on weekdays [11 (5-31) minutes versus 18 (6-45) minutes, p= 0.01; HR=1.28 (95% CI:1.04-1.58), p=0.021]. The median time to the first non-BZD ASM administration was shorter on weekends/holidays than on weekdays [63 (29-110.5) minutes versus 70 (40-131.5) minutes, p= 0.061; HR=1.24 (95% CI:1.004-1.53), p=0.046]. Patients with SE onset in-hospital during weekends/holidays had shorter times to the first BZD [6 (3-18) minutes versus 10 (5-27) minutes, p=0.02; HR=1.37 (95% CI:0.95-1.97), p=0.089] and to the first non-BZD ASM [30 (20-55.5) minutes versus 45 (25-79.5) minutes, p=0.043; HR=1.48 (95% CI:1.02-2.15), p=0.038] than those during weekdays (Figure 1).
CONCLUSIONS: Time-to-treatment of pediatric SE is shorter on weekends/holidays than on weekdays. These differences are mostly driven by shorter delays in patients with in-hospital SE onset during weekends/holidays.
KEYWORDS: Epilepsy

240. Valtoco® (Diazepam Nasal Spray) in Children With Epilepsy Aged 6-11 Years: Interim Subgroup Results By Frequency of Usage From a Phase 3, Open-Label, Repeat Dose Safety Study
Tarquinio Daniel (Atlanta, GA, United States) Segal Eric, Miller Ian, Dlugos Dennis, Wheless James, Desai Jay, Mauney Weldon, Ayala Ricardo, Cascino Gregory, Biton Victor, Cook David, Carrazana Enrique, Rabinowicz Adrian

OBJECTIVE: To assess repeat doses of diazepam nasal spray (Valtoco®, NRL-1) by monthly frequency of usage in pediatric subgroups (aged 6-11 years) of a long-term study in patients with seizure clusters.

METHODS: Patients aged 6-65 years with frequent seizure clusters were enrolled. Age- and weight-based doses of 5, 10, 15, or 20 mg of diazepam nasal spray were administered; second doses were permitted 4-12 hours later, if needed. Treatment emergent adverse events (TEAEs) were assessed for subgroups of patients aged 6-11 years based on monthly usage of diazepam nasal spray: moderate (1-2 doses) and frequent (≥2 doses).
RESULTS: Of 177 enrolled patients, 54 were aged 6-11 years with 41 in the safety analysis: 19 had moderate monthly use of diazepam nasal spray and 22 had frequent use. The percentage of patients with duration of exposure ≥12 months was somewhat higher in the moderate-use group (73.7%) than the frequent-use group (59.1%; Table 1). Across usage groups, total doses ranged from 1-188 (Day 365). Incidence of TEAEs was generally similar between groups, 82.4% in the moderate-use group and 77.3% in the frequent-use group (Table 2). No serious TEAEs were deemed treatment related. There were no discontinuations due to TEAEs. Three (15.8%) moderate-use and 1 (4.5%) frequent-use patients discontinued prematurely.
CONCLUSIONS: The safety profile of diazepam nasal spray in children ages 6-11 with seizure clusters was similar between moderate-use (<2 doses/month) and frequent-use (≥2 doses/month) subgroups and consistent with that expected for diazepam. Retention was high in both usage groups. For the DIAZ 001.05 Study Group
KEYWORDS: Epilepsy

241. Characteristics of Children with Epilepsy Failing More Than 2 ASMs Before Referral for Surgical Evaluation
Newell Grace (Fort Worth, TX, United States) Papadelis Christos, Malik Saleem, Keater Cynthia, Shahani Dave, Shandley Sabrina, Perry M. Scott

OBJECTIVE: Drug resistant epilepsy (DRE) is defined as failure of 2 antiseizure medications (ASM) and alternative treatments such as epilepsy surgery should be considered. Despite a diagnosis of DRE many patients continue treatment with additional ASM trials delaying surgical referral. We sought to characterize differences among children failing <2 and >2 ASMs before referral to identify opportunities to reduce time to surgical evaluation.
METHODS: We compared multiple sociodemographic and epilepsy variables from medical records derived from the Comprehensive Epilepsy Surgery Database of Cook Children's Medical Center in Fort Worth, Texas. The comparison was between patients failing < 2 and >2 ASMs at the time of initial epilepsy surgery evaluation. All variables were analyzed using SPSS to compare differences between the two groups (Table 1).
RESULTS: Ninety-seven patients met our inclusion/exclusion criteria. Children failing >2 ASMs met criteria for DRE on average 5.33 years earlier than children failing <2 ASMs ($p<0.05$) (Fig. 1a). Children failing >2 ASMs were on average 3.44 years younger at surgical referral ($p<0.05$) (Fig. 1b), but their referral was delayed an average of 1.23 years after DRE diagnosis compared to those failing <2 ASMs ($p=0.057$). No significant differences were observed between the two groups among the rest of the variables.
CONCLUSIONS: Younger children are delayed for epilepsy surgery referral and instead trial additional ASMs despite meeting criteria for DRE early in life. Improved recognition of young children with DRE is a viable target to reduce delay to epilepsy surgery.
KEYWORDS: Epilepsy

242. Peri-ictal headache in children with epilepsy - prospective diary study.

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OBJECTIVE: The aim of this prospective diary study was to analyze the correlation between demographic and clinical factors and the type of peri-ictal headache. Furthermore, an attempt was made to find trends in the headache duration, intensity or location.
METHODS: 57 with peri-ictal headaches were included in the prospective study. The participants' guardians were asked to keep a diary of the seizure and peri-ictal headache episodes during a 180-day period. In the 3rd and 6th month of follow-up, EEG examination was performed and systematic history regarding peri-ictal headaches was taken from the patients and their parents. 50 patients completed the 6 month follow-up.
RESULTS: Prospective analysis did not reveal any correlations between sex, age, duration of disease, EEG changes and type of peri-ictal headache. However a statistically significant correlation was noted between the age at onset of disease and the occurrence of ictal and post-ictal headaches: the patients with ictal headaches were younger at the time of epilepsy diagnosis. A total of 913 seizure and 325 peri-ictal headache episodes were noted during the study. Post-ictal headaches were most common, occurred up to 1 hour after the seizure, lasted minutes to hours, were migraine-type and 2,43 times more likely to occur after generalized seizures.
CONCLUSIONS: Peri-ictal headaches are a significant health problem for patients with epilepsy. The most common type are post-ictal headaches and they are most likely to appear after a generalized seizure episode.
KEYWORDS: Epilepsy, Headache/Migraine

243. Time to Second Doses in Children With Epilepsy Treated With Valtoco® (Diazepam Nasal Spray): Interim Subgroup Results From a Phase 3, Open-Label, Repeat Dose Safety Study

Miller Ian (Miami, FL, United States) Segal Eric, Tarquinio Daniel, Dlugos Dennis, Wheless James, Desai Jay, Mauney Weldon, Ayala Ricardo, Cascino Gregory, Biton Victor, Cook David, Carrazana Enrique, Rabinowicz Adrian

OBJECTIVE: Seizure clusters may persist 24 hours or longer, with 58.5% of clusters lasting 6-24 hours. Therapies providing long-lasting activity are needed. This analysis assessed time from first to second dose, if needed, through 24 hours in the 6-11 year-old subgroup of a long-term, repeat-dose safety study of diazepam nasal spray (Valtoco®, NRL-1).
METHODS: The study enrolled patients aged 6-65 years with frequent seizure clusters. Age- and weight-based doses (5, 10, 15, or 20 mg) of diazepam nasal spray were administered; second doses were permitted 4-12 hours later, if needed. Use of a second dose was assessed at 4, 6, 12, and 24 hours.
RESULTS: Among 177 enrolled patients, 54 were aged 6-11 years. Of 755 treated clusters, 19 (3%) received a second dose by 4 hours, 27 (4%) by 6 hours, 50 (7%) by 12 hours, and 90 (12%) by 24 hours (Figure). In the safety population, exposure was ≥12 months in 65.9% of patients, 6 to <12 months in 22.0%, and <6 months in 12.2%; 53.7% of patients averaged ≥2 doses/month. Adverse events (AEs) were reported for 80.5% of patients, 2 AEs were considered treatment-related (both mild and transient). Four of 54 discontinued, none due to an AE.
CONCLUSIONS: The need for second dose was low in children aged 6-11 years, with second doses given for only 12% of seizure clusters within 24 hours. These data support patients'

maintenance of control over 24 hours after the initial Valtoco dose. The retention rate in the study was high. For the DIAZ.001.05 Study Group
KEYWORDS: Epilepsy

244. Avoiding Premature Closure: Epilepsy in Pediatric Patients with Psychogenic Non-Epileptic Spells
Shear Talia (Chicago, IL, United States) Barajas Miguel, Tatachar Priya

OBJECTIVE: The prevalence of psychogenic non-epileptic spells (PNES) in patients with preexisting epilepsy has been well documented. Less well studied, however, are delays that occur when the diagnosis of PNES precedes that of epilepsy. Here we describe the utility of a thorough neurological evaluation and prolonged EEG studies in those presenting with new or ongoing spells of concern.
METHODS: An IRB-approved retrospective review of pediatric patients with a prior history of a psychiatric disorder with a recent diagnosis of epilepsy was conducted at Ann & Robert H. Lurie Children's Hospital (2019-2020). Clinical characteristics including demographics, prior neuro-diagnostic studies, medications, and time to diagnosis of epilepsy from onset of new symptoms were included. The diagnosis of epilepsy was based on neurological assessment and video-EEG, and was supplemented with neuroimaging.
RESULTS: Four patients (2 male) were included. Age ranged from 9-14 years. 3 of 4 (75%) had histories of normal EEGs. Average time from symptom onset to diagnosis and treatment of epilepsy was 15.3 ± 10.1 months (range: 7-30 months). All 4 underwent prolonged EEG recording ranging between 13 hours to 3 days, with spells of concern captured and consistent with seizure activity electrographically. Subsequent neuroimaging demonstrated definite structural abnormalities in 3 of 4 patients (75%).
CONCLUSIONS: Implicit bias and premature closure due to prior diagnosis of PNES may cause a delay in thorough evaluation and time to treatment of epilepsy. This case series emphasizes the need to investigate and capture spells of concern with prolonged video-EEG when new spells arise or new history is acquired.
KEYWORDS: Epilepsy

245. Auto-stimulation-VNS in Pediatric Patients with Lennox-Gastaut Syndrome
Abdelmoity Sherouk (Kansas City, MO, United States) Abdelmoity Ayman, Riordan Sean, Kaufman Christian, Le Pichon Jean Baptist, Abdelmoity Ahmed

OBJECTIVE: Lennox-Gastaut syndrome (LGS) is a severe childhood epilepsy commonly associated with drug-resistant epilepsy (DRE). The Vagus Nerve Stimulator (VNS) is established as a safe and effective treatment for DRE. This study assesses efficacy and tolerability of the auto-stimulation VNS models in pediatric patients with LGS.
METHODS: This retrospective chart review of LGS patients implanted with an auto-stimulation VNS model at a single level four pediatric epilepsy center. Patient responder's rate was the primary outcome. Improvement in five quality-of-life measures as reported by the patients and families. Efficacy and tolerability were assessed at 1, 3, 6, 12, 18 and 24 months compared to baseline.
RESULTS: 71 consecutive patients with LGS and implanted with an auto-stimulation VNS model. 55%, 67.7%, and 65% of children achieved greater than 50% reduction in seizures

frequency at 6, 12, and 24 months respectively. 11% of the patients were seizure free at 12 months and 17% were seizure free at 24 months. By 24 months post implantation most of the patient families reported at least a 50% improvement rate in one or more of the quality-of-life measures. The most commonly reported adverse events were dysphonia, paresthesia, and shortness of breath, all of which were tolerated and subsided by 24 months. Two patients had their device removed secondary to infection and no premature deaths were reported.
CONCLUSIONS: This study is the first observation that the auto-stimulation model of the VNS provides further improvements in both reduction in seizure frequency and improvement in quality-of-life when compared to previous treatment.
KEYWORDS: Epilepsy

246. PHARMACOKINETIC AND TOLERABILITY COMPARISON OF XEN496 PEDIATRIC FORMULATION WITH EZOGABINE ADULT TABLETS
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OBJECTIVE: XEN496 is a novel, immediate-release "sprinkle" (granule) oral formulation of ezogabine under development for seizures caused by heterozygous de novo KCNQ2 loss of function variants in pediatric patients ≥ 1 month of age. Ezogabine immediate-release tablets (e.g., Potiga®) are not suitable for use in this pediatric population, and are no longer commercially-available. XEN496 is intended to be mixed with milk, formula or soft foods prior to dosing. We sought to determine whether XEN496 and Potiga® exhibited comparable biopharmaceutical performance, therefore facilitating the extrapolation from historical Potiga® pharmacokinetic (PK) data to that of XEN496 for selection of a dosing regimen.
METHODS: Twenty-two fed healthy adult volunteer subjects underwent PK evaluation following a single 400 mg oral dose of ezogabine as XEN496. Subjects were monitored for adverse events (AEs). The results were compared with historical data available for single dose, oral ezogabine (Potiga®) at 400 mg in 23 adult subjects under similar conditions.
RESULTS: There were no significant differences in ezogabine C_{max}, T_{max} or AUC when given as Potiga® or as XEN496 (see Figure 1). Dizziness was the most frequent central nervous system adverse event with both studies, at 27% for XEN496 and 22% for Potiga®. Fatigue was reported in 32% of the XEN496 study subjects and somnolence was reported in 17% of the Potiga® study subjects. There were no clear differences in the AE profile across groups.
CONCLUSIONS: XEN496 has comparable single dose PK parameters to Potiga® in adult subjects and exhibited a similar AE profile.
KEYWORDS: Epilepsy, Genetics

247. Implementation of an EPIC SmartForm improves assessment of patient-centered outcome measures in childhood epilepsies
Fitzgerald Mark (Philadelphia, PA, United States) Fridinger Sara, Gonzalez Alexander, Melamed Susan, DiGiovine Marissa, Tefft Sarah, Tencer Jaclyn, Hagopian Samantha, Fried Lawrence, Dlugos Dennis, Kessler Sudha, Abend Nicholas, Helbig Ingo

OBJECTIVE: We created a standardized, EPIC-based Epilepsy SmartForm to document key data elements during clinic visits with the goals of improving patient care and enabling epilepsy-related quality improvement projects. We sought to implement this SmartForm, increase

utilization to at least 25% of visits within a 12-month period, and determine seizure frequency among our epilepsy patients.
METHODS: The SmartForm was created using variables recommended by the Epilepsy Learning Health System (ELHS) and Pediatric Epilepsy Learning Health System (PELHS). We analyzed CHOP Neurology office visits between 9/1/2019 to 3/1/2020 for patients with a primary diagnosis of epilepsy. Using a QlikView dashboard, SmartForm adoption was tracked on a weekly basis. Discrete data elements about seizure frequency and seizure freedom were analyzed in similar manner.
RESULTS: Since 9/6/19, the SmartForm has been used in 940 visits, which represents 20% of all office visits for patients with a primary diagnosis of epilepsy. Seizure frequency and freedom fields were completed in 80% of these visits. Of these patients, 11% are seizure free, defined as >2 years without a seizure. A large proportion of patients have ongoing seizures (89%), with 16% having daily seizures.
CONCLUSIONS: Our standardized Epilepsy SmartForm was adopted quickly by providers. For the first time, we systematically document that 89% of our patients have ongoing seizures with 16% of all children with epilepsy having multiple daily seizures. This indicates an urgent need to improve treatment of patients with intractable epilepsy and identify children who may benefit from surgical therapies, dietary strategies, and precision-medicine approaches.
KEYWORDS: Epilepsy

248. Efficacy of everolimus on epilepsy associated with tuberous sclerosis complex.
Ishihara Naoko (Toyoake, Japan) Shima Sayuri, Sasaki Hitomi

OBJECTIVE: Tuberous sclerosis complex (TSC) is caused by the releases of mTORC1 suppression due to dysfunction of protein complex encoded by causative genes *TSC1* and *TSC2*. It causes hamartomas in the body, such as subependymal giant cell astrocytoma (SEGA) and renal angiomyolipoma (AML). In Japan, everolimus (EVL), an mTORC1 inhibitor, was approved for use in SEGA and renal-AML in 2012 and was subsequently extended to whole TSC patients in 2019. As epilepsy is one of the most important non-neoplastic complications of TSC, we evaluated factors related to the effect of EVL on epilepsy.
METHODS: Twelve patients who had epileptic seizures at the initial administration of EVL were enrolled in the study. Clinical information was collected retrospectively from medical records.
RESULTS: The subjects were 5 males and 7 females, ages 5-41 (median 20), 5 with SEGA, and 8 with renal-AML. Seizure types were focal impaired awareness seizures (FIAS) in 5 cases, FIAS and generalized seizures (GS) in 3, FIAS and epileptic spasm (ES) in 2, and GS alone in 2. EVL doses were 2-10 mg/day and the serum trough levels were 3.4-12.1 ng/mL. Frequency of seizures decreased after administration of EVL in 8 cases, of which 5 were suggested to be effect of EVL. The average serum trough level for EVL-effective patients was 7.4 ng/mL, whereas for invalid patients was 5.9 ng/mL. The efficacy was high in FIAS, and less in ES and GS.
CONCLUSIONS: The efficacy of EVL was higher in high serum level, and in FIAS.
KEYWORDS: Epilepsy, Rare Diseases

249. Experience of implementing integrated services for children with epilepsy in primary health care and primary health nurse role in an outreach financially- constrained district in Pakistan.

Malik Muhammad (Lahore, Pakistan)

OBJECTIVE: The aim of this study was efficacy assessment of integration of childhood epilepsy in local primary health care in an outreach financially-constrained district in Pakistan.
METHODS: The data about childhood epilepsy treatment gap (CETG) and impact of integration of childhood epilepsy in primary health care to improve CETG was collected in free paediatric neurology camps on 7th and 8th December 2018. We evaluated 240 CWE (160 fully supported and 80 as control), treatment was initiated with AED(s) at least 3 months prior the study date. Tthree parts of data were: 1) demographical information ,2) AED(s) adherence profile using Morisky Medication Adherence Scale-8 (MMAS-8) and 3) intervention-effectiveness of the community childhood epilepsy center (CCEC) on bridging the treatment gap.
RESULTS: Age ranged from 04 months - 18 years with male to female ratio of 1.26:1. AED(s) adherence by self-report was 85% (was 42% in 2014 without community intervention) among the supported CWE and was 40% among the control: without any gender preference. After two years of intervention, CETG dropped to 20% (was ≥90% in 2014 without local community support), however still it was 82.5% without any support. Nonaffordability of treatment cost was the most important cause of non-adherence to AEDs; less important caused were lack of trained personals, parent's negligence and misbelieve. Treatment gap bridging was due to integration of childhood epilepsy services local primary health care.
CONCLUSIONS: Strengthening of the local primary health care service is an efficient approach in bridging treatment gap among CWE in financially poor settings.
KEYWORDS: Epilepsy, Teaching of Child Neurology, Neurorehabilitation

250. Neurodevelopmental and epilepsy outcomes of patients with infantile spasms treated in a tertiary care center

Bashiri Fahad (Riyadh, Saudi Arabia) Al-Sehemi Matar, Hamad Muddathir, Alshammari Nawaf, Aljumah Mujtaba, Kentab Amal, Salih Mustafa

OBJECTIVE: Infantile spasms (IS) are a rare form of epileptic encephalopathy. It is divided into three types; idiopathic, cryptogenic, and symptomatic. Neurodevelopmental regression is characteristic of IS.The aim of this study was to identify the patient and treatment factors that correlate with favorable neurodevelopmental and epilepsy outcomes.
METHODS: A retrospective chart review of all children with infantile spasms treated at King Khalid University Hospital (KKUH), Riyadh, Saudi Arabia between January 2000 and December 2017 was performed. The inclusion criteria were infants who were diagnosed with IS as per the International League Against Epilepsy (ILAE) definition. Patients who were lost to follow-up and those who did not receive treatment at KKUH were excluded. Statistical Analysis was done by using IBM SPSS.
RESULTS: A total of 53 patients were included and categorized into idiopathic, cryptogenic and symptomatic types of IS. The majority had a symptomatic etiology (71.7%).The type of etiology and delay in the initiation of treatment were significant predictors of motor and cognitive outcomes but not seizure control. Patients who had idiopathic IS were diagnosed earlier (0.72 months) and had better neurodevelopmental outcomes.Vigabatrin in combination with either adrenocorticotropic hormone (ACTH) or prednisolone resulted in greater epilepsy resolution than monotherapy and other combination modalities.

CONCLUSIONS: Neurodevelopmental outcomes of IS are strongly associated with the underlying etiology. Early initiation of treatment was associated with favorable cognitive and motor outcomes.Early response to combination therapy was associated with better seizure outcomes. However, motor and cognitive outcomes were not affected by the response to the combination therapy.
KEYWORDS: Epilepsy, Cognitive/Behavioral Disorders (including Autism), Movement Disorders (including Cerebral Palsy)

251. Clinical Characteristics and Risk Factors of Seizures Associated with Acute Gastroenteritis in Childhood
Chen Tai-Heng (Kaohsiung, Taiwan) Tseng Yung-Hao, Wu Yan-Zhang

OBJECTIVE: We investigated the clinical features of children with febrile or afebrile seizures during Acute gastroenteritis (AGE) and identify the impact of fever and potential risk factors.
METHODS: We retrospectively reviewed the medical charts of children admitted due to seizures associated with mild AGE. The patients were divided into two groups: an 'afebrile group' whose diagnosis was compatible with 'benign convulsion with mild gastroenteritis (CwG)' and a 'febrile group' who had a fever within 24 hours of the onset of an AGE-related seizure. We compared the two groups' clinical and laboratory features and outcomes.
RESULTS: There were 41 afebrile and 30 febrile cases, with a mean age of 32.2±27.6 months. The gender, seizure semiology, frequency, duration of seizures, the time interval between AGE symptoms onset and first seizure were different between the two groups. More seizure clusters and partial seizures and a shorter interval between the onset of AGE symptoms and seizures in afebrile patients than in febrile patients. Seizure clusters occurred more frequently in the afebrile patients who had a duration of AGE symptoms lasting two days or more, or white blood cell counts ≧10000/μL (p = 0.05 and 0.04, respectively). The most frequently identified enteropathogen was rotavirus (33%), especially in the male and febrile subjects. All cases had uneventful outcomes.
CONCLUSIONS: Although fever partially influenced the clinical features of AGE-related seizures, febrile CwG might have a pathophysiology distinctly different from that of febrile seizures. Comprehensive knowledge of febrile and afebrile CwG can help to avoid unnecessary diagnostics tests and anticonvulsants use.
KEYWORDS: Epilepsy, Infections/Neuroimmunology, Teaching of Child Neurology

252. Unusual double mutation in MECP2and CDKL5 genes in Rett-like Syndrome
Jdila Marwa Ben (Sfax, Tunisia) Charfi Triki Chahnez, Ghorbel Rania, Bouchaala Wafa, Ben Ncir Sihem, Kamoun Fatma, Fakhfakh Faiza

OBJECTIVE: Rett syndrome (RTT) is a neuro-developmental disorder divided into classical and atypical forms of the disease. RTT-like syndrome was also described and has been associated with several genes including MECP2 and CDKL5 but not in the same patient. Here we present a patient with double mutation in these two genes and will discuss the effect of mutations in genes expression.
METHODS: We report patient with Rett-like syndrome for whom clinical features and their progression guided toward the screening of two candidate genes *MECP2* and *CDKL5*. Severity score was evaluated by "Rett Assessment Rating Scale" (R.A.R.S.) and analysis of the genes was

performed by sequencing. Predictions of pahogenicity and functional effects used several bioinformatic tools and RT/QPCR was conducted to evaluate gene expression.
RESULTS: Mutational screening revealed two mutations in *MECP2* and *CDKL5* genes in the patient with a high R.A.R.S. Bioinformatic investigations predicted a moderate effect of MECP2 mutation but a more pathogenic one of mutation in*CDKL5* gene. Effect of CDKL5 mutation on structure and stability of mRNA was confirmed by RT/QPCR. Additionally, analysis of gene expression revealed a drastic effect of CDKL5 mutant on its MeCP2 and Dnmt1 substrates and also on its MYCN regulator.
CONCLUSIONS: The co-existence of the two mutations in CDKL5 and MECP2 genes could explain the severe phenotype in our patient with RTT and is consistent with the data related to the interactions of CDKL5 with MeCP2 and Dnmt1proteins.
KEYWORDS: Epilepsy, Cognitive/Behavioral Disorders (including Autism), Rare Diseases

253. The curious case of a familial epilepsy syndrome with a distinct different etiology in one individual of the same family
Chattopadhyay Arijit (Kolkata, India) Datta Dipanjana, Guha Roy Priyamvada

OBJECTIVE: *Mutations in KCNQ2 leads to channelopathy associated with familial epilepsy syndrome . However, we report a separate etiology in a 3-year-old boy from the same family, having infantile seizures in clusters with a prenatal h/o of reduced fetal movement. This is a case study of two different types of seizures present in the same family.*
METHODS: The 3-year-old boy visited the Pediatric Epilepsy clinic where clinical and genetic investigations were conducted. His uncle, who had been suffering from infantile seizure , attended the genetic clinic, to understand the risk of recurrence of epilepsy in his next generation and investigations were done on basis of the information. Their family history revealed that the paternal aunts and cousins all had episodes of benign infantile seizures.
RESULTS: Investigations indicated that while the 3-year-old had a missense mutation in *POMT1* gene, which has been reported in muscle-eye-brain disorder and milder forms have been associated with seizures, ataxia and pyridoxine dependent seizures and inhertited in an autosomal recessive manner. The uncle had a novel variant in *KCNQ2* gene associated with familial epilepsy. The grandparents were also investigated and the grandfather who also had the KCNQ2 mutation, was asymptomatic. The 3-year-old child did not have a *KCNQ2* mutation like other family members.
CONCLUSIONS: While family studies can predict the gene and the management, it is important to test every family member, as there could be other genetic component involved too. In this case the management of KCNQ 2 associated epilepsy would be different from those with POMT1 seizures.
KEYWORDS: Epilepsy, Genetics

254. Assessment of adrenal function after ACTH treatment in children with infantile spasms: a retrospective analysis of local practices and trends
Haridas Babitha (Buffalo, NY, United States) Haider Mohammad, Mastrandrea Lucy, Farooq Osman

OBJECTIVE: Infantile spasms (IS) is an age dependent epileptic encephalopathy. Treatment with high dose ACTH suppresses the hypothalamic-pituitary-adrenal axis necessitating stress-

steroid therapy during intercurrent infections/illnesses after ACTH treatment. Our goals were to: a) assess how often endocrinology was involved in patient care; b) identify predictors of hypsarrhythmia persistence on EEG following ACTH.
METHODS: We performed a five year retrospective chart review of all children admitted to a tertiary Childrens Hospital diagnosed with infantile spasms and treated with ACTH.
RESULTS: Of the 23 patients with infantile spasms, 10 underwent cosyntropin testing under the care of an endocrinologist. Of those, 80% of tests were done more than 3 months after completion of ACTH therapy, and 6 passed cosyntropin stimulation test. Female gender and the presence of modified hypsarrhythmia on pre-ACTH EEG had a higher incidence of persistent hypsarrhythmia following ACTH. Patients with symptomatic and cryptogenic IS had 67% and 69% incidence of developmental delay. Patients with symptomatic IS had a higher incidence of delays after ACTH treatment (89%) versus the cryptogenic group (69%; p=0.17).
CONCLUSIONS: Our study demonstrates the need for a multi-disciplinary team, involving endocrinology, in the care of patients with IS. Though not statistically significant, we noted a trend of an increase in incidence of developmental delay following ACTH therapy in the symptomatic IS sub-population, which should be explored in future studies.
KEYWORDS: Epilepsy

255. Extreme photosensitivity and self-induced seizures - new features of WDR45 encephalopathy with dramatic response to Lorazepam. Photosensitivity and self-induced seizures with dramatic response to Lorazepam in 10 year old girl with WDR45 epileptic encephalopathy .
Melikishvili Gia (Tbilisi, Georgia) Kurua Ekaterine, Melikishvili Mariam, Tabatadze Nazi, Dulac Olivier

OBJECTIVE: WDR45 mutation causes a broad range of neurodevelopmental disorders. Epilepsy occurs in patients, ranging from 66-75% adult to 91% in children. In addition to developmental delay (DD), the main feature in adults is dystonia and in pediatric patients is epilepsy, varying from infantile spasms (IS), febrile seizures (FS), focal seizures and drop attacks to myoclonic seizures. (1). Our aim was to delineate the phenotype of our patient's epilepsy.
METHODS: We evaluated a 10-year-old female patient with mild DD and epilepsy. Clinical history of development, seizure type, frequency, and treatments was reviewed. Routine, long-term video EEG monitoring and neuroimaging were conducted. The epilepsy gene panel was performed.
RESULTS: Our patient communicates relatively well, has a mild learning disability. At the age of 3, presentation with FS, including one status epilepticus, our patient had exhibited staring and drop attacks. Latter seizure type were frequent myoclonic jerks. On EEG focal and generalized interictal spike/polyspike wave complexes and focal slowing at the left temporal area were seen, frequent ictal myoclonic seizures were recorded, she showed extreme photosensitivity and interestingly flickering of the eyelids without EEG abnormalities were followed by epileptic myoclonic jerks - designation of self-induced seizures. MRI showed characteristic features of WDR45 encephalopathy. De novo mutation of WDR45 (c.183C>A (p.Asn61Lys) was revealed. Surprisingly oral Lorazepam stopped all seizures and photosensitivity disappeared.
CONCLUSIONS: Epileptic encephalopathy accounts for 90% of children with WDR45 variants. Prominent photosensitivity and self-induced seizures in WDR45 epilepsy have not been reported so far. An excellent response to Lorazepam was observed in our patient.

KEYWORDS: Epilepsy, Genetics, Rare Diseases

256. Psychogenic Nonepileptic Events in Pediatric Patients with Autism

Freedman Daniel (Columbus, OH, United States) Terry Debbie, Enciso Laurie, Trott Kristen, Burch Mary, Albert Dara

OBJECTIVE: There has been little description of Psychogenic Nonepileptic Events (PNEE) in pediatric patients with autism. Here we review and describe pediatric patients referred with PNEE and comorbid autism.
METHODS: This is a retrospective review of all patients referred to the PNEE clinic from January 2018-December 2019. The clinical characteristics were abstracted by chart review. Follow-up phone calls were made following the PNEE clinic visit.
RESULTS: Out of 191 PNEE referrals, nine had autism, eight attended the appointment. The mean age was 13 (range 7-20), 44% were male and 33% had a comorbid diagnosis of epilepsy. This is compared to the larger PNEE cohort without autism that had only 28% males and 18% with comorbid epilepsy. Using International League Against Epilepsy levels of diagnostic certainty, four patients had a diagnosis of documented PNEE, three had clinically established, one had possible diagnosis, and one patient had a probable diagnosis. Over half had bilateral convulsive movements during events. At one-month phone follow-up, eight patients had improvements in events or were event-free, one reported no change, five patients were seeing a counselor or psychologist and two were on a waitlist. The majority of parents were accepting of the diagnosis.
CONCLUSIONS: This case series of nine patients with PNEE and comorbid autism reveals unique characteristics in this population. First, we report that patients with autism can develop PNEE and can have improvement from events after diagnosis. Higher rates of of epilepsy and male gender were seen compared to non-autistic patients with PNEE.
KEYWORDS: Epilepsy

257. CAPTURING SEIZURES IN CLINICAL TRIALS OF ANTISEIZURE MEDICATIONS FOR KCNQ2-DEE

Harden Cynthia (Burnaby, British Columbia, Canada) Grayson Celene, Butterfield Noam, Chitra Rohini, Millichap John, Dlugos Dennis, Aycardi Ernesto

OBJECTIVE: We sought evidence as to whether seizures in infants and young children with *KCNQ2* developmental and epileptic encephalopathy (*KCNQ2*-DEE) could be reliably counted by clinical observation. This evidence would support using seizure diaries instead of video electroencephalography (VEEG) to assess the outcome of an anti-seizure medication (ASM) trial. The FDA typically recommends VEEG for assessing seizure counts in infants, however, the seizure characteristics of *KCNQ2*-DEE may enable seizure counting by clinical observation. Further, for patients who have seizures less than daily, VEEG presents feasibility challenges.
METHODS: All published reports of *KCNQ2*-DEE were reviewed for seizure and EEG descriptions. Caregivers from a patient advocacy group were surveyed for information regarding recognition of seizure occurrence.
RESULTS: Out of 137 *KCNQ2*-DEE patients described within 16 case series, 94% (129 patients) had clear motor seizures which correlated with EEG findings. Focal tonic was the most

common seizure type, present in 81% (n=111) of the patients (see Table 1). Other seizures were generalized tonic clonic, generalized tonic, focal motor, myoclonic and epileptic spasms, all clinically apparent motor seizure phenomena. Apnea was frequently associated with tonic seizures. There were no reports of subclinical seizures. The caregiver survey (n=51) revealed that 80% were very confident in their ability to recognize and count seizure occurrence.
CONCLUSIONS: We conclude that the seizures of *KCNQ2*-DEE are characteristic, clinically evident and families are recognizing seizures confidently. This evidence provides support for the accuracy of families using seizures diaries to count seizures in an ASM clinical trial of *KCNQ2*-DEE patients.
KEYWORDS: Epilepsy, Genetics, Rare Diseases

258. The importance of EEG findings as a risk factor of subsequent unprovoked seizure after febrile convulsion
Hye Won Park (Jeju, Republic of Korea) Kim Seunghyo

OBJECTIVE: We performed this study to identify the risk factors of unprovoked seizure in the specified situation of febrile seizure (FS) like as simple FS, complex FS, and FS plus on Jeju Island, South Korea.
METHODS: A hospital-based retrospective study of 494 children with FS whose first episode developed between July 2005 and June 2017 and who were seen in the Pediatric Department at the Jeju National University Hospital.
RESULTS: 195 boys and 299 girls were enrolled in this study. The average age at the first FS was 25.5±22.5months. The average total number of FSs was 3.2±2.9. 96.8% (478/494) of cases manifested as generalized seizure and 3.2% of cases showed focal seizure. 202 cases (40.9%) showed complex FS. 75 cases developed FS after 6 years of age.A family history of FS or epilepsy was found in 32.4% and 6.5% of patients, respectively. Abnormal findings of EEG were observed in 40.7% (156/383). Centrotemporal spikes and 3 Hz spike and wave complex features were frequently observed in 5.5% (21/383) and 2.6% (10/383) of total population, respectively. Subsequent unprovoked seizures occurred in 21.9%. They were subdivided in three groups such as simple FS, complex FS, and FS plus. For each and overall group, univariate and multivariate analyses showed that EEG abnormalities served as an independent risk factor for a subsequent unprovoked seizure (P=0.001, odds ratio 4.39, 95% CI 2.6-7.5).
CONCLUSIONS: EEG is the proper diagnostic tool to predict the risk of a subsequent unprovoked seizure in patients with FS regardless of specified situation.
KEYWORDS: Epilepsy

259. The risk of future epilepsy in infants with severe hyperbilirubinemia and seizures.
Husain Sumair (Wilmington, DE, United States) L'etoile Nathan, Khair Abdulhafeez, Mukarram Samira, Obeid Rawad

OBJECTIVE: Neonatal hyperbilirubinemia can lead to different neurological presentations including seizures. The development to epilepsy later in infancy is unknown.
METHODS: We reviewed charts of infants diagnosed with severe hyperbilirubinemia [Unconjugated Bilirubin (UB) level > 30 mg/dL] and neonatal seizures, and who were admitted to two neonatal intensive care units in Philadelphia PA and Wilmington DE between June 2019 and January 2020. We reviewed the treatments for the hyperbilirubinemia and seizures. We

followed the electroencephalogram (EEG) findings during the acute hyperbilirubinemia and on outpatient follow up.
RESULTS: Two infants met the inclusion criteria, both were males. Infant A, was born at 37 weeks gestation. On day of life 7 had max UB of 33.5 mg/dL. Infant B was born at 32 weeks gestation. On day of life 14 he had max UB of 34.3mg/dL. EEG for both infants showed frequent multifocal epileptiform discharges, as well as clinical and subclinical seizures emanating independently from the bilateral hemispheres. Both infants were initially treated with Levetiracetam, Fosphenytoin, and Phenobarbital. Seizures stopped on day 3 of admission for both. Infant A was discharged on Levetiracetam and Oxcarbazepine. At 6 months of age, he is maintained on Oxcarbazepine with no clinical seizures and normal EEG. Infant B was discharged on Phenobarbital and Oxcarbazepine. At 3 months of age, he continues on both medications, no clinical seizures, and normal EEG (Figure-1 and 2).
CONCLUSIONS: Infants with severe hyperbilirubinemia develop clinical and subclinical seizures acutely. Seizures become controlled with anti-epileptics and EEG tends to normalize.
KEYWORDS: Epilepsy, Neonatal & Fetal Neurology

260. Decreasing the Use of Isolated Free-Text Sigs in the Prescription of Intranasal Midazolam for Home Seizure Rescue
Kammeyer Ryan (Denver, CO, United States) Coffman Jennifer, Poppy Amy, Messer Ricka

OBJECTIVE: The electronic medical record (EMR) can offer important safety checks when discrete sig fields are utilized for outpatient prescriptions. However, over 60% of our Neurology department prescriptions for intranasal (IN) midazolam were written using only an isolated free-text sig. We aimed to decrease the proportion of isolated free-text sigs written for home rescue IN midazolam using an EMR-based discrete order set.
METHODS: An electronic order set ("SmartSet") was created in our EMR (Epic) for the prescription of IN midazolam and associated supplies (syringe, nasal atomizer), utilizing input from nurses, physicians, and pharmacists. These orders defaulted to a discrete sig for prescription and administration instructions. The SmartSet was added to the EMR in Dec 2018, and education on the SmartSet was provided to various Neurology, hospital and ED providers over the next year. Data on total, free-text, and discrete-text sigs for IN midazolam were obtained pre and post SmartSet implementation for outpatient and UC/ED settings.
RESULTS: The Neurology clinic was responsible for 90-94% of IN midazolam prescriptions from 2018-2019. Over the course of the first year after SmartSet implementation, Neurology-prescribed free text sigs for IN midazolam decreased from 60-70% to 15%, with a concurrent decrease in ED-prescribed free-text sigs from 10-20% to consistently <10%.
CONCLUSIONS: Use of an EMR-based order set providing discrete sig functionality for IN midazolam decreased the use of isolated free-text sigs. Further safety efforts will focus on tailoring of the SmartSet towards increased ease of use (speed buttons or auto-fill) or expansion to other commonly prescribed anti-seizure medications.
KEYWORDS: Epilepsy

261. Effective treatment of self-induced seizures and photosensitive epilepsy with Lorazepam
Melikishvili Gia (Tbilisi, Georgia) Gachechiladze Tamar, Tabatadze Nazi, Melikishvili Mariam, Gverdtsiteli Sopho, Kurua Ekaterine, Dulac Olivier

OBJECTIVE: Self-induced seizures produced by stimulation of natural light are rare and self-induction is a mode of seizure precipitation employed by either intellectually disabled or healthy photosensitive individuals (1). Absences and myoclonic jerks are the most common seizures in self-induction. Generalized tonic-clonic seizures (GTCS), when they occur, are very usual. Treatment of self-induced photosensitive epilepsy with Fenfluramine was first published in 1985 (2) and the effectiveness of Lorazepam was evaluated in 2001 (3).
METHODS: We evaluated 3 patients with self-induced seizures and photosensitivity caused by different gene mutations. Clinical history was obtained from parents, long-term video EEG monitoring was performed before and after oral Lorazepam treatment, neurologic examination, brain MRI and next-generation sequencing were done.
RESULTS: We report 3 patients: P1- 9 years old boy with *SCN1A* variant, P2 - 10 years old girl with a mutation in *WDR45* gene, P3 - 9 years old girl with the variant in *CHD2* gene. All 3 patients had myoclonic seizures, GTCS and mild to moderate developmental delay. MRI of P2 showed bilateral hypointense signal in the substantia nigra (characteristic of WDR45 encephalopathy). P1 and P2 had a history of febrile seizures. EEG revealed self-induced myoclonic seizures and photosensitivity in all 3 cases. Adding oral Lorazepam (3-6 mg/day) stopped either clinical and electroclinical seizures. Interestingly, photosensitivity disappeared in 2 cases as well.
CONCLUSIONS: The presence of self-induced seizures and photosensitivity were common features in our patients' series. Lorazepam should be considered as an effective treatment of self-induced photosensitive epilepsy.
KEYWORDS: Epilepsy, Rare Diseases, Genetics

262. Childhood Epilepsy with Centro-Temporal Spikes: Are They Really Benign?
Mohanlal Smilu (Kozhikode, India) Babu Sachin, Naushad Aleena, G Sruthi

OBJECTIVE: To determine the clinical spectrum and challenges in the management of children with Benign childhood epilepsy with centro- temporal spikes
METHODS: The Observational study was conducted at a tertiary care center Aster MIMS , Kozhikode ,India. Study duration from July 2019- April 2020. Children with seizure semiology of childhood epilepsy with centro temporal spikes were included and followed up for a minimum 3 month period.
RESULTS: 20 children were included. 11 boys and 9 girls. Mean age of seizure onset 6.5 yrs. Facial sensorimotor seizures -9, GTCS- 6,focal with bilateral motor clonic- 5. 19 – nocturnal episodes, 1- both nocturnal and awake episodes. H/o febrile seizure in 2(10%).2/20(10%) had ADHD premorbid ,7/20 (35%) has scholastic and behavioural issues.EEG showed right lateralised discharges in 11/20 (55%), bilateral 6/20(30%) ,left 3/20 (15%).Maximum negativity in central – 8(40%),parietal(P3/P4)-6 (30%),frontal- 5(25%), temporal-1(5%).Non dipolar discharges-4/20(20%) Interictal discharges activated by sleep were < 10%- 3, 10-50%-14, > 50%- 3.Awake AED was obtained in 3/20(15%). Neuroimaging MRI was done in 15/20 and all normal. No treatment- 3(15%), 1 antiepileptic drug – 9(45%), 2 antiepileptic drug -8(40%). Additional need of antipsychotic medications- 3/ 20 (15%).Follow up showed improvement in scholastic performance in 2/7 children , no improvement – 5/7, reduction in interictal spike percentage after addition of clobazam in 3.

CONCLUSIONS: The scholastic issues in children with centro -temporal spikes are challenging . Normal neuroimaging in all children questions whether there is really a need for imaging even though the epileptiform discharges are lateralised and are non dipolar
KEYWORDS: Epilepsy, Cognitive/Behavioral Disorders (including Autism)

263. AN ONLINE SURVEY OF CAREGIVERS OF PATIENTS WITH KCNQ2 DEVELOPMENTAL AND EPILEPTIC ENCEPHALOPATHY (KCNQ2-DEE)
Grayson Celene (Vancouver, British Columbia, Canada) Butterfield Noam, Harden Cynthia, Luzon Constanza, Helper Alix, Millichap John, Dlugos Dennis, Pimstone Simon, Aycardi Ernesto

OBJECTIVE: *KCNQ2* developmental and epileptic encephalopathy (*KCNQ2*-DEE) is an ultra-rare disorder caused by variants in the *KCNQ2* gene, encoding the Kv7.2 potassium channel. It is characterized by neonatal-onset focal tonic seizures and psychomotor impairment; there are no approved treatments. The Kv7.2 potentiator, anti-seizure medicine (ASM), ezogabine, has historically been used off-label in this disease, but never formally studied. In order to inform a clinical trial design using ezogabine as a precision-medicine in *KCNQ2*-DEE, we sought information from caregivers regarding their experiences and perceived gaps in pharmacologic treatment.
METHODS: A 28-question online survey was developed to obtain de-identified data from caregivers of children with *KCNQ2*-DEE, querying demographics, seizure onset and frequency, ASM use, and any experience with ezogabine.
RESULTS: Data from fifty-one caregivers revealed that thirty-two (63%) of *KCNQ2*-DEE patients described were at least 4 years of age at the time. Ninety percent had seizure onset within the first two days of life with a seizure frequency of >10 seizures/day; phenobarbital and levetiracetam were the most frequently used initial ASMs. Half of the respondents reported seizures in the past 6 months, with seizure rates from multiple daily to monthly. The most frequently used current ASMs were carbamazepine and oxcarbazepine. Seven respondents tried ezogabine to treat seizures or improve behaviors; ezogabine was perceived to be beneficial for both uses.
CONCLUSIONS: *KCNQ2*-DEE imposes a significant seizure burden at disease onset, with persistent seizures in half of patients. There is an unmet medical need, appropriate for a disease-targeting approach using a Kv7.2 potentiator.
KEYWORDS: Epilepsy, Rare Diseases. Genetics

264. THE RELATIONSHIP BETWEEN EPILEPSY AND AUTISM IN CHILDREN
JocicJakubi Bosanka (Muscat, Oman) Al Futaisis Amna, Jocic Darina

OBJECTIVE: While the prevalence of Autistic Spectrum disorder (ASD) in general population is 0.75% to 1.1% , recent study has found that 4%–5% of children with epilepsy had ASD. On the other hand the prevalence of epilepsy in children with ASD is varying widely from 5% to 38% . The aim of this study was to analyze characteristics of Epilepsy and EEG in children with ASD with specific reference to age, gender, type of epileptic seizure, seizure onset and EEG characteristics.
METHODS: We retrospectively analyzed 86 children with ASD , diagnosed and treated at SQUH, Muscat Oman. In 40 of them (Group A) ASD was primary diagnose and later one they

developed epileptic seizures while 46 children (Group B) developed ASD after epilepsy diagnose was established.
RESULTS: Among 40 children in Group A epilepsy was diagnosed in 45% of children . Seven patients (38.8%) had one or more episodes of SE and have required urgent treatment. The electroencephalogram was abnormal in 62.5% of children and in 37.5% showed no epileptiform abnormalities (EDs).
In Group B (46 children) the majority of patients (32%) had Infantile spasms and in 65% onset of seizure was during first year of life .In this group 26% children had normal EEG, while epileptiform abnormality was found in 74%.
CONCLUSIONS: The comorbidity of epilepsy and ASD is well recognized, but the mechanism of this association still remains unknown. It seems that increased risk of autism spectrum disorder is associated with early onset of epilepsy.
KEYWORDS: Epilepsy, Cognitive/Behavioral Disorders (including Autism)

265. Creating a center of excellence for patients with infantile epilepsy
Williams Brittany (Memphis, TN, United States)

OBJECTIVE: Infantile spasms (IS) is an age-specific epileptic encephalopathy with an incidence of 1.6-4.5 per 10,000 live births. If not treated in a timely manner, permanent developmental delay and refractory epilepsy can ensue. Our institution has treated 93 patients diagnosed with IS since 2016. On average, patients travel 110 miles to be seen, with 17 % of patients seeking a second opinion. With the objective to enhance quality of care and the quantity of patients that our center sees, it was decided to build and develop a center of excellence for patients with infantile epilepsy.
METHODS: A multidisciplinary team consisting of neurologists, pediatricians, neuroradiologists, neuropsychologists, neuro-ophthalmologists, geneticists, clinical dieticians, speech therapists, and nurse practitioners held regularly scheduled meetings to discuss the process and build and implement a center of excellence. A standardized approach to care to address the needs of these patients was discussed amongst the team.
RESULTS: A standardized inpatient protocol was developed for patients with IS assisting in facilitating communication and gathering data. Our center will be able to track results over time for this specific patient population.
CONCLUSIONS: The goal of the center of excellence is to decrease time to diagnosis while simultaneously decreasing the time to initiation of treatment. A retrospective database will be created within the center, aiding in identification of variables that may impede treatment, allowing for best practice implementation, and facilitating tracking of neurocognitive outcomes longitudinally.
KEYWORDS: Epilepsy

266. NOVEL MICROSAMPLING TECHNIQUE FOR USE IN A CLINICAL TRIAL OF PEDIATRIC PATIENTS WITH KCNQ2-DEE
Namdari Rostam (Burnaby, British Columbia, Canada) Cadieux Jay, Evans Steven, Butterfield Noam, Luzon Constanza, Harden Cynthia, Chitra Rohini, Aycardi Ernesto

OBJECTIVE: Drug levels obtained through blood sampling are critical for drug development. For pediatric subjects, pharmacokinetic (PK) evaluation using standard venous blood sampling

techniques tests the limits of feasibility and safety. Using a single-dose PK assessment, we sought to determine whether the levels of the pediatric investigational product XEN496, obtained by a capillary microsampling technique, differed from those obtained by a routine venous blood sample.
METHODS: 24 fasted healthy adult subjects were dosed a single 400 mg dose of XEN496 orally. Serial PK samples (prior to dosing and up to 48 hours post-dose) were obtained by both conventional venous blood sampling and by capillary micro-sampling using the Tasso^{TM} OnDemand^{TM} device, in which approximately 300 µL of whole blood is vacuum-drawn into a collection unit consisting of a retractable single-use lancet and detachable reservoir applied to the skin. XEN496 levels were determined using validated LC/MS-MS methods with appropriate corrections for red blood cell binding.
RESULTS: Adult subjects reported no pain or discomfort during the microsampling procedure. There were no significant differences in XEN496 concentrations obtained via the two techniques (Figure 1).
CONCLUSIONS: Micro-sampling with the Tasso^{TM} OnDemand^{TM} device is a viable alternative to routine venous blood sampling for assessment of drug levels. The use of the capillary microsampling technique in clinical research could be invaluable to minimize both the discomfort and the volume of blood draws in pediatric (or adult) subjects.
KEYWORDS: Epilepsy, Translational/Experimental Therapeutics

267. Genotyping Lissencephaly Patients May Help Predict Response to Therapy and Aid Future Prognosis
Hani Abeer (Beirut, Lebanon)

OBJECTIVE: Highlight the importance of the genetic diagnosis in different cases of lissencephaly in terms of seizure response to therapy and future neurodevelopment
METHODS: The charts of 2 children who presented at the same age with tonic flexion spasms and received a diagnosis of lissencephaly radiologically were reviewed. Subsequently genetic testing was done to help delineate the genetic etiology of their lissencephaly.
RESULTS: The first patient responded to the use of steroids and continued to have normal neurodevelopment with seizure freedom 2 years later. The second patient had an initial response to steroids with spasm recurrence few months later that were medically refractory and with continuing marked developmental delays. The first patient was found to have a heterozygous mutation in the PAFAH1B1 gene. The second patient had heterozygous variants in the LAMB1 and RELN genes.
CONCLUSIONS: In an era where genetic evaluation is becoming increasingly available, the use of genetic testing will help establish the prognosis and response to treatment potentially in many patients with neurological disorders. A wider correlation study is needed to further establish a genotype-phenotype association in patients with lissencephaly.
KEYWORDS: Epilepsy, Genetics, Neuroimaging

268. Complex Partial Seizure Mistaken for Stubbornness in an Adolescent Child
Jimoh Adenike (Jos, Nigeria) Okpataku Christopher, Eseigbe Edwin

OBJECTIVE: The report aims to describe how children with complex partial seizure can be mislabeled by parents and teachers, and the consequences on the child.

METHODS: A 12-year-old boy was brought to the Paediatric neurology clinic by his mother with complaints that child was very forgetful and wasted time in returning from simple errands. There were school reports of absent mindedness in class and inability to recall lessons taught. Mother noticed occasional fluttering of the eyes in child but thought nothing to it. Both parents felt he was being stubborn, and as a result the father constantly scolded and caned him. Review of child privately revealed that there was repeated loss of consciousness in-between receiving instructions at home and in school. Examination revealed a withdrawn but otherwise stable child. Hyperventilation test was negative. Electroencephalogram showed supportive evidence for diagnosis of complex partial seizure. Anticonvulsant was commenced, along with counselling sessions for both parents and the child.
RESULTS: Child did well, remained seizure free and relationship with his father became cordial.
CONCLUSIONS: Complex partial seizure can be missed by parents and teachers, making the child at risk of being treated unfairly and labeled wrongly, as it occurred in this case. This underpins the need for raising awareness of non-motor presentations of seizures among school teachers and general populace.
KEYWORDS: Epilepsy

269. Genetic cases of early infantile epileptic encephalopathies in Russian population
Kholin Alexey (Moscow, Russian Federation) Zavadenko Nikolay, Kholin Elena, Fedonyuk Inessa, Kolpakchi Larisa, Kozhanova Tatiana, Il`ina Elena

OBJECTIVE: The most severe forms of epileptic encephalopathies are represented by early infantile forms, leading to pronounced disturbances of both intellectual and motor functions. Currently, by 2020, OMIM includes 82 genetic variants of early infantile epileptic encephalopathies (EIEE): 40 variants with autosomal dominant, 35 variants with autosomal recessive, 4 variants with X-linked recessive and 3 variants with X-linked dominant types of inheritance.
METHODS: Next Generation Sequencing (NGS) was performed with the "Hereditary epilepsies" panel, clinical and whole exome sequencing on the platforms IlluminaNextSeq 500, Illumina HiSeq 1500 и Illumina HiSeq 2500 (USA). Dynamic video-EEG monitoring was done by means of "Encephalan-Video" RM-19/26 ("Medicom MTD", Russia).
RESULTS: Among the group of children with early onset epileptic encephalopathies 19 patients with EIEE was identified: 5 infants with EIEE type 6 (SCN1A gene mutations), 4 children with EIEE type 14 (KCNT1), 3 girls with EIEE type 16 (TBC1D24), 2 infants with EIEE type 4 (STXBP1), 2 boys with EIEE type 5 (SPTAN1), 1 case of EIEE type 7 (KCNQ2), 1 infants with EIEE type 9 (PCDH19) and 1 girl with EIEE type 18 (SZT2). Eight types of mutation was not previously described, including those in genes TBC1D24 (1499C>T, Ala500Val), TBC1D24 (chr:16:2546775 A>C, Tyr209Ser), STXBP1 (C.*96T>A, frameshift mutation), SZT2 (2371C>T, Arg791Cys), KCNQ2 (1742G>A, Arg581Gln), KCNT1 (1066C>T, Arg356Trp), KCNT1 (1439A>G, Asp480Gly) and SCN1A (1224delC, Phe408fs).
CONCLUSIONS: Modern genetic assessment by means of NGS methods is required for all the children with pharmacoresistant epileptic encephalopathies. For some forms of EIEE targeted pharmacotherapy approaches were recently elaborated.
KEYWORDS: Epilepsy, Genetics, Rare Diseases

ETHICS

270. The evaluation of vitamin K status in children with febrile seizure

Carman Kursat (Eskisehir, Turkey) Karal Yasemin, Mert Gul, Ekici Arzu, Perk Peren, Yarar Coskun, Nuhoglu Cagatay, Dinleyici Meltem, Tosun Ayse, Dinleyici Ener

OBJECTIVE: Febrile seizure (FS) is the most common neurological disorder of childhood. The exact pathophysiology of FS is unknown. Recent studies showed that the role of vitamin K in non-hematological and inflammatory disorders. The present study aimed to investigate serum vitamin K levels in children with FS.
METHODS: This prospective multicenter study examined representative populations in eight different cities in Turkey between April 1, 2018, and April 1, 2019. Blood samples were taken from all children at presentation. Vitamin K 1, Vitamin K2, tumor necrosis factor-alpha (TNF-α), interleukin 1 beta (IL-1β), and interleukin 6 (IL-6) levels by enzyme-linked immuno-sorbent assay.
RESULTS: The study was conducted with 155 children: 84 children with FS and 71 children in the febrile control group. Serum vitamin K1 and vitamin K2 were also higher in the FS group than the controls (Table). The results of statistical analysis showed that vitamin K1 and K2 levels were correlated with TNF-α, IL-1β and IL-6 levels. The median vitamin K1 and vitamin K2 levels of children experiencing their first FS was higher than children with recurrent FS. The type of FS has no effect on serum vitamin K1 and vitamin K2 levels.
CONCLUSIONS: This study demonstrates that the vitamin K levels in children with febrile seizures were higher than the control group. These new findings may contribute to clarifying the etiopathogenesis of FS.
KEYWORDS: Ethics

271. A Matter of Life or Death: How UAB Providers Make Resuscitation Decisions in Neonates and Critically Ill Patients

Hendrickson Elizabeth (Birmingham, AL, United States) Dure Leon

OBJECTIVE: Providers worldwide have made resuscitation decisions about neonates differently than patients of other ages [1], even when patients have identical outcomes. We investigated if UAB providers also treat neonates differently than older patients and what ethical factors they use to do so.
METHODS: We utilized, "Ethics of Resuscitation at Different Ages of Life[2]," a standardized questionnaire containing Likert scales concerning eight critical patients of different ages. Scenarios give chance of survival and their potential neurological impairments if survival occurs. Respondents also ranked the order they would resuscitate patients if all simultaneously required intubation and discussed which factors they considered in making decisions. We used χ^2 with Yates correction to compare proportions, with significance at $P < 0.01$.
RESULTS: 48 medical students and physicians at Children's of AL participated. Four subgroups gave the premie a median ranking of either fourth or fifth, with a total average of 4.79.The most significant factors among all subgroups were age, prognosis, and future quality of life.

CONCLUSIONS: In previous studies, the premie is resuscitated 7th or 8th out of 8 patients with 35% of respondents willing to "always intubate," even with equal or superior outcomes to other patients. Interestingly, UAB providers ranked the premie 5th out of 8 with 63% choosing to "always intubate." This aligns more closely with the principle of distributive justice and indicates a stronger sense of duty towards premature neonates than predicted from previous research.
KEYWORDS: Ethics, Neonatal & Fetal Neurology

GENETICS

272. PLXNA3 (Plexin A3) Variants Cause a Spectrum of Neurodevelopmental Disorders
Steele Jacqueline (Farmington, CT, United States) Heron Benedicte, Kamp Jiddeke, Kim Linda, Shankar Suma, Veerapandiyan Aravindhan, Graf William

OBJECTIVE: To describe the neurological and neurodevelopmental phenotypes of boys with likely pathogenic *PLXNA3* (Plexin A3) variants.
METHODS: The proband in this study is a 15-year-old boy with longstanding severe intellectual disabilities (ID), who has a hemizygous *PLXNA3* variant identified on a trio GeneDx Autism/ID Xpanded Panel. This study used a global data exchange platform, GeneMatcher, to identify and recruit other physicians caring for boys with hemizygous *PLXNA3*variants ("*PLXNA3* patients"). In this case-series, physicians completed questionnaires about the clinical features of their *PLXNA3* patients. *In silico* gene expression analysis was completed using Polyphen, Provean/Sift, and Mutation Taster to determine the likelihood of pathogenicity for each *PLXNA3* variant. Descriptive statistics were used to describe genotype/phenotype findings in an ongoing study.
RESULTS: Worldwide, GeneMatcher identified ~70 *PLXNA3* patients, of which approximately half had documented maternal inheritance. We studied six unrelated male *PLXNA3* patients (mean age, 9.7[range 2-15] years), who all had a diagnosis of ID and autism, ranging from mild to severe. Five patients (83%) had fine-motor dyspraxia; four patients (67%) had variable behavioral disorders including hyperkinesis, attentional deficits, and aggressive behaviors. Three patients (50%) were treated for epilepsy. All six *PLXNA3* patients showed "probably damaging/disease causing" variant pathogenicity in one or more gene expression profiles.
CONCLUSIONS: *PLXNA3* is a prenatally expressed signaling gene involved in axon pathfinding and pruning. This preliminary clinical study is the first to describe *PLXNA3*-related neurodevelopmental disorders in boys. Additional clinical and neurobiological studies are needed to determine the ramifications of "plexinopathies" in the developing brain.
KEYWORDS: Genetics, Cognitive/Behavioral Disorders (including Autism)

273. Shortening the time between symptom onset and diagnosis for CLN2 disease: Results from Behind the Seizure™, a no-cost epilepsy gene panel testing program
Chu Dorna (Novato, CA, United States) Volz Ashley, Gurnon Stephanie, Johnson Tiara, Ly Christine, Truty Rebecca, Aradhya Swaroop, Leal-Pardinas Fernanda

OBJECTIVE: CLN2 disease is characterized by language delay, epilepsy, progressive motor and cognitive decline, blindness, and premature death. Average age of diagnosis is 4.9 years

(DEM-CHILD database), which is ~2 years after seizure onset and when significant neurodegeneration has occurred. Genetic testing may shorten the time to diagnosis.
METHODS: Behind the Seizure™ (BTS) is a no-cost epilepsy gene panel testing program for children aged <5 years who experience an unprovoked seizure. Ordering physicians indicate if patients experience key signs/symptoms such as language delay or motor difficulty preceding seizure onset. Follow-up interviews were conducted with ordering physicians, other healthcare team members, and/or parents to elucidate patients' clinical presentations prior to diagnosis.
RESULTS: As of February 25th, 2019, 6 patients with CLN2 disease were diagnosed through BTS (n=682 screened). Average age of diagnosis was 3.9 years. First referred symptom of all patients prior to diagnosis was seizures; average age of onset was 2.8 years. Average time between first seizure to genetic testing and diagnosis was 13 months. All patients were noted to have language delay prior to seizure onset. Four patients had delay in developing a two-word sentence (occurring >24 months or never). All patients had delay in developing a whole sentence (occurring >36 months or never). Prior to diagnosis, in four patients, ataxia occurred after language delay and seizures, with no significant vision changes noted.
CONCLUSIONS: Genetic testing may facilitate earlier diagnosis of CLN2 disease. Genetic testing should be considered in children with early-onset language delay and unprovoked seizures.
KEYWORDS: Genetics, Rare Diseases, Neurometabolic Disorders

274. The Utility of Whole Exome Sequencing in Diagnosing Pediatric Neurological Disorders

Muthaffar Osama (Jeddah, Saudi Arabia)

OBJECTIVE: Pediatric neurological disorders have a wide spectrum of clinical presentations and can be challenging to diagnose. Whole exome sequencing (WES) is increasingly becoming an integral diagnostic tool in medicine. It is cost-effective and has high diagnostic yield especially in consanguineous populations. This study aims to review WES results and value in diagnosing neurological disorders.
METHODS: A retrospective chart review was performed for WES results between the period of January 2018 to November 2019. WES was requested for children with unexplained neurological signs and symptoms like epilepsy, developmental delay, visual impairment, spasticity, hypotonia and MRI brain changes. It was conducted for children in pediatric neurology clinic in a tertiary center, Jeddah, Saudi Arabia.
RESULTS: A 26 children with undiagnosed neurological conditions underwent WES were identified. Genetic diagnoses explaining the phenotype (i.e. pathogenic, likely pathogenic variants and variants of unknown clinical significance "VOUS" but explains the phenotype) were found in 20 patients (77%). Consanguinity was positive in 18 families of the cohort (69%). Seven patients showed homozygous mutations. Five patients had heterozygous mutations. Six patients with VOUS. Two patients had multiple genetic mutations and 6 patients had negative WES results.
CONCLUSIONS: WES showed high diagnostic rate in this group of children with variable neurological disorders.
KEYWORDS: Genetics

275. Neurodevelopmental Profiles in the NIH Pediatric Undiagnosed Diseases Program

Acosta Maria (Bethesda, MD, United States) Thurma Audrey, Macnamara Ellen, Carter Dennis, Wolfe Lynne, D'Souza Precilla, Estwick Tyra, Yang John, Johnston Jean, Kessler Riley, Toro Camilo, Adams David, Gahl William, Tifft Cynthia

OBJECTIVE: The NIH Undiagnosed Disease Program was established in 2008 to offer hope for patients who, despite exhaustive medical evaluation, remained undiagnosed. In undiagnosed children suspected of a genetic disorder, assessment of neurodevelopmental status is critical as most applicants to the program have an underlying neurologic problem.
METHODS: We describe the neurodevelopmental profiles of pediatric UDP patients from 2008-2019. At a minimum, patients had a parent interview for adaptive functioning. We used a hierarchical approach to cognitive testing, since many patients were developmentally unable to obtain basal scores on tests standardized for their age range.
RESULTS: Of the 4934 applications received by the UDP, 1228 were children and 371 were accepted to undergo comprehensive phenotyping during a one week inpatient admission to the NIH Clinical Center. Preliminary analyses include 229 patients younger than 18 years who had a neurodevelopmental assessment and a scorable measure of adaptative functioning. Mean Vineland composite score of 64.51+20.93, and IQ estimates and language scores that were obtained indicate that the cohort was generally impaired. In 34% of cases, low developmental functioning prohibited traditional IQ or developmental test scoring; however, alternative ratio scoring or out-of-age level testing established mental ages.
CONCLUSIONS: Neurodevelopmental problems were present in the majority of pediatric UDP patients indicating that patients with prolonged diagnostic odysseys have a high frequency of developmental disabilities. Current standardized cognitive assessment tools are lacking for patients with severe neurodevelopmental disorders to properly assess of level of functioning, and underscore the need for more focused psychometric research.
KEYWORDS: Genetics, Cognitive/Behavioral Disorders (including Autism)

276. Childhood leukodystrophies and genetic leukoencephalopathies: A Multicentric epidemiological study

Jha Ruchika (Pune, India) Dubey Rachana, V Pooja, Goswami Jyatindra, Roy Shuvendu, Gupta Aparajita, Ahmad Faiz, Nanda Subrat, Saxena Apoorv, Bhanu K, Rajesh U, Tewari Vishal, Devgan Amit, Sondhi Vishal

OBJECTIVE: This multicentric study aims to report the epidemiology of inherited white matter (WM) disorders among Indian children.
METHODS: All children with suspected leukodystrophy/ leukoencephalopathy presenting to either of the four centres from Jan 2018 onwards were screened. Leukodystrophy/ leukoencephalopathy was suspected based on clinical phenotype in association with neuroradiologically proven WM involvement. Only children with genetically and/or enzymatically confirmed diagnoses were included. The lifetime risk at birth was calculated by taking the number of observed cases divided by the number of live births during the diagnosis period.
RESULTS: Six-hundred-seventy-four children with suspected WM involvement were screened; 92 cases with confirmed leukodystrophy and 108 cases with confirmed leukoencephalopathies were identified. Sixteen different leukodystrophies and 22 different leukoencephalopathies were diagnosed. The estimated lifetime risk per 10 million Indian live births for the whole

leukodystrophy group was 37.9 and for leukoencephalopathy group was 44.5. The commonest leukodystrophies (percentage, life time risk per 10 million live births) included: metachromatic leukodystrophy(20.7%, 7.8), hypomyelinating disorders (17.4%, 6.6), peroxisomal disorders (16.3%, 6.2), Aicardi-Goutières(14.1%, 5.4) and megaencephalic leukoencephalopathy with subcortical cysts(10.9%, 4.1). The salient leukoencephalopathies (percentage, life time risk per 10 million live births) included mitochondrial disorders(19.4%, 8.7), homocystinuria(11.1%, 4.9), lissencephaly(11.1%, 4.9) and urea cycle disorders(8.3%, 3.7).
CONCLUSIONS: This paper provides noteworthy data from a developing country in context of inherited WM disorders of CNS. This also reports the lifetime risk/million live births for the leukodystrophies/ leukoencephalopathies, and hence provides a framework for comparison with other geographic regions.
KEYWORDS: Genetics, Neuroimaging

277. Using RNAseq for identification of aberrant splicing in patients with persistently undiagnosed rare genetic disorders.
Helman Guy (New Orleans, LA, United States) Stutterd Chloe, Vanderver Adeline, Taft Ryan, Pais Lynn, O'Donnell-Luria Anne, Eggers Stefanie, Clark Michael, Compton Alison, Thorburn David, Christodoulou John, Stark Zornitza, Tan Tiong, White Susan, Simons Cas

OBJECTIVE: Over the last decade genomic sequencing approaches have revolutionized the diagnosis of rare genetic disorders. However, few unbiased studies report diagnosis rates substantially higher than 50%. Pathogenic variants that result in aberrant mRNA splicing can be difficult to identify by DNA analysis. We investigated the utility of incorporating RNA sequencing analysis to facilitate the identification of pathogenic aberrant splicing events in patients with persistently undiagnosed rare genetic disorders.
METHODS: RNA sequencing was performed on individuals that remain undiagnosed after trio-exome or genome sequencing. We developed an integrated transcriptome-wide analysis workflow to identify features indicative of aberrant splicing including relative changes in exon:exon junction usage, allele-specific expression and differential gene expression. When combined with variant data from DNA sequencing, this approach enables rapid identification of patient-specific aberrant splicing events. Candidate disease associated events can then be validated using orthogonal methods including nanopore long-read cDNA amplicon sequencing and cell-based functional studies.
RESULTS: High confidence candidates in disease-associated genes in six individuals to date (6/19 [32%]). These include aberrant splicing in several nuclear-encoded mitochondrial genes (*NDUFB10*, *NDUFV1*, *PMPCA*), lysosomal enzymes (*TPP1*), vesicular trafficking proteins (*TRAPPC4*) and transcription regulatory proteins (*MED23*). Overlaying this analysis on genome sequencing data, the variants that cause the observed changes in splicing include deep intronic and exonic missense and synonymous variants, often not predicted to alter splicing when analyzed by *in silico* splicing prediction tools.
CONCLUSIONS: This study demonstrates the potential for increased diagnostic yield of rare genetic disorders through the integration of a transcriptome based analysis with existing genomic sequencing approaches.
KEYWORDS: Genetics, Rare Diseases

278. Genetic Modifiers of Disease Severity in Tuberous Sclerosis Complex

Sanchez-Castillo Meredith (Phoenix, AZ, United States) Rangasamy Sampathkumar, Ramsey Keri, Sekar Shobana, Adkins Jonathan, Cuyugan Lori, Monheim-Janss Cynthia, Liang Winnie, Narayanan Vinodh

OBJECTIVE: In Tuberous Sclerosis Complex (TSC), intra-familial phenotypic variability ranging from mild to severe has been observed within single families where all affected members have the same *TSC1* or *TSC2* mutation. We hypothesize that this could be due to (1) variants in genes other than *TSC1* and *TSC2*, or (2) differential expression of mTOR network genes.
METHODS: In our study, we have enrolled 10 parent-child pairs, both with TSC, where the child is severely affected but the parent is mildly affected. By using whole exome and RNA sequencing, we aim to identify genetic modifiers that could account for this variability.
RESULTS: Analysis of 10 families, have led to the identification of the following mTOR pathway gene variants in severely affected children and in mildly affected parents (Table 1). Additionally, increased expression of the *PIK3R5* and decreased allelic expression of the *RPTOR* mutation were also seen. In one family, a two-exon deletion was observed in *TSC2* across all subjects, with *TSC2* expression elevated only in the mildly affected parent.
CONCLUSIONS: To define the causality of genetic modifiers in phenotypic variability, we are examining the biological effect of the variants on the mTOR pathway using isogenic $TSC2^{-/+}$ iPSC-derived neuronal cells and patient-derived primary fibroblasts cells. The purpose of our research is to define a comprehensive set of modifier genes that could be used as genetic biomarkers to predict disease severity. Such a test may allow us to select patients for early initiation of disease modifying therapies.
KEYWORDS: Genetics, Translational/Experimental Therapeutics, Neuroscience

279. Phenotypic-genotypic spectrum of mitochondrial polymerase-gamma mutations: A multicentric retrospective review

Jha Ruchika (Pune, India) Devgan Amit, Dubey Rachana, Saini Lokesh, Sondhi Vishal

OBJECTIVE: This multicentric retrospective study examines the genotype-phenotype correlation of POLG mutations.
METHODS: A retrospective review of all genetic testing performed at three tertiary care centers since Jan 2018 was performed. All children with POLG variants and age ≤15 years were considered eligible. Patients were excluded if the mutations were non-pathogenic. Patient data including the demography, clinical features, laboratory data, neurophysiological characteristics, neuroimaging features, genetic mutations and therapeutic interventions were chronicled using a case record form. Patients were phenotypically classified into individual groups based on definitions of individual POLG syndromes.
RESULTS: We identified eight children (five male) with POLG mutations. These included the following phenotypes: (a) autosomal recessive progressive external opthalmoplegia (n=3); (b Alpers syndrome (n=2); (c) autosomal dominant progressive external opthalmoplegia (n=1); (d) leighs-like phenotype (n=1); and (e) leukoencephalopathy (n=1). The identified mutations included: POLG2 (c.G1092C/p.Lys364Asn, autosomal dominant), POLG2 (c26C>C/T autosomal recessive), POLG2 (c.19C>C/T, autosomal recessive), POLG (c413A>A/C, autosomal recessive), POLG (c.T911G, autosomal recessive), POLG (c.911T>T/G, autosomal recessive), POLG (c.3215C>C/T, autosomal recessive) and POLG (c.911T>G, autosomal

recessive. Only one patient had positive family history. No specific genotype-phenotype associations could be identified.
CONCLUSIONS: This study highlights the clinic-genetic heterogeneity among patients with POLG mutations. Identifying which individuals to screen for POLG mutations can be difficult. The majority of subjects in this study had no relevant family history, including those with limited phenotypes, indicating the importance of considering POLG mutations in a broad range of sporadic neuromuscular and neurodegenerative diseases.
KEYWORDS: Genetics

280. Epilepsy in patients admitted to the at the Undiagnosed Diseases Program : A Ten-Year Experience
Acosta Maria (Bethesda, MD, United States) Shimada Shino, Macnamara Ellen, Thurm Audrey, Wolfe Lynne, D'Souza Precilla, Johnston Jean, Estwick Tyra, Yang John, Toro Camilo, Adams David, Gahl William, Maclicdan May, Tifft Cynthia

OBJECTIVE: The NIH Undiagnosed Disease Program (UDP) was established in 2008 to offer hope for patients who, despite exhaustive medical evaluation, remained undiagnosed. Neurological manifestations, including epilepsy and seizures, are prevalent in pediatric UDP patients. We describe clinical manifestations and genetic diagnoses in UDP patients with seizure related presentation.
METHODS: We queried the UDP database of evaluated patients for human phenotype ontology (HPO) terms indicating a history of seizures or epilepsy. Information regarding seizures, neurological symptoms and developmental assessment is presented, as well as the genetic diagnosis in those whose in whom a diagnosis was established.
RESULTS: From 4934 applications received, 25% were pediatric cases. 30% pediatric cases were accepted and invited for a one-week inpatient evaluation at the NIH. Of these, 189 (50%) of patients had seizures identified as part of the clinical manifestations of their condition. A genetic or metabolic diagnosis was confirmed in 80 (42%) of patients with epilepsy, as compared to 33% in all pediatric cases. For patients with myoclonic seizures a diagnosis was made in 34 cases (70%) of cases.
CONCLUSIONS: Seizures are a prominent finding in patients admitted to the pediatric UDP. A detailed phenotypic description and unified terminology for seizure classification may yield better results in terms of genetic diagnosis in cases with significant neurological compromise. The presence of seizures seems to increase the probability of making a diagnosis with the highest likelihood in patients with myoclonic seizures. Finding a molecular diagnosis is critical to understanding the mechanism of disease and inform the design of targeted treatments.
KEYWORDS: Genetics, Epilepsy

281. CLN6 and White Matter Disease: Clinical Insights and IPSC-derived Oligodendroglial Models
Pierson Tyler Mark (Los Angeles, CA, United States) Oh Denise, Kim Jaemin, Kushwaha Yogesh

OBJECTIVE: Description of clinical and cellular phenotypes associated with CLN6 oligodendroglia.
METHODS: Diagnostic analysis included genetic testing, physical examinations, and neuroimaging. CLN6 IPSCs were differentiated along an oligodendroglial pathway over a 110-

day period. CLN6-IPSCs were assayed at timepoints consistent with different stages of oligodendroglial differentiation to evaluate pre-oligodendrocyte progenitor cells (OLIG2/ NKX2.2+), oligodendrocyte progenitor cells (PDGFRα/NG2+), immature oligodendrocytes (O4+) and mature oligodendrocytes (MBP+). CLN6 oligodendroglia were evaluated for increased storage by immunocytochemistry against subunit C (SUBC) of the mitochondrial ATP synthase, a predominant storage product in CLN6.
RESULTS: Several patients with clinical and genetic features consistent with CLN6 were noted to present with early neuroimaging findings consistent with white matter disease. Four CLN6 patient-derived IPSC lines were generated and differentiated along an oligodendroglia pathway over a 110-day period. Immunocytochemical data indicated all four CLN6 lines had efficient and chronological expression of oligodendroglial markers. These CLN6 lines expressed significant levels of SUBC storage material in terminally differentiated cells.
CONCLUSIONS: While Neuronal Ceroid Lipofuscinoses are primarily considered to be grey matter disorders, CLN6 was shown to present with early pathological changes in white matter. Neuroimaging of genetically-confirmed CLN6 patients contained white matter changes consistent with a leukodystrophy. CLN6-patient derived IPS cells underwent efficient oligodendroglia differentiation, with terminally-differentiated oligodendroglial cells possessing significantly increased SUBC storage in comparison to control lines. These subjects broaden the phenotypic and genotypic spectrum of *CLN6*-related disorders and indicate that both neurons and oligodendroglia are targets of disease pathology and that CLN6 should be included in the differential diagnosis of leukodystrophy.
KEYWORDS: Genetics, Rare Diseases, Translational/Experimental Therapeutics

282. Novel KDM5C Variant Associated with X-Linked Intellectual Disability: Expanding Clinical Phenotype

Tentler Kristen (Indianapolis, IN, United States) White Kerry, Curtin Michelle, Christensen Celanie

OBJECTIVE: We present a novel *KDM5C* variant, c.1425 C>A p.N475K, expressed in three full siblings (two males, one female), each displaying KDM5C-Related Disorder traits similar to those in the literature.
METHODS: Case Report
RESULTS: Siblings, mother, and father were tested via Autism/ID Xpanded panel (GeneDx^{TM}). Siblings and mother expressed the novel variant. The youngest also carried a second novel variant in *ZFHX4*. Father expressed no variants. *KDM5C* variants have been described in XLID Claes-Jensen type, characterized by intellectual disability (ID), spasticity, epilepsy, short stature, microcephaly, and autism; some of which the siblings display. Additionally two siblings display feeding difficulties and all exhibit visual difficulties, symptoms not previously described in KDM5C-Related Disorder. The female sibling appears to be a manifesting heterozygote of the *KDM5C* variant, while mother is asymptomatic. This may represent skewed X-inactivation. The youngest sibling showed a second novel variant in *ZFHX4* c.7975 C>T p.R2659W. He exhibits severe XLID and expresses new symptoms not previously described in KDM5C-Related Disorder. He does not have certain features reported in patients with *ZFHX4* deletion (e.g. facial dysmorphism, corneal opacities, and digital abnormalities).
CONCLUSIONS: Several aspects add to current scientific knowledge and expand the phenotype of KDM5C-Related Disorder. This report suggests: new features of KDM5C-Related

Disorder, phenotypic differences between female and male patients, potential skewed X-inactivation, and possible impact of an additional variant in *ZFHX4*. Changing the c.1425 C>A p.N475K variant from uncertain significance to pathogenic would help provide clarity to both clinicians and families. Further investigation could reveal deleterious synergistic effect between *KDM5C* and *ZFHX4*.
KEYWORDS: Genetics, Cognitive/Behavioral Disorders (including Autism), Rare Diseases

283. Results of the GNAO1 International Registry Survey
Axeen Erika (Charlottesville, VA, United States) Viehoever Amy, Sidiropoulos Christos, Schreiber John, Goodkin Howard

OBJECTIVE: *GNAO1* pathogenic variants are associated with a spectrum of neurodevelopmental disorders including epilepsy and movement disorders. To more fully understand the spectrum of the disorder, the *GNAO1* International Registry surveyed parents/guardians of individuals diagnosed with *GNAO1*-related disorders.
METHODS: Patient recruitment was via social media and an email generated by the Bow Foundation, a non-profit charitable organization dedicated to GNAO1-related disorders. The survey was drafted by E.A with revision by members of the Bow Foundation Scientific Advisory Board and hosted on an online platform. All data were de-identified.
RESULTS: 63 surveys were completed. Age of first concern for abnormal symptoms was under one year in all patients with 73% before 6 months. First abnormal symptoms were low muscle tone (70%), developmental delay (67%), seizure (25%) and abnormal movements (16%). All reported developmental delays. Feeding difficulties were common with 24 requiring gastrostomy tubes. Any history of seizure was reported in 49% with continued seizures in 24%. Recurrent status epilepticus was reported by 12 individuals. Movement disorders were reported in 76%, 14 of whom had required ICU admission for movements. Nine individuals have a deep brain stimulator.
CONCLUSIONS: This is the first parent-generated survey of this patient population. Individuals with GNAO1-related disorders presented with a range of clinical symptoms but uniformly have symptom onset before one year, most often before 6 months, and all have developmental delays.
KEYWORDS: Genetics, Movement Disorders (including Cerebral Palsy), Epilepsy

284. Primary Hemophagocytic Lymphohistiocytosis Masquerading as Recurrent Haemorrhagic Demyelination
Gupta Juhi (New Delhi, India) Singh Sonali, Sinha Rahul, Anand Vaishakh, Hauhari Prashant, Kumar Atin, Chakrabarty Biswaroop, Gulati Sheffali

OBJECTIVE: To describe an interesting case who was managed as CNS tuberculosis initially, then as multiple sclerosis and eventually found to have a underlying genetic aetiology.
METHODS: An eight year old boy presented with history of fever since 8 months and multiple focal neurological deficits. He was being treated as CNS tuberculosis outside. The radiology was reviewed which was suggestive of multiple areas of haemorrhagic tumefactive lesions with differentials being tumefactive demyelination and glioma. Therefore brain biopsy was done in collaboration with neurosurgery which was suggestive of chronic inflammatory infiltrate and negative stains for AFB. In view of multiple episodes of focal neurological deficits and

dissemination in time and space in MRI ,diagnosis of multiple sclerosis was made. He was given intravenous methylprednisolone pulse therapy followed by azathioprine. During steroid tapering, he had relapses of demyelination twice requiring repeat steroid pulses. Subsequently child presented with features of hemophagocytic lymphohistiocytosis (HLH) in the form of fever, pancytopenia, splenomegaly, elevated ferritin and triglycerides. Therefore genetic testing was sent suspecting primary HLH which would explain both CNS demyelination and HLH.
RESULTS: He was tested positive for *PRF1* mutation (*c.1519G>T; c.1349C>T,*compound heterozygous). This confirmed diagnosis of primary HLH presenting as CNS demyelination. Currently child has not developed any new neurological deficit for last one year and is planned for allogenic stem cell transplant.
CONCLUSIONS: Primary (familial) HLH may present solely with neurological features, therefore this entity should be considered in refractory cases of demyelination.
KEYWORDS: Genetics, Rare Diseases, Demyelinating Disorders

285. Biallelic variants in CSTB can cause a developmental and epileptic encephalopathy with dyskinesia

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OBJECTIVE: Biallelic *CSTB* (cystatin B) variants primarily cause Unverricht-Lundborg disease (ULD), a progressive myoclonic epilepsy. Individuals with ULD develop normally until disease onset between ages 6-15 and have normal cognition. Most cases (90-99%) have two dodecamer repeat expansions in the promoter region, with the remainder caused by a single dodacamer repeat plus a single nucleotide variant (SNV) or indel. More recently, four patients with homozygous *CSTB* variants causing premature stop codons were described with severe developmental delay, microcephaly, movement disorders, and seizures.
METHODS: Individuals with biallelic SNVs or indels in *CSTB* were identified in Baylor Genetics and GeneDx databases. All probands were diagnosed via index or trio exome sequencing with confirmation by Sanger sequencing.
RESULTS: We identified an additional eight individuals with infantile onset disease secondary to biallelic *CSTB* SNVs and/or indels (Table 1). All exhibited microcephaly, severe developmental delay, axial hypotonia and hyperkinetic movement disorders. Epilepsy, appendicular hypertonia and developmental regression were common. All had delayed myelination and reduced brain volume. When serial imaging was available, progressive brain atrophy was apparent. Molecular findings are summarized in Table 2. Two of the five variants identified (c.202C>T and c.67-1G>C) have been associated with ULD but not infantile onset disease. c.10G>A and c.66+2T>C represent novel variants.
CONCLUSIONS: Biallelic SNVs or indels in *CSTB* can cause a severe developmental and epileptic encephalopathy with dyskinesia distinct from ULD. This condition is characterized by severe developmental delay, microcephaly, hypotonia, hyperkinetic movement disorders, epilepsy, delayed myelination and progressive cerebral atrophy.
KEYWORDS: Genetics, Movement Disorders (including Cerebral Palsy), Rare Diseases

286. RNA sequencing identifies a cryptic exon caused by a deep intronic variant in NDUFB10 resulting in isolated Complex I deficiency.

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OBJECTIVE: The diagnosis of mitochondrial disorders remains a challenging and often unmet need. We sought to investigate a sibling pair with suspected mitochondrial disease and a clinical presentation notable for global developmental delay, poor growth, sensorineural hearing loss, and brain MRI abnormalities, both with early death.
METHODS: Following uninformative genome sequencing on the family quartet, RNA sequencing was pursued as an orthogonal testing strategy. Immunoblotting studies for mitochondrial oxidative phosphorylation (OXPHOS) expression and quantitative proteomics were performed to validate the RNA sequencing results.
RESULTS: RNA sequencing of fibroblasts from the older sibling identified the presence of a cryptic exon in intron 1 of *NDUFB10,* encoding a component of mitochondrial OXPHOS complex I. Differential expression analysis relative to control samples suggested significantly decreased expression. Immunoblotting analysis using an antibody against one subunit of each of the five mitochondrial OXPHOS complexes revealed complete loss of mitochondrial complex I. Genome sequencing revealed a homozygous intronic variant, NM_004548.3:c.131-442G>C, in both siblings and in a heterozygous state in both parents, which is absent from population allele frequency databases.
CONCLUSIONS: Variants in *NDUFB10* represent a rare cause of infantile-onset mitochondrial disease, only being reported previously once in the literature. We present data implicating a deep intronic variant in *NDUFB10* as the cause of mitochondrial disease in two further individuals. This variant results in total loss of expression and overall destabilization of mitochondrial OXPHOS complex I and highlights the importance of RNA sequencing as a complementary functional analysis tool in patients undergoing genome-wide diagnostic evaluation.
KEYWORDS: Genetics, Rare Diseases

287. A novel PYCR2 variant (c.757_758dupCT) causing Hypomyelinating Leukodystrophy 10 in two unrelated patients of Mexican ancestry

Keller Stephanie (Atlanta, GA, United States) Logan Rachel

OBJECTIVE: Hypomyelinating Leukodystrophy 10 is a rare disorder caused by variants in *PYCR2* following an autosomal recessive inheritance pattern. Symptoms include, progressive microcephaly, failure to thrive, severe developmental delay, cerebral atrophy, and hypomyelination with death in childhood[1-3]. We present two unrelated patients with the same previously unreported homozygous duplication within the *PYCR2* gene (c.757_758dupCT), including one patient with uniparental isodisomy of chromosome 1.
METHODS: Retrospective review of the clinical history, exam, laboratory studies, and imaging from 2 patients with the same mutation in *PYCR2*.
RESULTS: Two unrelated Hispanic males of Mexican ancestry with the same variant in the *PYCR2* gene (c.757_758dupCT) where detected via trio exome sequencing. Both patients presented with progressive microcephaly, failure to thrive, and severe developmental delay. Patient 1 also demonstrates spasticity, hyperreflexia, cortical vision impairment, and dysphagia. MRIs of the brain show cerebral hypomyelination, hypoplasia of the corpus callosum, and progressive cerebral volume loss. His exome revealed a homozygous variant (c.757_758dupCT)

in *PYCR2*, in trans. Patient 2 has a similar history with cortical vision impairment, spasticity, hyperreflexia, and dysphagia. Additionally, he has a history of hyperkinetic movements, tracheostomy dependence, and seizures. MRIs of the brain show hypomyelination with progressive volume loss and thinning of the corpus callosum. His exome showed maternal uniparental isodisomy for chromosome 1 with a homozygous c.757_758dupCT variant in the *PYCR2* gene.
CONCLUSIONS: Our cases expand the known causative genetic mutations and clinical account of patients with Hypomyelinating Leukodystrophy 10. Their clinical presentations are strikingly similar to one another and previously reported cases.
KEYWORDS: Genetics, Rare Diseases

288. Antenatal Bilateral Ventriculomegaly and Frontotemporal Hemorrhage in Fetus with Congenital Protein C Deficiency
Gong Paul (Louisville, KY, United States) Puri Vinay

OBJECTIVE: Severe protein C deficiency is a rare autosomal recessive disorder that commonly presents with neonatal purpura fulminans (PF). Patients are typically homozygous or compound heterozygous for PROC gene mutation, which encodes for Protein C. We describe a fetus found to have antenatal ventriculomegaly and intracranial hemorrhage and later discovered to be compound heterozygous with two PROC gene variants.
METHODS: Case report of patient seen as inpatient consult.
RESULTS: Patient was the 29-week-old female fetus of a 31-year-old G2P0100 mother with history of deep vein thrombosis (DVT) and found to have bilateral ventriculomegaly on prenatal ultrasound. Mother was referred for admission and fetal MRI, which revealed bilateral severe ventriculomegaly and frontotemporal parenchymal hemorrhage. Mother had a history of previous pregnancy complicated by abnormal fetal ultrasound concerning for ventriculomegaly. Mother's previous child died at 7 days of life with MRI brain findings of extensive encephalomalacia, intraventricular hemorrhage, and multiple foci of left-sided intraparenchymal hemorrhage. With maternal history of DVT and previous neonatal death, amniocentesis was recommended for fetal whole exome sequencing. Testing revealed maternally inherited pathogenic variant and paternally inherited variant of unknown significance of the PROC gene, confirming the diagnosis of severe congenital protein C deficiency.
CONCLUSIONS: This case illustrates a potential presentation of severe congenital protein C deficiency in the antenatal and neonatal period. Though commonly associated with PF, congenital protein C deficiency should be considered when evaluating a fetus with ventriculomegaly and intracranial thrombosis and hemorrhage as seen in our patient.
KEYWORDS: Genetics, Neonatal & Fetal Neurology, Stroke (including other Vascular Disorders)

289. Neurodevelopmental disorders caused by mutations in imprinted genes: MAGEL2
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OBJECTIVE: Emphasize the importance of examining imprinted genes when analyzing WES and WGS data.

METHODS: We present two unrelated patients with a complex neurodevelopmental disorder. Duo WES/WGS was performed on proband and mother. Proband genomic DNA was digested with SmaI, a segment of *MAGEL2* was amplified by PCR, and sequenced, to determine if the silenced (maternal) allele was variant or wild-type. Case 1: 18 y.o. male with intellectual disability. History of respiratory distress and feeding difficulty at birth. He vocalizes; cannot sit or walk, but can scoot on his back. Fed completely by G-tube. Exam showed dysmorphic features (flat midface, mandibular protrusion), distal contraction of fingers, tongue protrusion, and stereotyped hand wringing movements.Case 2: 6 y.o. male with prenatal polyhydramnios, respiratory distress and feeding difficulty at birth; arthrogryposis noted. He has a tracheostomy and is ventilated at night. Exam showed dysmorphic features (long face, broad nasal root, epicanthal folds, upslanted palpebral fissures), contractures of his fingers, diffuse hypotonia and hyporeflexia.
RESULTS: WES revealed a heterozygous variant in *MAGEL2* (case 1: c.1948C>T, p.Q650X; case 2: c.1996dupC, p. Q666PfsX47) not maternally inherited in either case.
CONCLUSIONS: *MAGEL2*-related disorders are caused by heterozygous mutations in the paternal *MAGEL-2* allele; silenced when on the maternal allele. When analyzing WES or WGS data, conventional filtering approaches may ignore heterozygous variants that are inherited from one of the two parents. It is important to include an analytical tool to systematically examine heterozygous, inherited variants occurring in imprinted genes, as potentially disease-causing.
KEYWORDS: Genetics, Rare Diseases, Translational/Experimental Therapeutics

290. EXPERIENCES AND ATTITUDES TOWARD VACCINATIONS IN FAMILIES AFFECTED BY MITOCHONDRIAL DISEASE

Kruk Shannon (Bethesda, MD, United States) Gordon-Lipkin Eliza, Sandon Rodrigo, McGuire Peter

OBJECTIVE: Given the morbidity associated with infection in mitochondrial disease (MD), we aim to understand patient experiences and family attitudes toward immunizations.
METHODS: Families with children 0-21 years with “probable”/“definite” MD by Walker criteria were included. The primary caregiver completed a questionnaire. Attitude questions used a Likert scale.
RESULTS: Eighteen families enrolled: 11 Leigh Syndrome, 1 POLG, 6 MD not otherwise specified. Mean age of children with MD at questionnaire completion was 8.0 years. Mean age of MD diagnosis was 3.6 years. 6/18 were diagnosed with MD after age 4. 15/18 reported up-to-date vaccines. 4 reported vaccine exemption for their child with MD, 2 of which receive IVIg. All agreed that “vaccinating family members is important,” “high rates of vaccination in the community is important,” and “proof of childhood vaccination should be required before entering school.” Half reported worrying about vaccinating their child with MD. Variable responses were reported regarding safety/efficacy of vaccines for MD. 7/18 reported fever/fatigue after some vaccines; no individual vaccine was consistently attributed. One family reported motor regression after flu vaccine.
CONCLUSIONS: Most families were compliant with the standard vaccination schedule. In this small sample, fever/fatigue were commonly reported after vaccines; neurologic symptoms were rare. While families consistently agreed regarding the importance of herd immunity, they varied in attitudes about safety/efficacy of vaccines for MD and in anxiety regarding vaccinating their

own children with MD. While this small sample may not be representative of all families, this study identifies concerns for families with MD which should be considered by practitioners.
KEYWORDS: Genetics, Rare Diseases

291. 17 year old with epilepsy presenting to office with recent decline in school performance and progressively decreasing vision
Bhayana Kriti (Cleveland, OH, United States) Parikh Sumit

OBJECTIVE: Neuronal ceroid lipofuscinosis (NCL) refers to a group of neurodegenerative storage disorders. The symptoms include intellectual and motor decline, epilepsy, and vision loss. When testing pediatric patients with focused gene panels for such disorders, parents are not routinely counseled of the risk of any secondary findings for them. We present a case of an autosomal recessive cause of NCL where heterozygous carrier state is associated with a different disease.
METHODS: Case Report
RESULTS: 17 year old boy with epilepsy, with increasing seizure frequency, dysphagia and recent decline in school performance who presented with progressively decreasing vision. His neurological exam was pertinent for being cognitively dull but otherwise non-focal. The fundus exam revealed a Bull's eye Maculopathy bilaterally.
Testing for neurodegenerative diseases, with a specific concern for NCL, was initiated. CBC, CMP, Organic acids, Acylcarnitine, CK, Pyruvate-lactate, PPT1/TPP1 levels, epilepsy gene panel, EM of leukocyte buffy coat, whole-genome oligonucleotide array were normal. A comprehensive brain disorder gene panel analysis showed pathogenic bi-allelic variants in *GRN* inherited from each parent, consistent with a diagnosis of NCL. Each parent carried a pathogenic variant, and were found to be at risk for GRN-associated early onset frontotemporal dementia (FTD).
CONCLUSIONS: Homozygous variants in *GRN* causes NCL whereas, heterozygous pathogenic variants results in FTD in older adults. One may need to adjust their pre-test genetic counseling to account for disorders that may cause separate diseases in autosomal dominant and recessive forms.
KEYWORDS: Genetics

292. FOXG1 triplication in a patient with West syndrome, hypotonia, severe developmental delay, postnatal microcephaly, and growth failure
Kim Hyo Jeong (Incheon, Republic of Korea)

OBJECTIVE: *FOXG1*–related disorders are associated with severe developmental delay, speech impairment, and epilepsy. Patients with deletions or intragenic mutations of *FOXG1* usually also present postnatal microcephaly, hyperkinetic movement disorders, structural brain lesions including abnormalities of the corpus callosum, pachygyria, and abnormal myelination. Duplications of 14q12 harboring *FOXG1* often present infantile spasms, developmental delay with normal head circumferences and normal brain MRI. Triplications of *FOXG1* are rarely reported. Herein, we report the case with 14q11.2q13.1 triplication including *FOXG1*.
METHODS: Clinical, electrographic, radiological and chromosomal microarray data of the patient were analyzed.

RESULTS: The 7-month-old girl has suffered from hypotonia, severe developmental delay of the inability of head control, no babble and swallowing difficulty. Postnatal growth failure (height 5P, weight 5P) and postnatal microcephaly (head circumference below 3P) were accompanied. Infantile spasms with hypsarrhythmia were presented at 8 months old. Brain MRI presented pachygyria. Infantile spasms were controlled with medication including valproic acid, topiramate, and vigabatrin. But the patient expired due to pneumonia at 16 months old. Chromosomal microarray revealed 14q11.2q13.1 triplication of 10.5 Mb.
CONCLUSIONS: We report a 14q11.2q13.1 triplication. The phenotype includes West syndrome, hypotonia, severe developmental delay, postnatal growth failure, postnatal microcephaly, and pachygyria.
KEYWORDS: Genetics

293. LEIGH SYNDROME ASSOCIATED TO MT-ND6 MITOCHONDRIAL GENE MUTATION: A CASE REPORT.
Medina Gabriela (Quito, Ecuador) Cardenas Karol, Espinosa Nicolas, Dueñas, Pinargote Nora

OBJECTIVE: Report the association between MTND6 mitochondrial gene mutation and developmental regression with ataxia in a preschool female with Leigh Syndrome (LS)
METHODS: Case report: A 2 years and 9 months old female patient, previously healthy, presented with gait instability, weight loss and feeding difficulty. Rapid progression of her symptoms resulted in inability to walk without assistance, dysarthria and irritability. Physical examination showed an axial and peripheral hypotonia, increased left patellar reflex and ataxic gait.
RESULTS: Biochemical tests showed normal plasmatic and CSF lactate levels and a negative https://catalyst.omnipress.com/#collection/585/round/1273/settingsacylcarnitine profile. Normal organic acids in urine proved no indication of a metabolic disorder. Brain Magnetic Resonance (MR) and MR Spectroscopy abnormalities are shown in Figure 1 and 2. The Exome Sequencing and MtDNA Analysis detected heteroplasmic levels of m.14459G>A MT-ND6 mutation.
CONCLUSIONS: Mutations in the mitochondrial DNA can lead to some mitochondrial diseases. Clinical outcome in patients with the m.14459G>A mutation varies enormously. Only 4 cases of this mutation in LS patients have been reported worldwide, and none in Ecuador. LS is a neurodegenerative disorder that presents in infancy or early childhood and is caused by an inherited mitochondrial dysfunction. Presentation is heterogeneous, consisting of psychomotor regression, hypotonia and ataxia. Bilateral lesions in the basal ganglia in imaging are characteristic. Although our patient presented clinical and radiological characteristics of LS, the diagnosis was difficult. In our country genetic testing is usually not available, but in this case we were able to use it to further support our diagnosis and avoid unnecessary additional tests.
KEYWORDS: Genetics, Neurometabolic Disorders, Rare Diseases

294. A Patient with xeroderma pigmentosum type A who has progressing heart complications.
Miyata Rie (Tokyo, Japan) Hayashi Masaharu, Ohara Tomoko, Yamaguchi Asuka, Kuranobu Dai

OBJECTIVE: Xeroderma pigmentosum (XP) is a genetic disorder in DNA nucleotide excision repair and characteristic symptoms are skin hypersensitivity and progressive neurological

impairment. We experienced a 30-years-old patient with XP type A (XPA), whose heart function is getting worse and suffered from Mobitz II second degree atrioventricular block. We cannot find the report of dysrhythmia in patient with XP.
METHODS: The patient was born with normal delivery. He was retarded and had sensitivity for sunlight. He was diagnosed at three by genetic test. His movement and intellectual function had been getting worse. He was operated tracheostomy and gastrostomy at the age of twenty-one. He had become bedridden. He started to show fatty liver from the middle of twenties and nutrition was controlled. He started to show bradycardia at the age of thirty. Mobitz II second degree atrioventricular block was demonstrated by electrocardiography (ECG) and ejection fraction was decline to 40% by echocardiography.
RESULTS: There are no report of heart diseases in XPA patients except for one sibling case of cardiomyopathy. It is unclear that the symptoms relating to the heart was related to the disease or his individual symptoms. But some XPA patients died during nighttime suddenly. Arrhythmia may be related with death of in nighttime.
CONCLUSIONS: It is important for XPA patients to check ECG and echocardiography regularly.
KEYWORDS: Genetics, Rare Diseases

295. A child with Fever-Induced Paroxysmal Weakness and Encephalopathy with ATP1A3 mutation
Ferman Diana (Los Angeles, CA, United States) Luc Quinn, Sanger Terence

OBJECTIVE: To support a newly described phenotype of ATP1A3 gene mutation. The ATP1A3 in the Gene c2266C>T,p. Arg756 has recently been described as a new phenotype, Fever-Induced Paroxysmal Weakness and Encephalopathy (FIPWE). This group of children have distinct symptoms and outcomes from alternating hemiplegia of childhood (AHC), rapid-onset dystonia-parkinsonism (RDP), and cerebellar ataxia areflexia, pes-cavus, optic atrophy, sensorineural hearing loss syndromes (CAPOS).
METHODS: Case Report
RESULTS: 10-year-old male presents to our movement disorders clinic with a history of fever cause by viral illness on two separate occurrences, one at 4.8 years and another at 9.11 years of life that caused a neurologic decline. Child developed a fever that led to sudden onset of weakness, loss of speech, and cognitive changes. At each occurrence child did not completely recover and with each insult was left with increased residual symptoms of dystonia, dysphagia cognitive changes. Patient was seen by our movement disorders specialist who recommended medical management for dystonia symptoms and ordered a dystonia panel that resulted a pathogenic variant in ATP1A3 variant.
CONCLUSIONS: We believe it is important to expand the phenotypic variation of ATP1A3 to help expedite treatments and awareness.
KEYWORDS: Genetics, Movement Disorders (including Cerebral Palsy)

296. REMOTE ACTIGRAPHY MONITORING AS A METHOD OF QUANTIFYING DISABILITY OVER TIME IN PATIENTS WITH MITOCHONDRIAL DISEASE
Gordon-Lipkin Eliza (Bethesda, MD, United States) Kruk Shannon, Sandon Rodrigo, McGuire Peter

OBJECTIVE: Mitochondrial diseases are a complex family of heterogenous multisystemic disorders frequently affecting the nervous system. Children with mitochondrial disease (MD) frequently experience chronic fatigue and prolonged recovery after illness. However, quantitative objective measures of these symptoms are lacking. We aimed to quantify daily activity of MD over time in their home environment using activity tracking technology, or actigraphy.
METHODS: Children were included if they met "probable" or "definite" MD by Walker criteria, were ambulatory and were able to wear the small wearable device daily at home. Sibling healthy controls (HS) were included, when available. The GarminVivofit3 was used to measure daily steps. Significant events were recorded by families. Normative data was extracted from Tudor-Locke et al. IJBPNA 2011. Percent expected daily steps (PEDS) was calculated by the mean daily steps divided by the age/sex matched normative value x10.
RESULTS: 11 MD and 3 HS were included. 10 subjects wore the devices for >3 months. For MD, PEDS ranged from 20% to 76%. For those MD with HS, 2 of 3 patients had lower PEDS than their HS. Over the initial 6 months of the study, one subject was hospitalized. PEDS decreased during illness to 33% and then gradually returned to baseline of 55%.
CONCLUSIONS: Remote actigraphy monitoring in children with MD is feasible and allows for non-invasive, objective, longitudinal data collection outside the hospital setting. It can be used to measure change over time and to compare across patients. This technology has excellent potential as a practical outcome measure for clinical trials.
KEYWORDS: Genetics, Neurometabolic Disorders

297. NEURODEGENERATIVE DISORDERS: GENOTYPE - PHENOTYPE SPECTRUM IN PAKISTAN
Sultan Tipu (Lahore, Pakistan)

OBJECTIVE: Neurodegenerative disorders are one of most common neurological disorders in children particularly in countries where consanguineous marriages are prevalent like Pakistan. The tremendous advancement in the field of molecular genetics has unrevealed many mysteries regarding most of these neurological disorders. To find out the genotype: phenotype correlation this study was conducted at the Pediatric Neurology department of Children's Hospital Lahore.
METHODS: After IRB approval, 200 families were selected. Blood specimen was sent from patients, healthy sibling and both parents to Lab for whole exom sequencing (WES). Skin biopsy samples were taken in selected patients.
RESULTS: There were 51% males and 49% females with age ranges from 5 months to 18 years. Out of these 55% patients had developmental delay and 45% were have regression. Hearing impairment was found in 7% patients while vision was affected in 12% patients. Speech was affected in 66% patients while 43% patients had history of fits. Autistic spectrum of disorders were observed in 20% patients. Microcephaly was seen in 19% cases. Out of all families, 41% had more than one sibling affected. On neuroimaging, leukodystrophy was seen in 19.5 %patients. Cerebellar atrophy was observed in 15% patients while 17% patients had cerebral atrophy. On further genetic analysis, (51%) patients had known gene mutation while (49%) patients had novel gene mutation.
CONCLUSIONS: Genetic analysis of the families having a sibling of inherited neurological disorder can help in precise diagnosing, management plan and genetic counseling.
KEYWORDS: Genetics

298. A noble de novo EFNB1 mutation in a patient with global developmental delay and schizencephaly

Han JiYoon (Daejeon, Republic of Korea)

OBJECTIVE: Craniofrontonasal syndrome (CFNS; OMIM 304110) was first reported by Cohen in 1979, and is a characterized typical manifestation including craniosynostosis, frontonasal dysplasia, craniofacial asymmetry, and various skeletal anomalies. CFNS is a rare, X-linked disorder in which heterozygous females ironically reported the majority of patients and are more severely affected than hemizygous males because of functionally mosaic state bring about X-inactivation. Family-based trio testing by whole exome sequencing can be used as a proper test for developmental delay in undiagnosed children testing negative to conventional work-up, previously.
METHODS: As no definite diagnosis had been made, we opted to perform trio-whole exome sequencing (WES) to reveal the underlying genetic cause of the patient's condition.
RESULTS: A 4-month-old female infant was referred to the department of pediatric neurology with a diagnosis of microcephaly and developmental delay. She could not control her head hold objects until 4 months of age. Brain resonance imaging (MRI) revealed schizencephaly and dysgenesis of corpus callosum. Audiometry was normal and her response to sound seems to appropriate. The result of visual evoked potential and ophthalmologic test were normal. Blood karyotype with G-banding and a genomic microarray showed no deletion/duplications. We revealed a novel *de novo* missense mutation located exon 5 in *EFNB1* (c.943C>T).
CONCLUSIONS: *EFNB1* mutation is considered for child with schizencephaly and further study focusing on phenotyping is required to understand the possible contribution of genetic modifier and environmental impact in the expression of *EFNB1*.
KEYWORDS: Genetics, Neuroimaging, Cognitive/Behavioral Disorders (including Autism)

299. GLUT1: Two Cases and a Broadening Clinical Spectrum

Whalen Danielle (San Diego, CA, United States) Friedman Jennifer

OBJECTIVE: Pathogenic variants in the SLC2A1 gene cause glucose transporter type 1 (GLUT1) deficiency syndrome, classically described as intractable seizures beginning in infancy and developmental encephalopathy. Recently milder GLUT1 variants have been described, showcasing a broadening spectrum of clinical phenotypes amenable to potential ketogenic diet therapy.
METHODS: A comprehensive chart review as well as literature review was performed.
RESULTS: Patient 1: 13 year old with very long chain acyl-CoA dehydrogenase deficiency (VLCADD) diagnosed on newborn screen, absence and focal seizures with secondary generalization. Whole exome sequencing obtained to evaluate previous VLCADD diagnosis given atypical course was consistent with VLCADD carrier status and de novo pathogenic c.376C>T (p.R126C) variant in SLC2A1 gene consistent with GLUT1. Diagnostic lumbar puncture with CSF to serum glucose ratio of 0.40 supportive of this diagnosis. Currently trialing modified Atkins diet given difficulty maintaining oral ketogenic diet and conflicts with previous low fat, high carbohydrate diet for presumed VLCADD.
Patient 2: 17 year old with intractable absence and generalized seizures, hemiplegic migraines worse with fasting. Whole genome sequencing with de novo likely pathogenic c.1202C>T

(p.Pro401Leu) variant in SLC2A1 associated with GLUT1 spectrum disorder. Headaches and seizures relatively well controlled, family declining diagnostic lumbar puncture and ketogenic diet at this time.
CONCLUSIONS: Given the broadening clinical spectrum of GLUT1 associated syndromes, evaluation for GLUT1 should be considered in patients with early onset absence epilepsies, paroxysmal dyskinesias, and genetic generalized epilepsies associated with intellectual disability. Despite their rarity, GLUT1 syndromes remain of high clinical interest given known effective therapy with ketogenic diet.
KEYWORDS: Genetics, Epilepsy, Rare Diseases

300. Case Report: Cockayne Syndrome type II/B with Infantile Spasms
Al Omari Mohammed (London, Ontario, Canada) Nouri Maryam, Prasad Asuri

OBJECTIVE: Cockayne syndrome type B (CSB) is mostly due to a pathogenic ERCC6 gene mutation. While seizure disorders are described in CSB, there are no prior reported cases of CSB with infantile spasms as the presenting seizure. We present the clinical, electrophysiological and neuroradiological results of a patient with CSB presenting with infantile spasms.
METHODS: Case Report
RESULTS: An Eleven months old female infant, presented in the neonatal period with classic small for gestational age, dysmorphic features, including; microcephaly, growth failure, hypotelorism, deep-set eyes, cataracts and retromicrognathia. Diagnosis of CSB was confirmed by genetic testing, which disclosed a homozygous ERCC6 mutation (duplication described as c.2096 dupC). She presented with infantile spasms at 8 months associated with EEG. She was started on vigabatrin when she was 10 months with partial response and required addition of prednisolone. Unfortunately, she died of severe septic shock, 4 weeks after started on steroids. Clinically, she responded to combination of vigabatrin and prednisolone, with no spasms reported 2 weeks after steroids initiation. Initial and follow up EEGs prior to steroid initiation revealed a classic hypsarrhythmic pattern. MRI imaging of the brain showed global hypomyelination, atrophy of supratentorial white matter, corpus callosum, and cerebellum.
CONCLUSIONS: This patient with Cockayne syndrome presented with early onset seizures, presenting as infantile spasm. In this single case, spasms were difficult to control with vigabatrin alone, and required steroids to achieve a good control of her spasms, however, given their short life span, the role of aggressive management of spasms remains debatable.
KEYWORDS: Genetics, Epilepsy, Rare Diseases

301. A case report of heterozygous COQ8A gene mutation in patient with seizures and cerebellar symptoms.
Mammadbayli Aytan (Baku, Azerbaijan) Taghiyeva Madina, Aliyeva Sona, Alakbarova Leyla

OBJECTIVE: Cerebellar ataxia is a common symptom of coenzyme Q10 (CoQ10) deficiency associated with COQ8A mutations. Onset is typically during infancy or childhood with ataxic features associated with developmental delay or regression. When disease onset is later in life, first symptoms can include incoordination, epilepsy, tremor, and deterioration of writing.
METHODS: We report the case of a boy that was born at term , parents are cousins. Pregnancy, birth history and developmental milestones were unremarkable . Before neurological manifestation he had night recurrent vomiting(1-2 times per month) not associated with food

intake. At 9 years he had his first focal seizure. After that he continued to had focal and generalized seizures and also epileptic status .Additional symptoms noted after epileptic status included left sided spastic hemiparesis, facial left sided palsy, positive oral automatism reflexes, positive pathological reflexes in the left , clonus in both legs and cerebellar symptoms(ataxia-dynamic and static, slurred speech, intention tremor).His cognitive functions were good before epileptic status.
Lab.examination reveals high levels of Lactic Acid and low levels of pyruvate. MRI was normal. EEG shows focal epileptic activity of the occipital lobe.
RESULTS: We perform a Whole exome sequence analysis to this patient: *COQ8A* gene p.R271L/p.L506W heterozygous mutation was identified.
CONCLUSIONS: This boy have a COQ8A pathogenic variant with seizures and cerebellar symptoms (ataxia-dynamic and static, slurred speech, intention tremor)and after CoQ10 supplementation remains stable.
KEYWORDS: Genetics, Epilepsy, Neurometabolic Disorders

302. Diagnosis and treatment of Pediatric onset Genetic Epilepsy: Experience Sharing of a Tertiary care centre of Bangladesh
Rahman Md Mizanur (Dhaka, Bangladesh) Fatema Kanij

OBJECTIVE: Childhood epilepsies are challenging to manage in terms of choosing appropriate antiepileptic drugs. The etiology is diverse namely structural disorder of brain, neurometabolic, neurocutaneous and genetic disorders. Genetic disorders are important yet under diagnosed etiology of pediatric epilepsy. This presentation will highlight the important of genetic test in pediatric epilepsy
METHODS: Thirty three cases of pediatric onset drug resistant epilepsy were taken in which structural or metabolic etiology were excluded . To detect the genetic etiology next generation sequencing was done. In all cases, detailed clinical history, examination, family pedigree, EEG, metabolic screening, MRI of brain were done.
RESULTS: In 20 case genetic mutations were detected. The important genetic mutations detected were SCN1A , *SCN8A , NPLR3 mutation, DOCK7 mutation, CDKL5, KCNQ2 etc*
CONCLUSIONS: Genetic mutations are not uncommon in Bangladeshi population. So, it is essential to search for genetic mutation in suspected cases of pediatric epilepsy
KEYWORDS: Genetics, Epilepsy

303. Heterozygous mutation variant in SCN9A gene for Congenital Insensitivity to pain - case study
Chayut Deena (Norwich, United Kingdom) Kalra Vivek, Chitre Manali, Woods Geoff, Sanghrajika Anish, Arora Ruchi, Armon Kate

OBJECTIVE: To share the case of a child diagnosed in retrospect, with Charcot joints secondary to congenital insensitivity to pain (CIP).
METHODS: A 6-year-old developmentally normal boy was first seen at age 19 months with self-mutilating behaviour and tongue-biting. He developed recurrent tongue ulcerations, tongue abscess and pyogenic granuloma. He demonstrated high thresholds for pain and temperature.
5 years later, he re-presented with an undisplaced tibial fracture following trivial trauma. After cast removal, he developed a swollen, erythematous ankle with features consistent with septic

arthritis of the ankle, which was treated with washout and antibiotics. Thereafter, radiographs demonstrated significant bony destruction of the talus, calcaneum and distal fibula.
RESULTS: MRI of the feet and ankles showed multifocal bony lesions. Various differentials were considered and investigations including a bone biopsy were planned. Extensive metabolic investigations and NCS/EMG were normal. Initial genetic tests included a normal microarray. A gene panel including HPRT1, NGF, NTRK1 and SCN9A revealed a heterozygous likely benign variant in SCN9A.
Following a neurogenetics review, the re-examined scans were felt to be Charcot-like. Trio whole genome analysis revealed a bi-allelic mutation in SCN9A gene providing the diagnostic genetic basis for CIP.
CONCLUSIONS: A delayed diagnosis was made because Charcot joints were not initially considered (and hence CIP) in the differential diagnosis. The SCN9A mutations required whole genome sequencing. Sensation of pain is crucial in protecting joints from recurrent trauma and irreversible damage. An early diagnosis of CIP is essential for protective measures to be put in place.
KEYWORDS: Genetics, Neuromuscular Disorders, Rare Diseases

304. Advancements in the clinical interpretation of variants in ion channel genes related to epilepsy through functional computational modeling of missense variants
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OBJECTIVE: Many genes encoding ion channel proteins are involved in monogenic epilepsy disorders. Extensive naturally existing missense variation in these genes poses a challenge to interpreting novel variants, leaving many classified as “variants of uncertain significance” (VUS) and therefore not clinically actionable. This study measures the utility of a computational functional modeling platform (FMP) to predict the effect of missense variants on protein function.
METHODS: We developed a novel, gene-specific FMP aimed at evaluating specific properties (sequence, biophysical, structural, and spatial relationships) of proteins that contribute to the pathogenicity of missense variants. We assessed the impact of the FMP on the classification of VUS in 17 epilepsy-related ion channel genes in which FMP accuracy was established.
RESULTS: FMP informed the clinical classification for 85% (1387/1648) of previously reported missense-VUS observed in 17 ion channel genes. FMP evidence resulted in reclassification of 6% of missense-VUS (78/1387): 26% toward pathogenic, 74% toward benign. Reclassifications impacted 248 patients, accounting for 9% of patients with a missense-VUS in these genes. FMP was most impactful for SCN1A with 19 reclassified missense-VUS (8% of SCN1A-missense-VUS) affecting results for 41 patients (10% of patients with SCN1A-missense-VUS).
CONCLUSIONS: Analyzing multiple aspects of protein biology through validated computational models guides the clinical interpretation of more missense variants than is otherwise possible. FMP performance is expected to increase as additional functional data becomes available for ion channel genes. These advances significantly improve the diagnostic yield and actionability of genetic testing in epilepsy, promoting precision medicine applications, and family testing.

KEYWORDS: Genetics, Epilepsy

305. Assessment of tuberous sclerosis-associated neuropsychiatric disorders using the MINI-KID tool: a pediatric cohort study

Ding Yifeng (Shanghai, China) Wang Ji, Zhou Hao, Li Taoli, Zhou Shuizhen, Wang Yi

OBJECTIVE: To assess neuropsychiatric disorders and their possible risk factors in children with tuberous sclerosis complex (TSC) in China.
METHODS: Cross-sectional study of 95 parents of Chinese children aged 6-16 years with TSC. Tuberous sclerosis-associated neuropsychiatric disorders (TAND) were assessed using the MINI-KID (parent version), and children with TAND were compared with children with asthma and healthy children. Logistic regression analysis was used to identify risk factors for TAND.
RESULTS: A total of 81.05% of patients (77/95) had at least one TAND, and 70.53% (67/95) had an intellectual disability. The MINI-KID tool diagnosed a total of 15 neuropsychiatric diseases, the most common of which were attention-deficit/hyperactivity disorder (ADHD) (51.58%, 49/95) and social anxiety disorder (41.05%, 39/95). The number of children with neuropsychiatric diseases in the TSC group was significantly greater than the numbers in normal development group ($P < 0.0001$). Epilepsy before the age of 2 years, an epilepsy duration exceeding 2 years, a seizure frequency of more than once a month, and use of more than 2 antiepileptic drugs were closely associated the occurrence of TAND.
CONCLUSIONS: The MINI-KID can be used for the screening and diagnosis of TAND in children with TSC aged 6-16 years. The incidence of neuropsychiatric diseases in children with TSC can arrive at 81.05%. Early onset of epilepsy, long duration of epilepsy, frequent seizures, and refractory epilepsy are risk factors for TAND. Early, reasonable, and rapid control of seizures may reduce the risk of neuropsychiatric illness in children with epilepsy.
KEYWORDS: Genetics, Cognitive/Behavioral Disorders (including Autism)

306. Whole exome sequencing in children with suspected neurogenetic disorders: An effective, cost- and time-saving diagnostic tool

Wassmer Evangeline (Birmingham, United Kingdom) Vogt Julie, Sanchis-Juan Alba, Raymond Lucy

OBJECTIVE: Many children attending a paediatric neurology clinic are suspected to have a neurogenetic disorder, however confirming this can be a challenge and can take many years. Even after extensive invasive and costly investigations, many do not have a molecular genetic diagnosis. Whole Exome Sequencing (WES) has proved to be a valuable tool in medical genetics and has become cheaper and faster. To assess the diagnostic yield of WES in children suspected of having a neurogenetic condition
METHODS: We performed whole genome sequence (WGS) analysis as part of the NIHR Bioresource Research Project on a cohort of children recruited in a paediatric neurology clinic. These children with developmental impairment were suspect of neurogenetic disorders based on radiology (atrophy or normal neuroimaging), clinical findings (sensorineural deafness, cataracts or dysmorphism) or family history (sibling with similar findings) or a progressive course
RESULTS: 29/ 46 children received a molecular diagnosis. Variants of uncertain significance were found in a further 6 children. The mean time elapsed from symptom onset to WES was 10 years (range 3–16).

CONCLUSIONS: We demonstrated the clinical utility of WES in our patient cohort, obtaining a diagnostic yield of 63%. WES for children with a suspected neurogenetic disorder proves to be an effective, cost- and time-saving approach for the molecular diagnosis
KEYWORDS: Genetics, Rare Diseases

307. Novel mutations identified by whole exome sequencing in ECHS1 from three Chinese patients with Leigh Syndrome
Wu Miaojuan (Wuhan, China) Liu Yongchu, Sun Dan, Liu Zhi-sheng

OBJECTIVE: To precisely identify the disease-causing variants of children who were diagnosed as Leigh Syndrome(LS).
METHODS: We implemented whole-exome sequencing in three Chinese patients diagnosed as LS to precisely identify the disease-causing variants. During the diagnosis, other examinations and biomedical measurements such as metabolic measurement, mitochondrial respiratory chain (MRC) enzyme activity measurement, oxygen consumption rate (OCR) measurement and brain magnetic resonance imagining (MRI), were also carried out.
RESULTS: WES analysis of three patients identified four distinct mutations in *ECHS1* to be the pathogenesis. Among the detected mutations, only one, c.583G>A (p.Gly195Ser), has been reported in previous studies; the other three, c.463G>A (p.Gly155Ser), c.557C>T (p.Ser186Leu) and c.476_c.477delAGinsGGCATAGA (p.Gln159delinsLeuTyrAla), are all novel. It is worth noting that one of the novel variants, c.463G>A (p.Gly155Ser), was detected in all three patients from unrelated families, indicating a potential founder effect, which has already been previously reported to be existing in LS in other mutations. Clinically, despite different initial presentations, all studied patients were with similar clinical syndromes such as development regression, paroxysmal exercise-induced dystonia, as well as common radiological features like symmetrical bilateral brain abnormalities, similar metabolic results like consistently elevated plasma. The presence of the marker metabolite 2-methyl-2,3-hydroxybutyric acid in urine organic acids have also been detected.
CONCLUSIONS: Our findings enriched the pathogenic mutation spectrum of *ECHS1* gene and confirmed the clinical and phenotypic presentations of Short-chain enoyl-CoA hydratase deficiency (ECHS1D) in LS. Further studies are required to look into the noteworthy novel mutation c.463G>A (p.Gly155Ser), especially in Chinese origin population.
KEYWORDS: Genetics

308. AUTOSOMAL DOMINANT TEMPORAL LOBE EPILEPSY WITH AUDITORY FEATURES: A UNIQUE FRAMESHIT MUTATION VARIANT
Otero Matheus (Salvador, Brazil) Shahid Syeda, Lakhani Shenela, Marquis Belinda

OBJECTIVE: Describe the association of a unique frameshift mutation variant in gene LGI1 with a clinical presentation compatible with autosomal dominant temporal lobe epilepsy with auditory features.
METHODS: 16 year old male presented with mild ADHD, learning disability and epilepsy since age 10 years. His seizure semiology consists of hearing a "loud beeping" sound, right gaze deviation, lower extremity jerking followed by generalization, lasting 2 minutes with postictal receptive aphasia. Patient was seizure-free for 3 years on oxcarbazepine, and subsequently weaned off. After remaining stable for 2 years, he presented with two seizure episodes of similar

semiology. Oxcarbazepine was restarted. Neurological exam revealed impaired calculation and concentration consistent with his neurocognitive delay. Several maternal family members have epilepsy with similar presentation.
RESULTS: Genetic analysis revealed a heterozygous mutation variant of LGI1 gene in exon 8, c.1649_1650delAT:p.His550ArgfsX4 (H550RfsX4). This was classified as a variant of unknown significance. Many affected individuals from this patient's family demonstrate the same frameshift variant that is predicted to result in protein truncation. This result along with family history is consistent with the diagnosis of autosomal dominant temporal lobe epilepsy with auditory features. Brain MRI was normal. Video electroencephalogram captured electro-clinical target events with focal onset from the left centro-temporal region, followed by secondary generalization.
CONCLUSIONS: The identified variant was initially considered of unknown significance, however that designation was reclassified when the family pedigree was examined, corroborating a direct familial association with the syndrome. In addition, this particular variant mutation has not previously been described for this gene.
KEYWORDS: Genetics, Epilepsy, Rare Diseases

309. Design of a comprehensive genetic and metabolic diagnostic platform for patients with AHC of unknown genetic cause
Gropman Andrea (Washington, DC, United States) Uittenbogaard Martine, Brantner Christine, Chiaramello Anne

OBJECTIVE: Alternating Hemiplegia of Childhood (AHC) is a rare neurodevelopmental disorder with an extensive phenotypic variability, resulting in a challenging clinical diagnosis. About 75% of AHC cases are caused by variants mapping in the *ATP1A3*, *ATP1A2* or *GLUT1* gene, leaving 25% of patients with undiagnosed AHC. Our objective is to design a genetic and metabolic diagnostic platform for patients with AHC of unknown etiology for decoding the genotype-phenotype correlation and personalizing therapeutic interventions.
METHODS: The 9-year-old male proband exhibits symptoms of AHC with a suspected mitochondrial etiology and unclear genetic diagnosis. We used fibroblasts derived from the proband's skin biopsy to design a diagnostic workup consisting of whole exome sequencing (WES), deep sequencing of the mitochondrial genome, mitochondrial morphometric analysis and live-cell metabolic assays.
RESULTS: Our WES analysis yielded novel genetic clues on his AHC with a mitochondrial etiology by pinpointing variants mapping in the *PNKD*, *MTO1* and *NDUFA2* genes, all involved in the mitochondrial energy metabolism. Deep sequencing of his mitochondrial genome revealed a novel mitochondrial variant mapping in the *MT-TL2* gene encoding the mt-tRNALeu$^{(CUN)}$ critical for normal oxidative phosphorylation (OXPHOS) functions, responsible for ATP synthesis. Our metabolic analysis highlighted a dysregulated OXPHOS and diminished metabolic plasticity, preventing an efficient switch from OXPHOS to glycolysis to maintain ATP homeostasis.
CONCLUSIONS: Our genetic and metabolic platform improves the diagnostic process of AHC with an unclear genotype-phenotype correlation. It provides critical insights into AHC in terms of genetic clues and bioenergetic deficit to ultimately personalize therapeutic options.
KEYWORDS: Genetics, Neurometabolic Disorders, Rare Diseases

310. COASY Protein Associated Neurodegeneration in Twin Females: A Case Report
Tran Catherine (Kansas City, MO, United States) Fitzgerald Keely

OBJECTIVE: Coenzyme A synthase protein associated neurodegeneration (CoPAN) is an inherited, progressive neurodegenerative disorder caused by mutation in coenzyme A synthase (COASY) gene. It is a subtype of neurodegeneration with brain iron accumulation (NBIA) disorders. Early imaging findings can suggest metabolic or mitochondrial disorder and not typical "eye of the tiger" sign associated with NBIA disorders. Few cases are reported in medical literature. We introduce a case of identical twin females with pathogenic variants.
METHODS: N/A
RESULTS: The twins were conceived naturally to non-consanguineous parents and delivered at 37 weeks after an uneventful pregnancy. Both had early feeding difficulty and required admission for failure-to-thrive at 2 years of age with gastrostomy tube placement. Development was globally delayed. MRI brain showed enlargement and hyperintense T2/FLAIR signals involving the putamen, caudate, and thalami bilaterally with restricted diffusion. Magnetic resonance spectroscopy and metabolic labs were normal. Whole exome sequencing identified compound heterozygous variants in COASY gene, c.394C>T (p.Q132X) and c.1495C>T (p.R499C). Both Twin A and B display dystonia in the feet and ataxic gait, and wear helmets due to frequent falls. Twin B has self-injurious behaviors. Neither developed spasticity.
CONCLUSIONS: CoPAN typically presents with gait difficulties caused by onset of spasticity and dystonia in the lower limbs in early childhood followed by progression of dystonia to the mouth/jaw, dysarthria, parkinsonism, spastic-dystonic paraparesis, axonal degeneration, and cognitive impairment. Treatment involves symptomatic management with regular developmental assessment and therapy. Early imaging and clinical features can be suggestive of metabolic or mitochondrial disorder, however, CoPAN should be considered.
KEYWORDS: Genetics

311. Novel GRLB mutation causing a syndrome of hyperekplexia and encephalopathy (SHEEPR) in Puerto Ricans: A Case Report
Abdelmoumen Imane (Philadelphia, PA, United States) Jimenez Sandra, Melvin Joseph, Valencia Ignacio, Schneider Michael

OBJECTIVE: To describe the clinical presentation and phenotype of two Puerto Rican children from different families with severe spastic encephalopathy and hyperekplexia who have homozygosity for the same novel frameshift mutation in the *GRLB* gene.
METHODS: A detailed retrospective chart review of two patients with the same frameshift homozygous *GRLB* gene mutation followed was performed. Variables included clinical presentation, age of onset, developmental assessment, neurological examination, electroencephalogram (EEG) and neuroimaging findings, treatment response and ancestry information.
RESULTS: While these two patients have Puerto Rican ancestry, none of the parents identifies consanguinity, nor do they originate from the same town. Hyperekplexia manifested during the neonatal period. Clonazepam alleviated the frequency of the stiffening attacks. Both patients have Intellectual disability, severe spasticity and epileptiform discharges on EEG.

CONCLUSIONS: Homozygosity for the frameshift mutation (c.1431_1452dup (p. F485Kfs*53) in the *GRLB* gene found in two patients of Puerto Rican descent, is associated with a severe form of hereditary hyperekplexia. We call this entity the syndrome of hyperekplexia and encephalopathy in Puerto Ricans (SHEEPR). We attribute the syndrome to an ancestral mutation in the Puerto Rican population.
KEYWORDS: Genetics, Rare Diseases, Neuroscience

312. Genetic epilepsy and epileptic encephalopathies: experience from a tertiary care center
Mohanlal Smilu (Kozhikode, India) Najiya, Pachat Divya, Babu Sachin, Kumar Suresh

OBJECTIVE: Our aim was to study the clinical profile of children with epilepsy / epileptic encephalopathies with a presumed genetic etiology.
METHODS: The study was conducted at a tertiary care center -Aster MIMS, Kozhikode (Kerala, southern part of India).Retro-prospective chart review from January 2019- February 2020.Children with epilepsies/ epileptic encephalopathies < 18 years with presumed genetic etiology were included and followed up for minimum 3-month period.
RESULTS: 34 children were included. M: F 18:16. Age of seizure onset ranged day of life -1 to 10 years. Positive family history in 5 .5 children required neonatal intensive care (preterm-4, neonatal hypoglycemia-1, neonatal seizures-2). 12 children had polymorphic seizures, Spasms-2, focal motor -10, focal non motor-2, tonic generalized-4 myoclonic- 2, atypical absences-1, generalized tonic / clonic-1. Examination revealed dysmorphism -8, Microcephaly-9, neurocutaneous markers-4, failure to thrive-8. Global developmental delay-15, cognitive delay-11, motor delay -2, Regression – 3, normal-3. Electroencephalogram showed Modified hypsarrhythmia-4, Lennox-gestaut like features- 6, non-specific diffuse slowing- 10, multifocal spike and slow waves- 11, 3-4 Hz spike and slow wave-1, photo paroxysmal response- 1, normal-1. Short term seizure outcomes were complete seizure control-3, partial control-15, refractory-16. MRI changes structural-7, non-specific cerebral atrophy-9, normal-18. Apart from routine antiepileptics, seizure control was achieved by pyridoxine and riboflavin-1, ketogenic diet-1, partial response to steroids initially-2. Genetic testing done in 30/34 patients and 28 /30 (93%) tested positive. Channelopathies-9, vitamin responsive-1, Neurocutaneous syndrome-4, Infantile epileptic encephalopathies-4, progressive myoclonic epilepsies-3, chromosomal-2, others-5.
CONCLUSIONS: Understanding the phenotype-genotypic correlation would be beneficial in the treatment and prognosis.
KEYWORDS: Genetics, Epilepsy

313. Novel mutation in SPTLC2 gene presenting as a mimicker of spinal muscular atrophy (SMA)
Shoup Jaime (Louisville, KY, United States) Lakhotia Arpita, Asamoah Alexander

OBJECTIVE: SPTLC2 pathogenic variants have been associated with hereditary sensory and autonomic neuropathy, 1C (HSAN1C). We describe a case of motor neuropathy/neuronopathy associated with SPTLC2 gene mutation, presenting as a mimicker of SMA in a pediatric patient.
METHODS: Chart review

RESULTS: A 3-year-old male presented for neurologic evaluation due to global developmental delay and abnormal gait. Patient demonstrated gross and fine motor delay since birth, along with language and social delay. Physical exam showed high-arched palate, tongue atrophy/fasciculations, proximal greater than distal weakness with Gower maneuver and hyperlordotic gait. He had normal deep tendon reflexes except absent Achilles reflexes. Creatine kinase, fragile X, chromosomal microarray, and brain magnetic resonance imaging were normal. Electromyography and nerve conduction study demonstrated acute and chronic neurogenic changes with low motor combined muscle action potentials. Muscle biopsy findings were consistent with SMA. Genetic testing for 5q SMA was negative. Further genetic testing with Invitae comprehensive neuropathies and neuromuscular panels showed three variants of unknown significance at ISPD, PMP22, and SPTLC2 genes. Whole genome sequencing re-demonstrated three variants of unknown significance, two of which were paternally inherited, but one was a *de novo* mutation in the SPTLC2 gene and predicted to be deleterious by prediction algorithms.
CONCLUSIONS: SPTLC2 gene mutation is associated with HSAN1C with presentation typically in the third decade. This case highlights a novel mutation in the SPTLC2 gene that presents as a motor neuropathy/neuronopathy in the first decade of life. It should be considered in patients who have a SMA phenotype with negative genetic testing for 5q-SMA.
KEYWORDS: Genetics, Rare Diseases, Neurometabolic Disorders

314. Genetic testing in child neurology: A rare case of Optic atrophy secondary to Primary Co-enzyme Q defeciency.
Avula Sreenivas (Peoria, IL, United States)

OBJECTIVE: A set of clinical findings in rare genetic diseases may suggest a possible diagnosis but confirmatory genetic testing is needed for a definitive diagnosis to improve the out comes if the genetic condition is treatable and also in genetic counselling.
METHODS: A 15 year old boy with a diagnosis of Type 2 Usher syndrome and bilateral optic atrophy presented to the neurology clinic for further evaluation. His exam showed significant pale discs bilaterally. Optic atrophy panel genetic testing was ordered to determine the underlying etiology as he also has congenital sensorineural hearing loss.
RESULTS: Optic atrophy panel was positive for two variants in the PDSS1 gene that encodes prenyldiphosphatase synthase, an enzyme involved in the coenzyme Q synthesis pathway that plays a role in the oxidative phosphorylation in mitochondria1. The variants noted were p.Gly330Arg (G330R) (GGG>AGG): c.988 G>A in exon 10 of the PDSS1gene and p.Met171Val (M171V) (ATG>GTG): c.511 A>G in exon 6 of the PDSS1 gene. Targeted testing of the parents showed that he inherited one variant from each parent. His Co enzyme Q10 level was reduced 215.2 mcg/L (ref range (320-1376) and Leucocyte coenzyme Q10 level was severely low 30 pmol/mg protein (Ref range (66-183) confirming the defect affecting coenzyme Q10 metabolism.
CONCLUSIONS: Primary coenzyme Q10 deficiency is an autosomal recessive condition with clinical features that encompasses multisystem involvement, including neurologic and cardiac manifestations. Early diagnosis can limit disease progression. Advances in next generation sequencing technologies with panels have significantly enabled the discovery of genetic mutations.
KEYWORDS: Genetics, Neurometabolic Disorders, Rare Diseases

HEADACHE/MIGRAINE

315. Pediatric tension-type headaches: co-morbidity with emotional, behavioral and sleep disorders.

Nesterovskiy Yuriy (Moscow, Russian Federation) Zavadenko Nikolay, Shipilova Elena

OBJECTIVE: To assess in pediatric patients with frequent episodic or chronic tension-type headaches (TTH) the incidence of co-morbid emotional, behavioral and sleep disorders.
METHODS: 150 patients with TTH (75 male and 75 female) aged 8-16 years were asessed. The severity of emotional and behavioral problems was analyzed in comparison with their healthy peers (103 boys, 117 girls) by means of parents' interviewing with the «Strengths and Difficulties Questionnaire» (SDQ) [Goodman R., 2001]. For categorization of sleep disorders the Sleep Disturbance Scale for Children (SDSC) [Bruni O. et al., 2001] was used.
RESULTS: Total difficulties scores measured by SDQ were significantly higher in boys (16,2±0,7) and girls (14,3±0,7) with TTH compared with their peers (respectively 7,9±0,4 and 7,7±0,4, $p<0,001$). Clinical assessment revealed the following externalizing disorders in pediatric patients with TTH: ADHD (45,3% boys, 13,3% girls), oppositional defiant disorder – ODD (26,7% boys, 18,7% girls), co-occurrence of ADHD and ODD (17,3% boys, 10,7% girls). Regarding the internalizing disorders, most patients with TTH had anxiety disorders (68,0% boys, 77,3% girls) and some suffered dysthymic disorder (4,0% boys, 2,7% girls).
Many patients with TTH had clinically significant sleep problems, including disorders of initiating and maintaining sleep (36% boys, 37,3% girls), disorders of arousal/nightmares (20,0% boys, 20,0% girls), sleep wake transition disorders (53,3% boys, 28,0% girls), disorders of excessive somnolence (42,7% boys, 34,7% girls).
CONCLUSIONS: Pediatric TTH clinical manifestations may be dependent on the co-morbid emotional, behavioral and sleep disorders. These comorbid disorders must be considered for individualized treatment program including drug therapy and non-pharmacological approaches.
KEYWORDS: Headache/Migraine

316. Establishing a National Real-World Data Pediatric Migraine Registry: Proof of Principle

Gelfand Amy (Wilmington, DE, United States) Szperka Christina, Pezzuto Tara, Hammett Alex, Kessel Shirley, Benjamin Daniel, Cohen-Wolkowiez Michael, Hornik Christoph

OBJECTIVE: Evaluate the use of real world data collected in a prospective multi-site, pediatric migraine registry collecting real world data to support regulatory submissions and facilitate conduct of future clinical trials in children and adolescents with migraine.
METHODS: Those aged 4-17 years who met International Classification of Headache Disorders, 3rd edition for migraine were eligible. There were no restrictions with regards to frequency, severity, or aura status. Enrollment goal was *n*=200. The enrollment period ran from 12/2018 to 01/2020. Participants provided headache and clinical data for the initial visit and will

be followed for 4 additional follow-up visits in person and provide headache diary data via an app. Baseline characteristics and medications used at enrollment are reported here.
RESULTS: 19 of 20 sites activated and enrolled, for a total of 201 participants enrolled over 13 months. Median age of participants was 14 years (IQR 11-16), and two-thirds were female (134/197, 68%). Median headache days/month at enrollment was 13 (IQR 8-25). Preventives used prior to or during enrollment were recorded. Acute treatments were recorded from both pre-enrollment and during the enrollment period.
CONCLUSIONS: Acute and preventive treatment of migraine in children and adolescents is highly variable, highlighting the need for more trials to guide treatment selection. A pediatric migraine registry that collects real-world data is feasible to create and maintain. In addition to collecting data in a regulatory compliant manner, the registry creates a ready for use infrastructure for the conduct of future clinical trials in children and adolescents with migraine.
KEYWORDS: Headache/Migraine

317. Neuroimaging yield in pediatric headache
Serdaroglu Esra (Ankara, Turkey)

OBJECTIVE: Headache is the most common neurological symptom in childhood. Neuroimaging is recommended in case of critical signs. Red flag symptoms such as younger age (<4 years), progressive frequency and severity, occipital pain, and early-morning waking should prompt careful investigation.
METHODS: Children and adolescents presenting with headache to a pediatric neurology clinic during a 6-month period were analyzed.
RESULTS: A hundred patients aged between 3-17 years (mean: 12.5 years) were analysed. Male/female ratio was 49/51. Mean duration of headache was 15.7 months with a frequency of 2.8 headache per week. Mean number of pediatric neurology visits was 2.6 times. Accompanying complaints were vomiting (n=17), vertigo (n=13), visual aura (n=14), photophobia (n=55), phonophobia (n=61), and motion sickness (n=35). Family history of migraine was observed nearly half of the patients (n=45). All patients had normal neurological examination. Neuroimaging was performed in 58 patients (58%) for occipital pain (n=13), headache waking the patient up (n=21), increasing frequency of headache (n=17), and young age at presentation (n=3) and the remaining few were priorly ordered by pediatricians. Neuroimaging was normal in 42 patients (72%). Remaining images revealed nonspecific T2 hyperintense millimetric lesions in five (9%), sinus inflammation in ten (17%) and coincidental findings.
CONCLUSIONS: Neuroimaging for pediatric headache is not very informative even in the case of red flag symptoms with normal neurological examination.
KEYWORDS: Headache/Migraine, Neuroimaging

318. Pseudotumor Cerebri Syndrome: From Childhood to Adulthood Risk Factors and Clinical Presentation
Mahajnah Muhammad (Hadera, Israel) Genizi Jacob, Zahalka Hazar, Andreus Ronza, Zelnik Nathanel

OBJECTIVE: Although considered uncommon, pseudotumor cerebri syndrome (PTC) is a significant cause of headache among children and adults. However, the presenting symptoms

may be different among diverse age groups. In the present study, we compared the risk factors and clinical presentation of PTC across life-from childhood to adulthood
METHODS: A retrospective survey of PTC patients aged 7 years or older between 2011 and 2013 was carried out. Pooled analyses were performed comparing characteristics from our data with those of published data subdivided into 3 age groups: pre-young children, adolescents, and adults.
RESULTS: Our cohort consisted of 72 patients: 32 children (10 pre-young children, 22 adolescents) and 40 adults. Within the pre-young children age group: 20% were females versus 82% in the adolescent age group and 85% of the adult age group. Obesity was found in 10% of the young children group, 64% of the adolescents, and 80% of the adults. Headache was reported in 70% young children, 82% adolescents, and 83% adults. Pooled analysis of 1499 patients showed that young children with PTC tend to complain less about headache compared with older ones. Vomiting and visual impairment were most common among adolescents, and dizziness and tinnitus were most common in adults.
CONCLUSIONS: PTC has different risk factors and clinical presentation throughout life. In young children, there is no gender preference and most patients are not obese. Risk factors in adolescents resemble those of adults.
KEYWORDS: Headache/Migraine

319. Impact of an innovative telementoring program about pediatric headache and migraine for community medical providers
Foxen-Craft Emily (Ann Arbor, MI, United States) Joshi Sucheta, Leber Steven

OBJECTIVE: The prevalence of pediatric headache and migraine exceeds the capacity of tertiary care centers to provide timely evaluation and treatment. Project ECHO (Extension of Community Healthcare Outcomes) virtually connects primary care providers to centralized experts, providing training to improve care they can provide in their local communities. This study aimed to examine the efficacy of Project ECHO adapted, with the American Academy of Pediatrics, for pediatric headache.
METHODS: Providers were recruited from around the state of Michigan in three cohorts, from May 2018 to July 2019. The program involved eight 1-hour videoconference sessions of didactic presentation and case discussion. Topics included evaluation; pharmacological, neutraceutical, and behavioral treatment; school planning; sleep; concussion; and procedural management, presented by institutional faculty, co-facilitated by a pediatric neurologist and a pediatric pain psychologist. Participants completed pre- and post- surveys, self-rating perceived knowledge and confidence in evaluating and treating pediatric headache.
RESULTS: Participants (n = 34) attended on average 4.75 sessions. Most completed both pre-program and post-program self-ratings (n = 24). Changes in self-ratings were all positive, and all but one were statistically significant, with effect sizes ranging from .31 - .64, suggesting improvements in perceived knowledge and confidence in independently evaluating and treating pediatric headache.
CONCLUSIONS: Results from the first three cohorts support the efficacy and potential of the telementoring approach in improving local care for a population often referred to specialty clinics, improving access to efficient, high-quality care for children in pain. Future research may assess impact on wait times and referrals.

KEYWORDS: Headache/Migraine, Teaching of Child Neurology

320. Pediatric Trigeminal Neuralgia - Consider MPZ Mutations Causing CMT With Cranial Nerve Involvement

Otallah Scott (Winston Salem, NC, United States)

OBJECTIVE: This report is intended to raise awareness of an unusual cause of trigeminal neuralgia (TN) in pediatric patients and an association with CMT-1b due to MPZ mutations.
METHODS: A 16 year old patient with previously diagnosed TN presented to our clinic in 10/2017. Her symptoms had first been assessed at age 13. She had been previously diagnosed with Parry Romberg syndrome as the etiology of her TN. She had subtle mid-face atrophy on the left which is also where she experienced her trigeminal neuralgia pain. The diagnosis of TN was confirmed, however, on exam she was noted to be areflexic. This had not been noted on prior neurology evaluations. Notably mother was also areflexic and maternal grandfather had a history of CMT.
RESULTS: EMG/NCS was consistent with Charcot- Marie-Tooth (CMT) disease. On analysis of an extensive family tree this patient was found to be a distant relative of a recently re-reported family in Western North Carolina with a known G163R MPZ mutation causing CMT and a high rate of TN and/or facial hemi-spasm in adults[1]. Genetic testing confirmed that the patient in question carried this mutation.
CONCLUSIONS: When TN is diagnosed in a child a careful assessment for evidence of CMT and other secondary etiologies should be performed and genetic etiologies including this rare MPZ mutation should be considered. A recent series described at least 12 CMT families with a similar association between TN and CMT[2]. However, the case described here is the first presenting in a pediatric patient to the author's knowledge.
KEYWORDS: Headache/Migraine, Neuromuscular Disorders, Genetics

321. Correlation of pediatric headache-related functional disability inventory (FDI) and prolonged school absence

Candee Meghan (Salt Lake City, UT, United States) Ruth Corrine, Kerr Lynne, Caplin Deirdre

OBJECTIVE: Headaches are common in the pediatric population and account for significant disability, resulting in school absence and impaired school performance. The Functional Disability Inventory (FDI) measures the degree to which children experience difficulty in physical/psychosocial functioning due to their health status. Respondents rate their perception of difficulty completing a variety of everyday activities over the previous 3 months. FDI has previously been shown to predict longer emergency stays, increased medication use, and increased admission rates in children with headache. We hypothesize that patients with higher FDI scores (measured by parent proxy) will have missed more school.
METHODS: Analysis of 264 consecutive new patient intake forms completed by parents of children (ranging from 5 to 18 years of age) seen in the University of Utah interdisciplinary Pediatric Headache Clinic between December 2017 and July 2018.
RESULTS: Higher FDI scores were significantly correlated with more missed days of school in the last three months (r = .04). There was a significant interaction effect for increasing age and female gender.

CONCLUSIONS: Measurement of FDI in pediatric headache clinic may allow for enhanced allocation of time and resources (e.g. psychology, nursing, social work, return to school plans, etc.) during a patient's initial headache clinic visit. It may also highlight factors impacting difficulty in returning to school or other routine activities. This study was limited by parental difficulty completing forms (due to time constraints, recall bias, text (rather than numerical) responses and variation in response rate/clarity based on the time of year.
KEYWORDS: Headache/Migraine

322. Brain MRI White Matter Hyperintensities in Cyclical Vomiting Syndrome with or without Migraine
Weaver Samantha (Birmingham, AL, United States) Al Robaidi Kahled, Singh Sumit, Rashid Salman

OBJECTIVE: Cyclic vomiting syndrome (CVS) has been linked to headaches with or without history of migraine. To our knowledge, brain magnetic resonance imaging (bMRI) findings of patients with CVS have not been previously compared to those of patients with migraines/headaches alone.
METHODS: We searched all outpatient pediatric records with a diagnosis code for CVS (January 2008 to October 2018). We excluded all patients who did not have reviewable bMRI or had confounding neurosurgical issues. A designated pediatric neuroradiologist interpreted all the bMRI studies. We compared our results to an age matched control sample (1 CVS patient: >2 control patients). Control group patients had bMRIs obtained for headaches/migraine.
RESULTS: A total of 183 patients were given a diagnosis of CVS during the above time period. Only 31 of these patients received a bMRI. Our final sample included 24 CVS patients (Ages 0-18) with 33 bMRIs on record. Migraine-like white matter hyperintensities (MWMH) were found in 13% patients. Cerebellar ectopia (lower edge of the cerebellum >1 mm below foramen magnum) was found in 38% patients. Our control group included 57 patients (Ages 0-18) with 60 bMRIs on record. MWMH were found in 10% patients while cerebellar ectopia was found in 28% patients.
CONCLUSIONS: Less than 20% patients with CVS underwent bMRI. In our small sample size, we noted that the incidence of MWMH in patients with CVS was similar to the age matched control group. This may mean that the CVS and migraine/headaches possibly share their underlying pathophysiologic mechanisms.
KEYWORDS: Headache/Migraine, Neuroimaging

323. Increasing Parent Education of Outpatient Migraine Treatments with Pediatric Migraine Action Plan
Brown Yvette (Phoenix, AZ, United States) Little Robert, Gogia Rastogi Reena, Olenski Klari

OBJECTIVE: In this study we ask the question, does a home-based treatment algorithm discussed in an initial outpatient neurology consultation improve caregiver awareness of treatment options? We hypothesize that receiving a pediatric migraine action plan will have a statistically significant increase in caregiver headache self-efficacy scores compared to caregivers that did not receive the pediatric migraine action plan.
METHODS: During odd weeks of the study, the provider will review a pediatric migraine action plan, adapted from American Headache Society adult and pediatric guidelines, with the

patient and caregiver during the initial headache consultation. Whereas during even weeks of the study, patients and caregivers will be given patient education material without the migraine action plan. A standardized survey based on the validated acute medication self-efficacy for headache will be given to recruited caregivers after the appointment, in the absence of the provider, in the consultation room prior to departure. The caregiver will answer an 11-question survey based on their comfort of decision-making processes for acute headache medication adherence for their child.
RESULTS: Data collection is ongoing. Preliminary data not yet available.
CONCLUSIONS: In an effort to maximize outpatient management of migraine, our goal is to increase parent awareness of home-based treatments in hopes of decreasing emergency department visits and thereby decreasing the number of inpatient admissions for migraine in the pediatric population. We hope to achieve this goal by incorporating a standardized pediatric migraine action plan during initial headache consultations in an ambulatory pediatric neurology clinic.
KEYWORDS: Headache/Migraine

324. Cost effectiveness and outcome of a pediatric headache infusion center
Maag Logan (Dayton, OH, United States) Payne Asia, MacDonald Sarah, Kumar Gogi

OBJECTIVE: We opened a Headache Infusion Center (HIC) in June 2017 with the goal of reducing emergency room (ER) visits and admissions.
METHODS: Data was collected prospectively on medications used, efficacy of medications, admission rate, recurrence of headache within 2 weeks leading to a ER visit or inpatient admission. We collected information on demographics, medications, duration of diagnosis and billing information. Patients received the first pathway consisting of an intravenous fluid bolus, ketorolac, prochlorperazine and diphenhydramine. If no relief, the second pathway of a dose of intravenous valproate sodium was administered after which they were admitted if the headache persisted.
RESULTS: 297 patients were seen from June 7, 2017 – June 30, 2019. 89% were Caucasian and 78% were female with a mean age 15 years. 39% patients needed the second pathway.7% patients needed to be admitted. 8.4% patients visited ER within 2 weeks of HIC visit while 6.7% were admitted within 2 weeks of HIC visit. 46% patients were on one preventative medication while 48% were on more than 1. Two most frequently used medications were amitriptyline and topiramate. The bill to a private payor was 3727 dollars for an ER visit and 1842 for HIC visit. The payment by the private payer for the ER visit was 50% more than for the HIC.
CONCLUSIONS: A pediatric headache infusion center is a cost effective way of decreasing ER visits and should be established as a standard of care for patients suffering from headaches
KEYWORDS: Headache/Migraine, Neuroscience

325. Childhood Adversity and Headache in Adolescents
Anto Marissa (Philadelphia, PA, United States) Szperka Christina

OBJECTIVE: The relationship between exposure to adverse childhood experiences (ACEs) and headache has been well characterized in the adult population. Childhood adversity and its effect on headache has not been investigated as robustly in children. This study examines the relationship of ACEs to frequent headache in a large cohort of adolescents.

METHODS: The National Longitudinal Study of Adolescent to Adult (Add) Health followed a nationally representative sample of adolescents from 1994 to 2018 assessing health and social issues. We used publicly available data from Wave I of Add Health (N=6,504) to examine a variety of ACE exposures and their potential relationship to frequent headache. Logistic regression was used analyze the relationship between cumulative ACE score and frequent headache while controlling for age, sex, race, food insecurity, and housing insecurity.
RESULTS: Frequent headache was reported in 29.3% of respondents, 45% of respondents reported one or more ACE exposures. For each increase in cumulative ACE score, odds of frequent headache increased by 1.2 (odds ratio 1.2, 95% confidence interval 1.15-1.3). The ACEs that showed strongest association with headache frequency were lack of maternal and paternal warmth, family member suicide attempt, experiencing community violence, and living in an unsafe neighborhood.
CONCLUSIONS: A variety of ACE exposures was associated with frequent headache in adolescents. An increase in cumulative ACE exposure increased odds of having frequent headache. Further investigation should be performed in children to both clarify the relationship between childhood adversity and headache and to inform our understanding of pathophysiology and potential treatments.
KEYWORDS: Headache/Migraine

326. The efficacy and safety of remote electrical neuromodulation for the acute treatment of migraine in adolescents with migraine
Hershey Andrew (Cincinnati, OH, United States) Lin Tamar, Gruper Yaron, Berenson Frank

OBJECTIVE: Remote electrical neuromodulation (REN) is a novel acute treatment of migraine. The REN device (Nerivio™, Theranica Bio-Electronics LTD., Israel) is FDA-authorized for acute treatment of migraine in adults. The current study assessed the efficacy and safety of REN in adolescents with migraine.
METHODS: This was an open-label, single-arm, multi-center study in adolescents (ages 12-17 years) with migraine. Participants underwent a 4-weekrun-in phase during which the headaches were treated according to usual care and recorded in an electronic migraine diary. Eligible participants continued to an 8-week treatment phase in which they were asked to treat their headaches with the device. Pain severity levels, associated symptoms and functional disability were recorded at treatment initiation, 2- and 24-hours post-treatment.
RESULTS: Sixty participants were enrolled, of these 14 failed to meet the run-in criteria, 1 was lost to follow-up, and 3 are still in the run-in phase. 35 participants completed a test treatment with REN. Pain relief and pain-free at 2 hours were achieved by 71.4% (25/35) and 34.3% (12/35) participants, respectively. Pain relief and pan-free responses were sustained at 24 hours in 89.5% (17/19) of participants and 88.9% (8/9) of participants, respectively. Nausea, photophobia, and phonophobia disappeared at 2 hours in 50.0% (10/20), 41.4% (12/29), and 40.0% (10/25) of participants, respectively. 65.5% (19/29) participants experienced improvement in functional ability at 2 hours. No device-related adverse events were reported.
CONCLUSIONS: REN provides clinically meaningful relief of migraine pain and associated symptoms, offering a safe and effective non-pharmacological alternative for acute treatment in adolescents.
KEYWORDS: Headache/Migraine

327. INCREASE IN THE COST OF MIGRAINE HEADACHE TREATMENT IN PEDIATRIC HOSPITALS

Santiago Jason (Phoenix, AZ, United States) Gage Sandra, Mirea Lucia, Kafle Maheshwor

OBJECTIVE: The objectives of this study were to describe national trends in admission rates, length of stay (LOS), and total costs associated with hospitalization for pediatric patients with migraine headache at Major Children's Hospitals across the United States and to compare the rate of change in cost with national trends in healthcare expenditures.
METHODS: Patients admitted to 40 tertiary care Children's Hospitals were identified using Pediatric Health Information System (PHIS) database. Patients aged 1-18 with ICD 9 and 10 codes for migraine headache as the principal diagnosis hospitalized between 2010 and 2018 were selected for review. Institutional IRB approved this study. PHIS approved data sharing. Data was analyzed using SAS/STAT® software.
RESULTS: Study subjects included 19,093 inpatients with mean age of 14.1 years. The majority were female (16030; 72%). Most of the patients identified as white race (78%) and non-Hispanic (85%) ethnicity. Absolute number of hospitalizations for migraine headache increased from 1,700 in 2010 to 2,800 in 2017 ($p = 0.003$). The cost of hospitalization increased from $5,113 in 2010 to $10,822 in 2017 ($p < 0.001$). The average LOS over the study period was 2.2 days (range 2.07-2.35 days; $p = 0.15$).
CONCLUSIONS: While LOS for migraine headache has not significantly changed over the past decade, the rate of increase in cost of hospitalization has greatly exceeded the rate of increase in overall healthcare costs based on data from the Center for Medicare and Medicaid services. Further studies are needed to ascertain potential causes for this disproportionate increase.
KEYWORDS: Headache/Migraine

328. Microglial marker molecule CX3CR1 Polymorphisms in Pediatric Migraine Patients.

Saygi Semra (Adana, Turkey) Baysan Pinar, Yalcin Yaprak, Kubat Gozde

OBJECTIVE: The pathogenesis of migraine is still unclear, but relevant data suggest the impact of neurogenic inflammation on pain generation. In the literature, many studies show that cytokines play an important role in the process of neurogenic inflammation. Fractalkine is small, proinflammatory cytokines almost exclusively expressed in the brain, where it plays an important role in neuroinflammation. CX3CR1 is the spesific receptor for fractalkine. Genetic polymorphisms of CX3CR1 may significantly modify the biological roles of fractalkine. Therefore, we investigate the possible association between V249I and T280M variants of CX3CR1 genotype and pediatric migraine patients.
METHODS: This study included 58 consecutive children and adolescents in whom migraine was diagnosed and 90 healthy children and adolescents. The isolated genomic DNA was used as a template for CX3CR1 (V249I and T280M) genotyping. Differences in the frequencies were estimated by the chi-square test.
RESULTS: There was no significant difference in genotype distributions of V249I and T280M polymorphisms of the CX3CR1 gene between patients and controls.
CONCLUSIONS: Our study does not support any significant association between the CX3CR1 polymorphism and migraine in the pediatric age group. Further studies related to this subject are needed, along with a search for new therapeutic agents with anti-inflammatory properties.
KEYWORDS: Headache/Migraine, Genetics

329. Utility of "Migraine Cocktail" in the Pediatric Emergency Department
Ghosh Ankita (Houston, TX, United States) Gourishankar Anand, Flemmons Karly, Mehta Malvi

OBJECTIVE: Assess the utilization of "migraine cocktail" in acute headache management at a tertiary level emergency department (ED).
METHODS: We did retrospective chart review of patients seeking acute headache treatment in ED from July 2017- 2019. Inclusion criteria was acute primary headache patients from age 5-18 years. Patients with secondary causes of headache were excluded. Primary outcome was reduction in headache pain score within 4 hours of treatment. Secondary outcome measures included length of ED stay, hospital admission rate, and ED readmission within 48 hours.
RESULTS: Among 47 patients, 60% of them had a diagnosis of migraine. Mean age was 12.7 years (SD 3), and 70% were female. Mean ED length of stay was 4.6 hours (SD 1.97, $p<0.05$). Nineteen percent of patients were hospitalized. Most commonly used combination treatment was Benadryl, Metoclopramide and Ketorolac (23%). Metoclopramide was substituted with Prochlorperazine based on physician preference. Fluid bolus was given to 74% of patients, among which 77% were discharged home from ED. Mean pre-treatment pain score was 7.6 (SD 1.6) and post-treatment pain score was 3 (SD 2.4). Mean difference between the two scores was 4.5 (CI, 3.9-5.2), $p<0.05$. Pain score improvement is associated with ED discharge (Odds ratio 0.25). Age, gender, type of cocktail class, headache duration before ED visit did not affect the discharge from ED
CONCLUSIONS: Two third patients were discharged with diagnosis of migraine. Migraine cocktail is effective in reducing pain score and hospital admission rates. Pain improvement predicts ED discharge.
KEYWORDS: Headache/Migraine

330. Pediatric Trigeminal Neuralgia Treatment: A Case Series
Iser Courtney (Oklahoma City, OK, United States) Parker Amy, Chrusciel Deepti

OBJECTIVE: Describe three pediatric patients with trigeminal neuralgia (TN) and their treatment course.
METHODS: We performed a retrospective chart review and found three patients under the age of 18 years with a diagnosis of TN. We described age of onset, initial symptoms, initial imaging, follow up imaging, pharmacotherapy, and surgical interventions.
RESULTS: In this case series of three patients with a clinical diagnosis of pediatric trigeminal neuralgia (TN), the most common clinical presentation was facial pain accompanied by decreased oral intake. All three cases were initially evaluated with MR brain imaging, and were unremarkable. They were treated with medical management consisting of various pharmacotherapy regimens. Two cases had periods of symptom freedom with medical therapy, but both experienced frequent exacerbations and eventual unresponsiveness, prompting titration or switching of therapy. Given the refractory nature of the three cases, brain MRI was repeated and two cases were concerning for neurovascular conflict. Two of the three cases underwent microvascular decompression (despite a normal MRI in one of the cases) with resolution of symptoms allowing for weaning of all TN medications.
CONCLUSIONS: Based on our literature review and the results of this case series, we recommend early referral to neurosurgery even if initial MRI is normal. Medical management is

typically unsuccessful, and microvascular decompression in our patients and in other case series was a definitive treatment.
KEYWORDS: Headache/Migraine

331. Relationship of Opening Pressure and Sonographic Markers of Increased Intracranial Pressure in Pediatric Papilledema
Larsh Travis (Cleveland, OH, United States) Hsich Gary

OBJECTIVE: B-scan ultrasonography is often used to help differentiate true papilledema due to increased intracranial pressure (ICP) versus "pseudo-papilledema". No previous report has assessed the relationship between ultrasonographic findings suggestive of increased ICP and lumbar puncture (LP) opening pressure (OP) in the pediatric population. We aimed to assess this relationship.
METHODS: We retrospectively reviewed charts of pediatric patients who presented between January 2012 and August 2019 with suspected papilledema. We collected demographic information, imaging findings, LP OP, and b-scan findings, which included the 30-degree test and crescent sign.
RESULTS: 172 patients with suspected papilledema were identified. 30-degree test: 28 patients had both a documented OP and 30 degree test. 6 patients had a negative 30 degree test; among these patients, the average OP was 21cmH_2O and no patients had an OP greater than 25 cmH_2O. Twenty-two patients had a positive 30 degree test; average OP was 24.4cmH_2O (p=0.22), greater than 25cmH_2O in 7 patients, between 20 to 25cmH_2O in 11, and less than 20cmH_2O in 4. Crescent sign test: Twenty-three patients had both a documented OP and a crescent sign test. Ten patients had a negative crescent sign; average OP was 19.7cmH_2O. One of these patients had an OP greater than 25cmH_2O (26cmH_2O). Thirteen patients had a positive crescent sign; average OP was 22.3cmH_2O (p=0.26), greater than 25cmH_2O in 3 patients, between 20 to 25cmH_2O in 6, and less than 20cmH_2O in 4.
CONCLUSIONS: Sonographic markers of increased ICP appear to be sensitive, but less specific, in the evaluation of borderline pediatric papilledema.
KEYWORDS: Headache/Migraine, Neuroimaging

HISTORY OF CHILD NEUROLOGY

332. PROFESSIONAL AND DEMOGRAPHIC PROFILE OF US NATIVE SPANISH-SPEAKING CHILD NEUROLOGISTS IN THE CHILD NEUROLOGY SOCIETY
Torres Alcy (Boston, MA, United States) Mohanty Mugdha, Salvador Carla, Chavez Wilson, Mora Mauricio, Kuban Karl

OBJECTIVE: To ascertain the prevalence of culturally native Spanish-speaking US child neurologists in the Child Neurology Society (CNS).
METHODS: Prevalence statistics regarding demographic and work profile were applied to data obtained from a cross-sectional electronic survey of CNS members.
RESULTS: With the exception of ethnicity, demographics of the 135 respondents were comparable to a previous CNS survey (Table 1). 53% were male and 24% were over age 60.

Approximately a quarter was represented each from East, South, Midwest, and Western US. 42% self-identified as Spanish, Hispanic, or Latino. 62% spoke English as their primary language, and 39% spoke Spanish as their primary language. Two-thirds graduated from a US medical school, 51% practice general neurology, and epilepsy was the most common subspecialty (18%). Two-thirds of respondents practice at a major teaching hospital, and 93% hold university academic appointments. 79% are AAN members. 76% did not have medical student debt at the time of the survey. 47% earn more than $200,000 while 12% earn more than $300,000. 29% report signs consistent with burnout. 87% would choose Child Neurology again and 96% would recommend child neurology to a medical student.
CONCLUSIONS: Although 40% self-identified as Hispanic, Latino, or Spanish and spoke Spanish as the primary language, these individuals were more likely to partake in the survey. Enhancing the ability of child neurologists to provide optimal care to the primary Spanish-speaking population, calls for further ascertainment of the number of clinicians in the CNS of both Hispanic native and non-Hispanic fluent Spanish speakers.
KEYWORDS: History of Child Neurology

333. Expansion of Pediatric Neurology Service to New Frontiers via Teleneurology and Outreach Clinics; a Pilot Project Proposal
Hlaing Chaw (Yangon, Myanmar) Aye Aye Mya Min, Ko Khine Mi Mi, Saan Aye Mu, Aung Hnin Wint Wint, Linn Kyaw, Mar Soe

OBJECTIVE: To create a model to serve children with epilepsy and other chronic neurological problems in Shan state
METHODS: Pediatric neurology as a subspecialty, started in Yangon, Myanmar in 2011, with one child neurologist, expanding presently to seven; serving a country of 55 million. Because of systemic infrastructure problems and poverty, we started mobile clinics to 3 surrounding states 3 years ago, covering a 100-mile, radius, and we are planning to expand to Shan state, the largest state in Myanmar with 5.8 million people. With our limited mobile capacity, we are still unable to serve their need for pediatric neurology service.
A pilot project will be launched to establish teleneurology service for Taungyi, the largest city in Shan state. We will partner with general pediatricians in Taungyi. The pediatric neurology service at Yangon Children's Hospital will provide monthly: 3 hours web cam internet based neurological care live consult, serving approximately 30 patients; Additionally, 2 child neurologists will travel to the local clinic in Taungyi for full one-day clinics every 4 months, providing specialized clinical care education for local general pediatricians for seizure management, fostering local sustainability.
RESULTS: We expect to improve neurological care of children in Shan State, reducing the burden of travel, as well as enhancing the skill and knowledge of local pediatricians.
CONCLUSIONS: This will be the first model for implementation of systemic teleneurology service in Myanmar and it will benefit both the acute and chronic need for expanded pediatric neurology service in Myanmar.
KEYWORDS: History of Child Neurology, Teaching of Child Neurology

INFECTIONS/NEUROIMMUNOLOGY

334. EEG and MRI findings in pediatric patients with GAD65 encephalitis and epilepsy: A case series

Tran Linh (Durham, NC, United States) Stingl Cory, Van Mater Heather, Pizoli Carolyn

OBJECTIVE: To describe electroencephalograms (EEG), seizure patterns, and magnetic resonance imaging (MRI) findings in pediatric patients diagnosed with drug-resistant GAD65-related epilepsy and to assess seizure response to immunomodulation.
METHODS: Retrospective chart review was performed on children and adolescents less than 21 years of age diagnosed with GAD65 encephalitis and epilepsy in the Duke Autoimmune Brain Disease Clinic between January 2010 and January 2018. Diagnosis of GAD65 encephalitis was based on elevated serum GAD65 antibody (>20 nmol/L) with positive GAD65 antibody in cerebral spinal fluid (CSF). Descriptive tables were used to describe demographics, EEG and MRI findings, number of anti-seizure medications, and if improvement was seen following immunomodulation.
RESULTS: Out of the eleven patients with suspected diagnosis of GAD65 encephalitis, six patients were identified to have drug-resistant epilepsy. Within this subgroup, all patients had abnormal EEG and MRI findings. Each had discharges originating from the left or right temporal regions. Five out of six had captured seizures originating from the temporal region. One patient had a probable captured seizure from the right centrotemporal region but lateralization was unclear. MRI findings consisted of T2 and/or FLAIR hyperintensity within the temporal lobe (3/6), hippocampal atrophy (3/6), and diffuse atrophy (1/6). All patients received immunomodulation with improvement in seizure frequency.
CONCLUSIONS: Our patients with GAD65-resistant epilepsy had predominantly temporal lobe seizures in addition to MRI changes affecting temporal lobe. GAD65 encephalitis should strongly be considered in pediatric patients presenting with cognitive changes and acute onset of refractory temporal lobe seizures. Immunotherapy may provide improvement in seizure control.
KEYWORDS: Infections/Neuroimmunology, Epilepsy, Neuroimaging

335. Evaluation of Zika-exposed Pregnant Women, Fetuses and Infants In a US Congenital Zika Program

Mulkey Sarah (Washington, DC, United States) Ansusinha Emily, Cristante Caitlin, Russo Stephanie, Biddle Cara, Kousa Youssef, Pesacreta Lindsay, Vezina Gilbert, Bulas Dorothy, Wessel David, du Plessis Adre, Debiasi Roberta

OBJECTIVE: To describe a United States (US) Congenital Zika Program's evaluation of Zika-exposed pregnant women/fetuses and infants.
METHODS: All pregnant women/fetuses and/or infants referred for clinical evaluation to the Congenital Zika Program at Children's National (Washington, DC) from January 2016 to June 2018 were included. We recorded the timing of maternal Zika-virus (ZIKV) exposure and ZIKV laboratory testing results. Based on laboratory testing the cases were confirmed, possible, or unlikely ZIKV infection. Prenatal and postnatal imaging findings by ultrasound and/or MRI were categorized as normal, nonspecific (e.g. germinolytic cysts, lenticulostriate vasculopathy), or as congenital Zika syndrome (CZS).
RESULTS: Of 81 women-fetus/infant pairs evaluated, 72 (89%) had confirmed ZIKV exposure. 62% were continental US residents with travel-related ZIKV exposure, 38% had exposure prior to emigration. 18% were symptomatic, only a minority presented for evaluation within time

limits for laboratory detection. ZIKV could only be confirmed in 30 (42%) cases, was possible in 26 (36%) cases, and could be confidently excluded in 16 (22%) cases. Five cases (7%) had prenatal US and MRI findings of CZS. Postnatal cranial US had non-specific findings in 8 of 17 cases (47%) and brain MRI found non-specific abnormalities in 8 of 14 cases (57%).
CONCLUSIONS: Due to variation in timing of exposure to presentation, ZIKV infection was unable to be excluded in the majority of cases. Neuroimaging found CZS in 7% and in many there were non-specific changes that warrant long-term follow-up. These challenges are instructive to future infectious/non-infectious threats to pregnant women and their infants.
KEYWORDS: Infections/Neuroimmunology, Neuroimaging, Neonatal & Fetal Neurology

336. Acute Necrotizing Encephalopathy of Childhood: A single center experience from South India

Yoganathan Sangeetha (Vellore, India) Bharathi Narmadham, Mallik Prateek, Thomas Maya, Muthusamy Karthik, Jacob Ebor

OBJECTIVE: Acute necrotizing encephalopathy of childhood (ANEC) is a rare entity with specific clinical and radiological features. The objectives of this study are to describe the clinical profile and assess the outcome of children and adolescents with ANEC.
METHODS: The clinical profile, laboratory parameters, radiological findings and outcome of children and adolescents, aged 6 months to 18 years, with a diagnosis of ANEC from January 2015 to December 2019 were collected from database of our hospital.
RESULTS: Among 24 patients included for analysis, the female: male ratio was 1.2:1. The mean age at presentation was 66.9±50.6 months. All patients had prodromal illness followed by altered sensorium and seizures. Multiorgan dysfunction, thrombocytopenia, elevated liver enzymes were identified in 60-70% cases. CSF pleocytosis and elevated protein were detected in 6 out of 15 patients. Among 21 patients, dengue serology was positive in 8 and PCR for influenza virus was positive in 13 patients. Bihemispherical slow waves were the commonest EEG finding. Near symmetrical signal changes involving thalami, putamen, brainstem, cerebellum, internal capsule, and white matter were detected on brain MRI. RANBP2 mutation was identified in 2 cases. Our patients were managed with supportive measures, anticonvulsants, oseltamivir, methylprednisolone or dexamethasone and/or immunoglobulin therapy. The mean follow-up duration was 14.7±20.4 months. The mean Glasgow outcome score for children at follow-up with influenza-associated ANEC was lower than in children with dengue-related ANEC.
CONCLUSIONS: Influenza and dengue virus infection were identified as common triggers for ANEC in our cohort. The long-term neurological outcome might be variable in ANEC patients.
KEYWORDS: Infections/Neuroimmunology, Rare Diseases

337. Rising Trend of Subacute Sclerosing Panencephalitis in Children below 5 years of Age: A Six Years Experience in Bangladesh

Chowdhury Yamin (Dhaka, Bangladesh) Alam Sarah, Hoque Sheikh, Islam Ariful, Yusuf Abdullah, Chowdhury Rajib, Hossain Mohammad, Haque Nazmul, Saha Narayan

OBJECTIVE: To see the trend of subacute sclerosing panencephalitis (SSPE) below 5 years of age children with or without previous history of measles vaccination.

METHODS: This descriptive cross-sectional study was conducted in the Department of Paediatric Neurology, National Institute of Neurosciences & Hospital, Dhaka, Bangladesh from January 2014 to December 2019 for a period of six (6) years. All the children with the age of 12 years presented with SSPE were selected as study population. The details of clinical characteristics were recorded among the less than 5 years of age group children.
RESULTS: A total number of 42 cases of SSPE children were recruited for this study of which 8(19.1%) cases were below 5 years of age. Interestingly, these 8 cases were found only in last 2 years (2 in 2018 and 6 in 2019 respectively). The mean age (±SD) was 47.0(±7.58) months. The mean age of occurrence of measles was 16.0(±7.09) months. The latent period of SSPE development was 29.75±10.63 months. The mean(±SD) age of onset of SSPE were44.14(±6.64) months. History of measles was found in 7(87.5%) cases among whom only 1 had no H/O measles vaccination. All (100.0%) cases were confirmed by EEG and Anti-Measles IgG antibodyin CSF. Furthermore, all (100.0%)c ases were presented with cognition and speech difficulties with myoclonic jerks.
CONCLUSIONS: In conclusion there is a rising trend of SSPE among children with less than 5 years of age even in previously vaccinated cases.
KEYWORDS: Infections/Neuroimmunology, Rare Diseases

338. Autoimmunity in 1st and 2nd Degree Relatives of Children with Opsoclonus-Myoclonus Syndrome
Santoro Jonathan (Los Angeles, CA, United States) Kerr Lauren, Kong Sek Won, Mandl Kenneth, Gorman Mark

OBJECTIVE: Opsoclonus-myoclonus syndrome (OMS) is a rare autoimmune disorder in children. Only one study has previously assessed familial autoimmunity and this was in a small, homogenous, European cohort which noted a rate of autoimmune disease of 15.8% in first degree relatives. These findings have not been replicated in other, more diverse OMS populations. This study sought to investigate the prevalence of autoimmune disease in pediatric patients with OMS and their first and second-degree relatives and to compare the rates in those with and without a paraneoplastic cause.
METHODS: A single center cohort study of consecutively evaluated children with OMS was performed. Parents of patients were administered surveys on familial autoimmunity. The Fisher's exact test and parametric and non-parametric t-test were used to compare groups.
RESULTS: Thirty-five patients (18 paraneoplastic, median onset 19.0 months; 17 idiopathic, median onset 25.0 months) and 68 first-degree relatives (median age 41.9 years) were enrolled. One patient developed systemic lupus erythematosus 7 years after OMS onset. Among 68 first-degree relatives, 18 (26%) had autoimmune disease. Paraneoplastic OMS was associated with a 38% rate of autoimmunity in a first-degree relative compared with 29% in idiopathic OMS (p=0.49). Amongst second-degree relatives, 33 had autoimmune disease, with thyroid and rheumatologic conditions being the most commonly reported.
CONCLUSIONS: In a cohort of pediatric patients with OMS, there were elevated rates of first- and second-degree autoimmune disease with no difference in rates observed between paraneoplastic and idiopathic etiologies, suggesting a genetic autoimmunity contribution to the development of OMS in children.
KEYWORDS: Infections/Neuroimmunology, Rare Diseases, Movement Disorders (including Cerebral Palsy)

339. Clinical, laboratory, radiological features and outcome of autoimmune encephalitis in children and adolescents: A descriptive study

Thomas Maya (Vellore, India) Malhotra Mukul, Jain Shikha, Yoganathan Sangeetha, Muthusamy Karthik

OBJECTIVE: To describe the clinical profile and outcome of autoimmune encephalitis in children and adolescents.
METHODS: Details of children and adolescents with definite, probable and seronegative autoimmune encephalitis from July 2010 to July 2018 were obtained from the hospital electronic data base.
RESULTS: A total of 59 children with a female to male ratio of 1.18 fulfilled the criteria for entry into this 8 year retrospective study. Mean age at presentation was 77.87 ± 54.23 months. Antecedent fever prior to onset of neurological symptoms was observed in 71% (42/59). Neurological manifestations included neuropsychiatric symptoms in 84% (50/59), seizures in 81% (58/59), sleep disturbances in 95% (56/59), movement disorder in 66% (39/59) and dysautonomia in 15% (9/59). Antibodies detected were Anti N-methyl-D-aspartate receptor antibodies 57% (34/59), antibasal ganglia antibodies in 2 children, anti-VGKC, anti-Tr (DNER), anti-CASPR 2 and anti-Hu antibodies in one child each. Rest 43% (25/59) were seronegative. Neuroimaging was normal in 49% (29/59) children while 22% (13/59) had diffuse cerebral atrophy. Electroencephalogram was normal in 42% (25/59) children. First line treatment modalities included IVIG and pulse methylprednisolone in all children and all were on continued immunomodulation with either mycophenolate or rituximab. Three children (5%) succumbed to the illness, 6 (10%) were lost to follow up and the rest 85 % (50/59) survived with minor sequelae.
CONCLUSIONS: Autoimmune encephalitis is a new entity in the ocean of etiologies for encephalitis. Clinical, laboratory and radiological characteristics and treatment modalities instituted in this study can guide early identification and treatment.
KEYWORDS: Infections/Neuroimmunology

340. Anti-glycine receptor antibody associated progressive encephalomyelitis with rigidity and myoclonus (PERM) revealing a variant in the autoimmune regulator (AIRE) gene in a four month old

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OBJECTIVE: Report anti-glycine receptor (GlyR) antibody associated PERM revealing a variant in *AIRE*
METHODS: Case report
RESULTS: A healthy four-month-old girl developed rapidly progressive, new onset, whole body stiffness and increased startle requiring benzodiazepine drip and intubation, consistent with PERM, a variant of stiff person syndrome (SPS). Given the very young age, genetic and autoimmune causes were simultaneously pursued. While awaiting test results, the patient was treated with 2g/kg IVIg and high dose intravenous methylprednisolone and 8 week steroid taper with gradual improvement allowing for benzodiazepine weaning. Anti-GlyR antibodies were positive in serum and negative in CSF. Serum anti-GAD 65 antibody was 204.4 IU/mL (normal

0-5). Whole exome sequencing revealed homozygous missense variants (predicted deleterious by in silico analyses); c.1370G>A (p.C457Y), in *AIRE*, the gene associated with autoimmune polyglandular syndrome type 1 (APS1). She had no primary endocrinopathies, candidiasis, or ectodermal dystrophy. At age 13 months, development and exam were normal on IVIg every 3 weeks and off oral benzodiazepines and baclofen.
CONCLUSIONS: This is the youngest reported case of autoimmune SPS/PERM with anti-GlyR antibodies. There is one published case of anti-GAD limbic encephalitis with an *AIRE* variant but no reports of *AIRE* variants with anti-GlyR antibodies. Anti-GlyR antibodies cause a subset of SPS/PERM, targeting the same glycine-gated chloride ion channel mutated in hereditary hyperekplexia, which causes symptoms from birth. New onset stiffness and increased startle beyond this time frame warrants autoantibody testing. Very early onset autoimmune disease should also prompt workup for genetic causes of autoimmunity including *AIRE* variants.
KEYWORDS: Infections/Neuroimmunology, Genetics

341. Presence of P/Q voltage-gated calcium channel (VGCC) antibodies in pediatric autoimmune encephalitis
Fisher Kristen (Houston, TX, United States) Shukla Nikita

OBJECTIVE: P/Q and N-type VGCC antibodies have been implicated in autoimmune neurological disorders, and are commonly paraneoplastic. In pediatrics, the clinical presentation is less clear. We present two pediatric patients who presented to Texas Children's Hospital with varying neurologic symptoms and ultimately diagnosed with VGCC antibody-mediated autoimmune encephalitis.
METHODS: A retrospective chart review was performed with collection of demographic and clinical data.
RESULTS: A 12 year old male presented with neurologic exam consistent with cerebellar ataxia, dysmetria, slowed speech, and behavior change. The second, a 14 year old male with neurologic exam consistent with myelitis, with weakness, hyperreflexia, and sensory level. Both patients underwent MRI, one demonstrating mild smooth enhancement of the cauda equina. Laboratory evaluation for both patients included lumbar puncture, one with elevated WBC (7) and elevated protein (55). Both with oligoclonal bands present. On paraneoplastic panel, both were found to have elevated P/Q-type VGCC antibodies, and diagnosed with VGCC antibody-mediated autoimmune encephalitis. Clinical work up additionally included metabolic studies which were unremarkable. Patient 2 was also found to have N-type VGCC antibodies, but at low levels and felt to be non-contributory. Both patients received immunotherapy (IVMP and IVIG) with improvement, but continued to have deficits. Both patients underwent oncologic screening, which was unrevealing.
CONCLUSIONS: Pediatric patients with VGCC antibodies can present with an array of neurologic symptoms, including cerebellar ataxia, myelitis, and cognitive changes. In the pediatric population, there appears to be less correlation with oncologic disease. Patients show improvements with immune therapy, but with residual deficits in follow up.
KEYWORDS: Infections/Neuroimmunology

342. A role for NLPR3 inflammasome in demyelinating lesions in cerebral adrenoleukodystrophy

Srivastava Isha (Palo Alto, CA, United States) Aguirre Alejandro, Cayrol Romain, Lund Troy, Vogel Hannes, Van Haren Keith

OBJECTIVE: X-linked adrenoleukodystrophy (ALD) is a neurometabolic disorder due to genetic mutation resulting in accumulation of very long chain fatty acids (VLCFA). In ALD, this accumulation leads to progressive, inflammatory brain demyelination by an unknown mechanism. We hypothesize that VLCFA-containing crystals induce the NLRP3 inflammasome, a potent pro-inflammatory activator, resulting in the devastating neuroinflammatory cascade and lesion expansion in ALD.
METHODS: We visualized cholesterol crystal deposition and clefts within cells in ALD and control brain tissue using light and polarized microscopy. We evaluated NLRP3 effector cytokines, IL-18 and IL-1b, in cerebrospinal fluid (CSF) of ALD (n=20) and control (n=9) patients using multiplex assay and in brain tissue using immunohistochemistry (IHC) in ALD (n=5) and control (n=4).
RESULTS: We identified VLCFA crystals and clefts within ALD, but not control brain tissue. These clefts localized to microglia (Iba1+) and astrocytes (GFAP+) in ALD tissue (n=1). Interestingly, the clefts were present in IL-18+ cells resembling microglia and macrophages. We found elevated IL-18 in both brain and CSF of ALD patients compared to controls. In CSF, IL-1bwas elevated in ALD, but this was not statistically significant.
CONCLUSIONS: We demonstrate increased cholesterol crystals within glial cells and co-localization with NLRP3 effector proteins in ALD tissue. Our data provides initial evidence of increased NLRP3 inflammasome activity in brain and CSF of ALD patients. This invites further investigation into the role of NLRP3 and cell death pathways within ALD brain lesion as possible new therapeutic targets to inhibit disease progression.
KEYWORDS: Infections/Neuroimmunology, Neurometabolic Disorders

343. Video-based eye tracking distinguishes follow up OMAS patients from controls
Parbhoo Kaajal (Toronto, Ontario, Canada) Brien Donald, White Brian, Berenbaum Tara, Munoz Douglas, Yeh Eluen Ann

OBJECTIVE: Opsoclonus myoclonus ataxia syndrome (OMAS) is a rare immune-mediated neurological disorder affecting predominantly young children resulting in long-term behavioural and learning problems despite resolution of other neurological symptoms. Video-based eye tracking metrics correlate with attention and cognitive function in other populations. Our aim was to assess whether eye tracking differentiated patients with a history of OMAS from controls.
METHODS: This cross-sectional study included children (n=12, 8F, median 67mo. (IQR44-72)) with a history of OMAS and healthy age and sex matched controls (n=12, 8F, median 60.5mo. (IQR44-97)). Video-based eye tracking was performed using the Eyelink1000 eye tracker (SR Research Ltd, Ottawa, Canada). Statistical analysis was performed using JASP (version 0.11.1). Normalized Scanpath Saliency (NSS) scores were derived from computational saliency models using feature maps in luminance, flicker, motion, faces and colours. Saccades at the start of each new clip were evaluated based on whether they indicated bottom up (saccades 1-3) or top down (saccades 4+) processing.
RESULTS: OMAS patients and controls differed in mean NSS parameters including: flicker(1-3) (3.55 vs 4.26, p=0.037), orientation(1-3) (2.36 vs 2.67, p=0.044), red-green(1-3) (3.2 vs 3.6,

p=0.043), blue-yellow(4+) (2.5 vs 3.0, p=0.022), luminance(4+) (2.4 vs 2.8, p=0.044), and face(4+) (2.7 vs 3.9 p=0.004).
CONCLUSIONS: Video-based eye tracking distinguishes OMAS patients from controls, particularly when looking at bottom-up and top-down saliency measures suggesting differences in both attention and cognitive processing. This may manifest clinically in reaction time metrics. Future studies are needed to confirm these findings and investigate correlations between cognitive metrics and eye tracking results.
KEYWORDS: Infections/Neuroimmunology

344. Clinical features and outcome in single live parenchymal neurocysticercosis and their correlation with serum matrix metalloproteinase-9: a longitudinal observational study
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OBJECTIVE: The objective of the current study is to prospectively describe clinical features and outcome in a cohort of neurocysticercosis (NCC), and study their correlation with serum matrix metalloproteinase-9 (MMP-9).
METHODS: Children aged 5-18 years, with treatment naive, single, parenchymal, live, probable or definite, NCC, presenting to a tertiary care teaching centre in north India, between June 2017 and June 2019 were included after ethical approval. A baseline serum MMP-9 was done. Subsequently oral albendazole (7 days), dexamethasone (5 days) and antiepileptic drugs were started. A CECT was done at 6 months and serum MMP-9 was repeated in calcified cases.
RESULTS: Overall, 66 children were analysed (median follow up:18 months, range: 6-24 months). The commonest seizure type was focal (87.9%) and location was parietal (45.5%). Electroencephalogram was abnormal in two-third cases. Most received phenytoin (37, 56%) monotherapy. Follow up CECT revealed 46 calcified and 20 resolved cases. Breakthrough seizures (BTS) were seen in 19 cases (18 within initial 4 months and 1 post calcification documentation). Serum MMP-9 was significantly elevated in treatment naive live state compared to calcified state (p=0.0009). Baseline serum MMP-9 didn't differ significantly in calcified versus resolved cases and those with versus without BTS.
CONCLUSIONS: This cohort describes a higher rate of calcification (69.7 %) compared to past (25-30 %) and early occurrence of BTS. These may be a reflection of increased inflammation at baseline (high serum MMP-9 levels) and/or reduced duration of albendazole therapy (7 days) practised currently or other novel mechanisms which should be evaluated in larger multicentric studies.
KEYWORDS: Infections/Neuroimmunology, Epilepsy

345. Low clearance rates in Neurocysticercosis: Is it time to review guidelines?
Sankhyan Naveen (Chandigarh, India) Barman Prabal, Suthar Renu, Vyas Sameer

OBJECTIVE: Our objective was to prospectivey study if post-treatment MRI clearance rates of Neurocysticercosis were similar to those reported in the literature using CT scan, after using the recommended anti-helmenthic drugs.

METHODS: A prospective, observational study, was conducted in consecutive children with NCC (non- calcified) from March 2018 to June 2019. Standard treatment was initiated, and they were followed up at six months clinically and with MRI brain.
RESULTS: Of 128 consecutive children with NCC screened, 80 children fulfilled the enrolment criteria. Baseline neuroimaging showed a single lesion in 65 and multiple lesions (≥2) in 15 children. Seizure-73(91.2%) was the most common presentation, followed by headache-5(6.2%). Clinical assessment and MRI brain were done in 72 children (both single and multiple lesions) at six months post-treatment. During the first 6-months, seizure recurrence was seen in 5(6.2%). MRI brain showed clearance of lesions in 10(13.9%) and persistence of lesions in 62(86.1%) children. In the single lesion NCC cohort (65 children), the lesions resolved in 9(15.3%, 95% CI of 6.1 - 24.4) and persisted in 50(84.7%, CI of 75.6 - 93.9). On follow up, disc lesions were seen in 14(23.7%), granulo-nodular in 15(25.4%) and calcified in 21(35.6%). Among children with multiple lesions, except for one child, all had persistence of lesions at six months.
CONCLUSIONS: Children with a single degenerating cysticercus granuloma, treated with a combination of anti-helminthics and corticosteroids as per the standard guidelines, have a low lesion resolution rate (15%) at 6-months. Thus, there is a need to evaluate newer therapeutic regimens.
KEYWORDS: Infections/Neuroimmunology, Neuroimaging, Epilepsy

346. Sleep Disturbance as an Initial Presenting Symptom in Patients with Autoimmune Encephalitis: A Multicenter Study
Shah Yash (Manhesset, NY, United States) Hong Annie, Khasgiwala Surabhi, Morse Anne, Troester Matthew, Kothare Sanjeev

OBJECTIVE: Autoimmune encephalitis (AIE) is becoming more widely recognized as a cause of encephalopathy in both adults and children. Incidence and prevalence of sleep disturbances in AIE patients remains unknown. Objective of this study was to determine the prevalence of sleep issues in patients presenting with AIE.
METHODS: This was a retrospective review of clinical data from pediatric and adult patients with a diagnosis of autoimmune encephalitis from three medical centers. Electronic medical records were reviewed for demographic details, co-existing autoimmunity, clinical data, electroencephalogram (EEG) results, and radiologic findings. Autoimmune encephalitis (AIE) diagnosis utilized the criteria from a 2016 position paper on a clinical approach to this diagnosis published in Lancet Neurology.
RESULTS: There were a total of 102 patients, and the median age of diagnosis of AIE was 14 years (range 1- 88years). Autoantibodies against N-methyl-D-aspartate receptor (NMDAR) were found in 34.3%, against Voltage gated potassium channel antibodies (VGKC Abs) in 10.8%, and against glutamic acid decarboxylase (GAD) in 8.8%. Forty-three (42.2%) patients had sleep disturbance as the initial presenting symptom. Of these, 30 (29.4%) had insomnia and 13 (12.7%) had hypersomnia. Also it was noted that sleep abnormalities were more common in Pediatric population (53.7%) compared to adults (42.9%) [$p < 0.001$]
CONCLUSIONS: Insomnia and hypersomnia are common sleep problems associated with AIE. Patients presenting with new onset sleep disturbances in an appropriate clinical context can provide a helpful clue in the early diagnosis of AIE. In addition, our findings emphasize the importance of screening for sleep disturbances in AIE patients.
KEYWORDS: Infections/Neuroimmunology

347. Consequentialism: Long term outcome in childhood encephalitis is defined by aetiology and clinical course

Thomas Terrence (Singapore, Singapore) Lim Jocelyn, Thoon Koh Cheng, Das Lena, Tan Natalie, Chan Derrick, Arkachaisri Thaschawee

OBJECTIVE: We evaluate long term outcome in children surviving encephalitis, a reversible neurological disease with a high risk for disability.
METHODS: Retrospective study of patients aged 1 month to 18 years (2008 - 2012, 5 years) with encephalitis of an infectious (as defined by Granerod), immune (by Graus, and clinicoradiological phenotyping) or indeterminate aetiology. Clinical course was either uncomplicated (rapid improvement, hospitalization ≤ 10 days) or protracted, and Liverpool Outcome Score (neurodevelopmental sequelae or epilepsy) was dichotomized to normal or symptomatic.
RESULTS: A total of 168 children (median age 7.0 (range 0.1-16.7) years) met inclusion criteria. There were 12 deaths (4 and 8 with infectious and immune encephalitis) and 68%, 65% and 43% children with infectious (of total 53 patients), immune (75 patients) and indeterminate (40 patients) encephalitis had a protracted clinical course.
In 131 survivors (78%) followed for a median of 6.1 (range 0.5-9.7) years,
univariate analysis identified female gender (p=0.0035), focal neurological signs (p<0.0001), intensive care therapy (p<0.0001), protracted clinical course (p=0.0004) and a defined aetiology (p=0.0024) as predictors for disability. In multivariate analysis, only focal neurological signs in the acute illness (OR 3.16, 95%CI 1.35-7.39) and protracted clinical course (OR 3.62, 95%CI 1.48-8.85) remained significant. Survivors of bacterial encephalitis had global developmental delay (43%) whilst cognitive impairment (100%) and refractory epilepsy (75%) characterised survival from autoimmune encephalitis.
CONCLUSIONS: Encephalitis treatment is *time-sensitive,* as children with a protracted clinical course have a high risk of disability. Survival from infectious and immune encephalitis manifests different sequelae.
KEYWORDS: Infections/Neuroimmunology

348. Evaluation of the FilmArray Meningitis/encephalitis Panel in Children in a Tertiary Center in South Korea

Lee Yun Jin (Yangsan, Republic of Korea) Park Su Eun, Nam Sang Ook, Ko Ara, Kong Juhyun

OBJECTIVE: FilmArray meningitis/encephalitis panel (FA-MEP) is a multiplexed polymerase chain reaction for the simultaneous, rapid detection of 14 common pathogens from cerebrospinal fluid (CSF). We retrospectively evaluated the pathogen of pediatric meningitis/encephalitis (M/E) by FA-MEP in South Korea, and the characteristics between children with FA-MEP positive and negative results.
METHODS: FA-MEP and conventional tests were performed in children who presented with symptoms of M/E in a tertiary hospital. Clinical and laboratory data were reviewed and analyzed to evaluate the characteristics of children with detected pathogens by FA-MEP.
RESULTS: The CSF specimens of 110 pediatric M/E were finally enrolled. Mean age was 5.9±5.2 years old. Overall positive rate by FA-MEP was 46.4% (51/110). The most frequently detected pathogens were enterovirus (23/51, 45.1%), parechovirus (10/51, 19.6%), *S.*

pneumonia (7/51, 13.7%), human herpesvirus type 6 (6/51, 11.8%), *S. agalactiae* (3/51, 5.9%), herpes simplex virus type 2 (1/51, 2.0%), and *E. Coli* (1/51, 2.0%). Meningitis than encephalitis (OR, 28.71, 95% CI, 6.04−182.55), and duration from onset to CSF test within 2 days (OR, 3.2, 95% CI, 0.1−0.91) were significantly associated with detection of pathogens on the FA-MEP. Of 14 children with empiric antibiotics before CSF test, the detection rate was significantly higher in the FA-MEP than in the conventional test (28.6% vs. 0.0%, $p = 0.031$).
CONCLUSIONS: The FA-MEP had a higher detection rate in children of M/E, particularly meningitis than encephalitis and shorter duration of time-to-test. This test was helpful in pediatric M/E with previous empiric antibiotics than the conventional test.
KEYWORDS: Infections/Neuroimmunology

349. Comparison of clinical profile of children with infectious and autoimmune encephalitis: experience from a tertiary care center in north India
Panda Prateek (Rishikesh, India) Sharma Vishakha, Lourembam Radhapyari, Verma Henuka, Sharawat Indar

OBJECTIVE: To compare the clinical profile and treatment outcome of children with infectious and autoimmune encephalitis/encephalopathy in a tertiary healthcare institute located in a hilly state of north India.
METHODS: Clinical profile, treatment response and cognitive/neuromotor outcome of all children with autoimmune and infectious encephalitis (symptom duration <4 weeks) admitted under two Pediatric Neurology Super specialists between August 2019 and January 2020 were determined by retrospective chart review.
RESULTS: Out of 70 cases of acute/subacute encephalopathy, 5 cases were excluded (1-neurometabolic (mitochondrial) cytopathy, 1-hypernatremia, 3-toxic encephalopathy) and 65 were included in analysis (34(52%) infectious etiology, 27 (48%) autoimmune etiology).Tuberculosis (16), bacterial meningoencephalitis (5), scrub typhus (4), Dengue encephalopathy (3), HSV (2) and Japanese encephalitis (1) constituted majority of infectious cases.
Anti-NMDAR encephalitis (2), ADEM (6), PANS (5), ANEC(2),anti-basal ganglia encephalitis (3),Hashimoto encephalopathy (3), optic neuritis (2), SLE (1) and seronegative autoimmune encephalitis (7) constituted autoimmune cases and treated with corticosteroid±IVIG. Profound encephalopathy (GCS<10) (p=0.02), seizure(p=0.03), requirement of mechanical ventilation (p=0.01), systemic manifestations (p=0.01), CSF pleocytosis>20/uL (p=0.01), increased CSF protein>100 mg/dl(p=0.03) and cerebral cortical affection in neuroimaging (p=0.01) were common in infectious cases. Neuropsychiatric features (p=0.02), autonomic instability (p=0.04), extrapyramidal features (p=0.03) and basal ganglia/thalamus affection in neuroimaging (p0.03) were more prevalent in autoimmune cases. Recovery was slower in autoimmune cases (p=0.03), but had higher proportion (p=0.04) with good clinical outcome (Pediatric Cerebral Performance Category scale1-2).
CONCLUSIONS: About half of acute/subacute encephalitis cases have autoimmune etiology, with more extrapyramidal and neuropsychiatric features and more favorable outcome as compared to infectious cases, if administered timely immunotherapy.
KEYWORDS: Infections/Neuroimmunology, Demyelinating Disorders

350. Feasibility & Safety of Plasma Exchange in Pediatric Neuro-immunology: A Single Center Experience

Shah Yash (Manhasset, NY, United States) Eksambe Padma, Fomani Katayoun, Karkare Shefali, Louie James, Kothare Sanjeev

OBJECTIVE: There is limited data available on the safety of therapeutic plasma exchange (TPE) for pediatric neuro-immunological disorders (PNID). Initial IVIG followed by TPE will result in removal of administered IVIG. Thus, TPE should be considered as an earlier treatment of choice over IVIG. However, there is a general belief that application of TPE in paediatric patients is more difficult due to more frequent technical problems regarding vascular access, lower blood volume and higher incidence of adverse events in children. In this study, we report our data on safety and feasibility of TPE for these disorders.
METHODS: Retrospective chart review was performed to include all patient who received TPE for four major PNID conditions: autoimmune encephalitis, ADEM, NMOSD and transverse myelitis. We recorded minor and major adverse effects (AEs) associated with each TPE procedure.
RESULTS: Thirty-two patients with PNID received a total of 186 TPE cycles. Out of these, only 1 cycle (0.89%) in AIE subgroup, 1(4.3%) in NMOSD and 1 (4.5%) in TM had AEs. No patients had major side effects. Twenty-one kids (65.6%) had significant improvement in symptoms after 5-7 day course of TPE. Three (9.3%) had moderate improvement from baseline.
CONCLUSIONS: In this study, we have shown that with a skilled and experienced team, TPE is an effective life-saving therapeutic intervention with minimal AEs in various PNID even when used early. In centers with experience in performing TPE, it should be considered earlier in the course of the disease, and possibly before IVIG use.
KEYWORDS: Infections/Neuroimmunology, Demyelinating Disorders

351. Sub-Acute Progressive Encephalopathy Associated with Antiphospholipid Syndrome

Otallah Scott (Winston Salem, NC, United States) Alam Umar

OBJECTIVE: To utilize a case of antiphospholipid syndrome (APS) and systematic literature review to expand the spectrum of neurologic manifestations of APS in children.
METHODS: A case of progressive encephalopathy associated with APS in a child lead to a systematic review of the literature.
RESULTS: Based on systematic review, although neuropsychiatric illness, cognitive decline, and rare cases of aphasia have been correlated with APS in adults, no sub-acute progressive encephalopathy has yet been identified in the literature in a child to our knowledge. In our case, a 16 year old young woman presented with multi-focal strokes (right superior M2 and left P2). Within the first week after stroke the patient had experienced steady improvement of a resultant hemiparesis and a mild transcortical motor aphasia. However, after transfer to acute rehab the patient experienced a sub-acute decline in mental status with profound impairments in language and alertness over 10 days. Interestingly this coincided with the development of hemi-chorea. After an extensive workup for recurrent stroke, seizure, and delirium, among other etiologies; concern arose for a direct interaction of antibodies with cortex. The patient was presumptively treated with a 5 day course of IVIG and high dose IV methylprednisolone with a rapid and sustained improvement in her cognition. Hemi-chorea gradually improved over

several weeks independent of cognition. Repeat testing at 12 weeks confirmed her APS diagnosis.
CONCLUSIONS: In patients with APS or suspected APS, treatment of sub-acute progressive encephalopathy with steroids and IVIG is reasonable. Further study is needed to more fully characterize this entity.
KEYWORDS: Infections/Neuroimmunology, Cognitive/Behavioral Disorders (including Autism), Stroke (including other Vascular Disorders)

352. Clinical Features of Pediatric and Adult Autoimmune Encephalitis: A Multicenter Sample

Hong Annie (New Hyde Park, NY, United States) Shah Yash, Morse Ann, Pickle Jacob, Lynch Rebecca, Troester Matthew, Fernandez-Carbonell Cristina, Kothare Sanjeev, Fisher Ciaran

OBJECTIVE: Distinguishing features between pediatric and adult patients with autoimmune encephalitis are not well characterized. The purpose of this study was to compare the clinical presentation of pediatric and adult patients diagnosed with autoimmune encephalitis.
METHODS: This was a retrospective review of clinical data from pediatric and adult patients with a diagnosis of autoimmune encephalitis from three medical centers. Electronic medical records were reviewed for demographic information, CSF autoantibody status, clinical data, electroencephalogram (EEG) results, radiologic findings, and treatment. Patients with positive CSF autoantibody results and autoantibody-negative but probable autoimmune encephalitis were included utilizing criteria from a recent position paper on a clinical approach to the diagnosis of autoimmune encephalitis (Lancet Neurology 2016).
RESULTS: There was a total of 102 patients, of which 67 were pediatric (65.7%). Initial clinical presentation included disturbances in cognition/memory (76%), psychiatric symptoms (50%), seizure (45%), sleep (42.2%), gait instability/weakness (34.3%), movement disorder (25%), and/or dysautonomia (10%). Seizures were present in 54 (53%) patients, classified as either focal (66.7%), generalized (16.7%), or undetermined (16.7%). Status epilepticus was present in 15% of patients. Differences between demographics, clinical presentation, imaging, and CSF autoantibody results in adults versus children are described in Table 1.
CONCLUSIONS: MRI abnormalities are significantly higher in adult patients with autoimmune encephalitis ($p=0.001$). Pediatric patients with autoimmune encephalitis are more likely to present with psychiatric symptoms, focal seizures, and/or status epilepticus compared to adult patients ($p < 0.05$).
KEYWORDS: Infections/Neuroimmunology

353. Efficacy and Tolerability of Valganciclovir for Six Months in Symptomatic CMV Infection

Ruby Naznin (Dhaka, Bangladesh) Rahman Muhammad, Akhter Shaheen

OBJECTIVE: CMV infection is the most common form of congenital infection which is being treated with oral valgnciclovir, but 6 weeks therapy is not sufficient for visual, audiologic and psychomotor improvement, some studies have shown better outcome with 6 months oral valganciclovir on infant with symptomatic CMV infection.
METHODS: This prospective interventional study was conducted in the department of pediatrics of DMCH among infants aged 1 month to 12 months with symptomatic CMV

infection. Among 75 infants 62 were completed 6 months treatment. We assessed pretreatment virus load, visual, hearing, psychomotor status of the infants. They were followed up at 3 months interval up to 12 months period regarding their post treatment viral load, visual, hearing, psychomotor status and the side effects of drugs.
RESULTS: Mean age of the infants was 6.7± 2.2, presented with developmental delay (85%), seizure (71%), microcephaly (66.1%), 65.4% had visual abnormalities including CVI, chorioretinitis. Common movement disorder was dystonia. Seventy one percent came with different grade of hearing impairment 1 with severe impairment and 23 had moderate impairment. Majority was delivered at home at term with PNA (67.7%) among them 45.2% had neonatal seizure. Cortical atrophy (80%) and intracranial calcification (58.1%) were the most common neuroradiologic abnormalities. None of our children discontinued treatment due to any side effects of drugs; rather patient has shown significant psychomotor, audiologic and visual improvement at the end of 12 months follow up.
CONCLUSIONS: Prolonged therapy of symptomatic CMV infection with oral valganciclovir is safe and effective and allows better auditory and psychomotor development
KEYWORDS: Infections/Neuroimmunology, Neuroimaging, Movement Disorders (including Cerebral Palsy)

354. A Rare Case of Pediatric Autoimmune GFAP Astrocytopathy Presenting As Meningoencephalitis and Acute Flaccid Paralysis
Lin Jenny (Atlanta, GA, United States) Elkins Kathryn, Upadhyayula Saila, Gombolay Grace

OBJECTIVE: Discuss clinical course in a pediatric case of autoimmune GFAP astrocytopathy.
METHODS: Chart review.
RESULTS: Sixteen-year-old girl presented with fevers, vomiting, diarrhea, nuchal rigidity and was started on antibiotics. CSF showed 284 WBCs with lymphocytic predominance, 55 glucose, 101 protein. On day 3, she was noted to have ophthalmoplegia (bilateral cranial nerve VI palsies, ocular dipping), papilledema, encephalopathy, and was intubated. MRI brain showed leptomeningeal enhancement (Figure 1). High-dose solumedrol was administered after infections were ruled out. On day 6, she developed acute-onset flaccid paraplegia of the legs, T10 sensory level, and bilateral upper extremity weakness. MRI spine showed holocord deep grey matter hyperintensity. Extensive serum and CSF evaluation revealed CSF 1:16 GFAP IFA titer. Repeat MRI spine a week later showed transverse myelitis T7-conus and persistent spinal cord enhancement 6 weeks later (Figure 1). EMG/NCV demonstrated an evolving predominantly motor neuropathic process. At two-month follow-up, mental status and upper extremity strength had normalized with residual dense paraplegia and incontinence. Immunotherapy included plasmapheresis, monthly IVIG, rituximab, cyclophosphamide and mycophenolate mofetil.
CONCLUSIONS: A rare case of autoimmune GFAP astrocytopathy in a pediatric patient with meningoencephalomyelitis, ophthalmoplegia, and flaccid paraplegia is presented. One pediatric case series describes 3/10 with meningoencephalomyelitis. While steroid-responsive, T-cell targeted immunosuppressants can be considered as T-cells are implicated in animal models. Majority improve with immunotherapy. One adult case of GFAP astrocytopathy treatment-refractory flaccid paralysis has been reported. This case illustrates the overlap of acute flaccid myelitis and transverse myelitis.
KEYWORDS: Infections/Neuroimmunology, Neuroimaging

355. Thrombocytopenia in children with AES and its effect on outcome: a prospective observational study from a tertiary care centre of northern India

Kanta Chandra (Lucknow, India) Pal Mahendra, Kumar Rashmi, Jain Amita, Verma Sanjeev

OBJECTIVE: Agents causing Acute Encephalitis Syndrome (AES) varies from region to region and time to time leading to variable presentation. Thrombocytopenia is a common laboratory finding observed in AES cases in our region. This study was done to find out prevalence of thrombocytopenia in AES and its association with clinical features, causative organisms and outcome that can help in deciding management of children with AES.
METHODS: This hospital based prospective observational study was conducted at a tertiary care teaching hospital of northern India from September 2018 to August 2019. Children between 6 months to 14 years of age diagnosed as AES according to WHO definition (2006) were enrolled after informed consent and followed till discharge. Cases of trauma, toxin exposure, cerebro vascular accident, malignancy, epilepsy or suspected metabolic disorder were excluded. They were investigated for dengue, Japanese encephalitis, Herpes simplex, scrub typhus, leptospirosis, typhoid and malaria.
RESULTS: A total of 128 children of AES were enrolled and investigated. Pyogenic meningitis and tuberculous meningitis cases were excluded. Mean age of patients was 72.8 ± 38.59 months and male to female ratio was 1.6:1. Thrombocytopenia was found in 67(52.3%) of cases (platelet count <1.5 lac/mm^3). Rash, bleeding, swelling, hepatomegaly, splenomegaly, low haemoglobin, low serum protein, raised liver enzymes- serum AST and serum ALT were significantly more in thrombocytopenic group in comparison to non thrombocytopenic group. But, no difference in etiology and outcome was found.
CONCLUSIONS: Thrombocytopenia is common among children with AES but do not affect the outcome of disease.
KEYWORDS: Infections/Neuroimmunology

356. Subacute Sclerosing Panencephalitis: Management challenge in developing countries

Sultan Tipu (Lahore, Pakistan)

OBJECTIVE: Subacute sclerosing panencephalitis (SSPE) is a chronic degenerative disorder of invariably fatal outcome. To find out the role of EEG in the early diagnosis and management of SSPE, this study was planned.
METHODS: After IRB approval, it was started at Department of Neurology Children's Hospital, Lahore from January 1st, 2011 to December 31, 2018. Children between the ages of 2 to 18 years (n=355) with myoclonic jerks were admitted in Neurology department. History and clinical examination was carried out and EEG and CSF antimeasles antibodies were performed. Children may have EEG findings consistent with SSPE (EEG abnormalities having burst suppression in high amplitude slow and sharp waves recur at 3-5 second interval on slow background) or other EEG findings like myoclonic epilepsy with normal back ground, normal EEG etc. CSF of all children was sent for antimeasles antibodies for further confirmation which was considered diagnostic. Brain imaging was done in all children to exclude other possible diagnosis.
RESULTS: Total of 138 patients with EEG findings of subacute sclerosing panencephalitis were further confirmed with CSF anti measles antibodies. It was positive in 107 children, while 31

children had negative EEG findings and all of them had negative results for CSF antimeasles antibodies. Male to female ratio was 1.5:1.
CONCLUSIONS: Subacute sclerosing panencephalitis is not an uncommon entity in our population with quite variable clinical presentation and electroencephlography has significant valve in early, cost effective and reliable diagnosis. Once diagnosed earlier, treatment may be initiated which may be helpful.
KEYWORDS: Infections/Neuroimmunology

357. CNS infection due to Streptococcus anginosus. A case series from a single center.
Madathil Sujana (Iowa City, IA, United States) Matsumoto Satsuki, Mathews Katherine, Glykys Joseph

OBJECTIVE: To present four cases of CNS infection due to *Streptococcus anginosus* seen at a single institution from 2014- 2019, and to raise awareness of this potentially fatal CNS infection among the pediatric neurologists.
METHODS: The electronic medical record was reviewed for all cases of *Streptococcus anginosus* CNS infection. Four cases were identified, and clinical information, including presentation, course of illness, laboratory tests, imaging, and treatment, was abstracted from the medical records.
RESULTS: All four patients (male; ages: 8,14,16 and 22 years) presented with severe headache and fever. The variable symptoms at presentation included nausea, vomiting, encephalopathy, right leg weakness, and intermittent speech difficulty. Brain imaging showed abscesses in 3 cases and subdural empyema in one. Cultures obtained through neurosurgical intervention grew *Streptococcus anginosus*. The 8-year-old boy with encephalopathy progressed to brain herniation and died. The 14 and 22-year-olds recovered without any neurological deficit. The 16-year-old boy with left temporal lobe abscess and speech difficulty at presentation had cognitive and speech impairment at discharge but recovered to baseline at one-year follow-up.
CONCLUSIONS: The *Streptococcus anginosus* group comprises three distinct species: *Streptococcus anginosus*, *Streptococcus constellatus*, and *Streptococcus intermedius*. They are part of normal human bacterial flora in mouth, throat, stool, and vagina.
The *Streptococcus anginosus* group are known for their pathogenicity and a strong tendency for abscess formation. CNS infections due to this organism are life-threatening. The early symptoms in our cases were non-specific. Early identification of brain abscess with neuroimaging, prompt surgical intervention as needed, and timely initiation of appropriate antimicrobial therapy are essential.
KEYWORDS: Infections/Neuroimmunology, Rare Diseases, Neuroimaging

358. Comparison of Socio-demographic, Clinical profile of Subacute Sclerosing Panencephalitis (SSPE) patients admitted in Paediatric and Adult Neurology unit of a referral Neuroscience Hospital in Bangladesh.
Debnath Bithi (Dhaka, Bangladesh) Hussain Mohammad, Khan Masum, Saha Narayan, Chowdhury Rajib

OBJECTIVE: To find out any difference of socio-demographic and clinical profiles between the patients admitted in Pediatric (upto age 14 years) and Adult Neurology (>14 years) unit of a referral Neuroscience hospital in Bangladesh.

METHODS: This study was conducted in the National Institute of Neurosciences, Dhaka, Bangladesh from September 2014 to August 2017. Patients of SSPE diagnosed by Dyken´s Criteria were selected as study population.
RESULTS: A total of 34 SSPE patients were recruited for this study of which 24 cases were from Pediatric Neurology unit (less than 14 years, Group-1) and the rest 10 patients were from Adult Neurology unit (more than 14 years of age, Group-2). Male patients outnumbered females in both groups [18(75.0%) and7(70.0%) respectively]. Most of the patients were from rural areas [Gr 1- 17(70.8%) and Gr 2- 7(70%)] and low socio-economic group [Gr 1- 12 (50%), Gr 2- 6 (60%)]. History of definite Measles infection was present in 10 (41.7%) patients in Group-1 and 3 (30%) patients in Group-2. Frequency of vaccination against measles was 22 (91.7%) & 10 (100%) respectively. Fall was the commonest presenting symptom in both groups [11 (45.8%) & 5 (50 %) respectively]. Visual disturbance was more common in Group-2 patients [4 (16.7%) & 5 (50%) respectively, p-value 0.045].
CONCLUSIONS: The profile of SSPE patients admitted in pediatric Neurology unit did not differ from those admitted in the adult Neurology unit except visual disturbance which was found to be more common (p value 0.045) in the late onset group.
KEYWORDS: Infections/Neuroimmunology

359. Powassan Virus: An Emerging Cause of Tickborne Encephalitis in Infancy
Kalsner Louisa (Farmington, CT, United States) Asad Daniyal

OBJECTIVE: Powassan virus (POWV) encephalitis is a tickborne infection, previously reported primarily in adults. We describe clinical and neuroradiological features of POWV in two infants with history of tick exposure in Connecticut.
METHODS: We report 2 cases of POWV encephalitis.
RESULTS: Patient 1 is a 5 -month old boy who presented with 4 days of fever and vomiting. He had seizures involving right facial twitching, becoming frequent on the day of admission, controlled with leviteracetam and fosphenytoin. CSF had 125 wbc and tested positive for POWV IgM. MRI Brain [Fig. 1] showed restricted diffusion in the basal ganglia and thalami. At 3.5 years of age he has receptive/expressive language delay with subtle dystonia and is seizure free off of medication. Patient 2 is 2 month-old boy who presented with fever and focal seizures involving tonic left arm extension and right gaze deviation. He had frequent seizures controlled with leviteracetam, fosphenytoin and phenobarbital. CSF had 215 wbc and tested positive for POWV IgM and antigen. MRI Brain [Fig. 2] showed patchy areas of restricted diffusion primarily involving the thalami. At 4 months of age he is seizure free on leviteracetam.
CONCLUSIONS: POWV is a rare tickborne illness reported primarily in adults with meningoencephalitis but should be considered in infants and children, particularly in endemic areas including New England. Unlike Lyme disease, transmission can occur after only minutes of tick exposure. The infants presented here both had fever, frequent focal seizures and a distinct pattern of restricted diffusion in the thalami and basal ganglia.
KEYWORDS: Infections/Neuroimmunology, Neuroimaging

360. To study the clinical profile and the response to immunotherapy in autoimmune encephalitis in children in a tertiary care centre of North India
Sinha Rahul (Delhi, India) Panda Prateek, Sondhi Vishal, Gupta Juhi, Jauhari Prashant, Chakrabarty Biswaroop, Gulati Sheffali

OBJECTIVE: To study the clinical profile and the response to immunotherapy in autoimmune encephalitis in children in a tertiary care centre.
METHODS: The data of 40 pediatric patients of autoimmune encephalitis (AE) were retrospectively analysed from March 2017 to Dec 2019. The clinical profile and response to immunotherapy in autoimmune encephalitis were studied.
RESULTS: Forty subjects (18 males: 22 females) were identified with a mean age of 6.5 years. Seizures (95%) and movement disorder (75%) was the most common presenting symptoms. 24 children who tested antibody positive were classified as definite-AIE (Anti-NMDAR, n=23; Anti-GAD, n=1) Clinical presentation for Anti-NMDAR encephalitis included behavioural abnormalities (20/23), seizures (23/23), dyskinesia (20/23), sleep-disturbance (20/23), and emotional-lability (20/23). EEG abnormality was seen in 55% (22/40) cases. MRI(Brain) abnormality was seen in 25% (10/40) cases. Anti-GAD syndromes presented with behavioural abnormalities and refractory epilepsy. Sixteen seronegative patients who showed improvement with immunotherapy were categorized as probable-AIE. Immunotherapy (Intravenous methyl prednisolone and intravenous immunoglobulin) was administered to all and titrated according to clinical response (initial co-administration of methylprednisolone and intravenous-gamma-globulin followed by tapering oral steroids; in non responders plasma-exchange and then rituximab was given). The average response rate to immunotherapy was 4-6 weeks in seropositive AE and 3-4 weeks in seronegative. The requirement of 2nd line therapy was seen in 10/40 patients with NMDA and GAD positive AE
CONCLUSIONS: The critical theme in the treatment of autoimmune encephalitis is that the early institution of immunotherapy is closely linked to reducing long-term sequelae and relapses thus improving outcomes.
KEYWORDS: Infections/Neuroimmunology

361. Clinical & Neuro-Imaging Changes of Subacute sclerosing panencephalitis- Experience 30 Cases in Tertiary Care Center in Bangladesh
Kundu Gopen (Dhaka, Bangladesh) Akhter Shaheen

OBJECTIVE: To see the clinical and neuro-imaging findings in children with Subacute sclerosing panencephalitis.
METHODS: This retrospective study was conducted at Bangabandhu Sheikh Mujib Medical University (BSMMU), Dhaka, Bangladesh. Thirty (30) SSPE children were evaluated at paediatric neurology ward from January 2010 to December 2017. Diagnosis was based on the characteristic features myoclonus , electroencephalographic evidence of periodic complexes, and raised IgG anti-measles antibody in CSF.
RESULTS: Total number of studied children were 30. Mean age was 10.2 ± 3.1 year and Male female ratio was 5:1. Among them 46.67% had history of measles infection during early childhood . Progressive deterioration of school performance (50%), gait disturbance (70%), myoclonus (83%) dysarthria(43%) and Ocular manifestations like optic atrophy& papilloedema (83.33%) were the main presenting feature of our studied children. All of the patients (100%) showed positive measles specific antibody IgG in CSF and On EEG findings showed periodic burst suppression in 90.90% cases. Most of the children (56.6%) were in stage II category and other 3.3%, 33.3%,6.6%,were stage I, stage III, stage IV category respectively.

Neuroimmaging study showed abnormalities in 45.83% cases included periventricular white matter hyper intense signal changes, cortical atrophy and ischaemic change.
CONCLUSIONS: In our study most of the SSPE patient were in stage II .About half of the patient had history of measles infection during early childhood. Neuroimmaging abnormalities found in majority cases of stage II and commonest finding was periventricular white matter hyper intense signal changes. The severity of clinical findings does not always correlate the of MR changes.
KEYWORDS: Infections/Neuroimmunology

362. The Forgotten TORCH
Bricker Katelyn (Chapel Hill, NC, United States) Shiloh-Malawsky Yael

OBJECTIVE: We aim to assess and increase awareness to congenital lymphocytic choriomeningitis virus (LCMV) infection, and its neurological sequelae. LCMV is a lesser known virus that can cause birth defects. It was once suggested that LCMV be added to the TORCHES (toxoplasmosis, rubella, cytomegalovirus, herpes simplex virus, enteroviruses, and syphilis). Despite multiple epidemic outbreaks in the last century, awareness of the virus is lacking. Transmission of this arenavirus is usually from the common house mouse (Mus musculus), and can be aerosolized. LCMV has predominantly been linked to congenital intrauterine infection, hydrocephalus, and chorioretinitis. Neuroimaging abnormalities included microcephaly, periventricular calcifications, ventriculomegaly, pachygyria, cerebellar hypoplasia, porencephalic cysts, periventricular cysts, and hydrocephalus.
METHODS: We present clinical and radiographic findings of three confirmed cases of LCMV and one suspected case. Clinical histories are detailed for each patient with an accompanying table to summarize comparative symptoms. Imaging for each patient is provided to accompany the clinical briefs. We provide data from a brief standardized survey of child neurologists, neonatologists, and radiologists to determine the likelihood of recognizing this diagnosis.
RESULTS: Our standardized survey supports congenital LCMV is likely under-recognized and under-diagnosed. Radiographic findings, including hydrocephalus, microcephaly, and periventricular calcifications are demonstrated in the varying clinical cases.
CONCLUSIONS: Despite it causing substantial neurological manifestations, clinicians across multiple specialties are frequently unfamiliar with LCMV. The possibility of LCMV infection should be considered in all patients with evidence of congenital microcephaly, periventricular calcifications, and hydrocephalus. Increased awareness among medical providers may reduce exposure during pregnancy, and therefore reduce risks of congenital LCMV.
KEYWORDS: Infections/Neuroimmunology, Neuroimaging, Rare Diseases

363. Clinical differences between seronegative and seropositive (CSF+) NMDA receptor autoimmune encephalitis
Sandweiss Alexander (Houston, TX, United States) Erickson Timothy, Murray Kristy, Muscal Eyal

OBJECTIVE: Pediatric NMDA receptor autoimmune encephalitis (NMDAR AE) presents with cognitive deficits, movement disorders, seizures, and psychiatric dysfunction. It is diagnosed clinically and confirmed by presence of serum/CSF anti-NMDAR antibodies. We compared the clinical features of seronegative to seropositive NMDAR AE patients.

METHODS: After IRB approval, we reviewed diagnostic work up and clinical features of all NMDAR AE patients admitted at a single tertiary care institution between 2010-2017. We compared clinical features between seronegative (anti-NMDAR CSF+/serum-) and seropositive (anti-NMDAR CSF+/serum+) patients.
RESULTS: 32 children were admitted with CSF NMDAR antibodies present (70% female, 12% Caucasian/56% Hispanic/26% African American); 3 patients (9%) were seronegative and 29 (91%) were seropositive (preadmission days of symptoms; mean, median, range: 4.66, 5, 0-9 vs 7, 13.6 0-90). Seronegative children were younger at presentation (mean 7.3 vs 10.7 years of age), fewer had coordination or movement problems (0% vs 72%), fewer had seizures (67% vs 76%), fewer were febrile (0% vs 17%), and they had significantly shorter hospitalizations than the seropositive group (median 17, range 12-19 vs median 25, range 5-101).
CONCLUSIONS: We found that those with CSF anti-NMDAR Ab without serum positivity had a less severe phenotype than the seropositive patients. We agree with the hypothesis of other large AE groups that a less robust CSF production of anti-NMDAR Ab by CNS B-cells may lead to undetectable serum antibodies and thus categorize those patients as seronegative. Our data complements existing adult data. This may have implications for mechanisms of pathogenicity and treatment options for the less severe cohort.
KEYWORDS: Infections/Neuroimmunology

364. Dominant ADAR c.3019G>A mutations are an important mimic of Hereditary Spastic Paraplegia and Cerebral Palsy

Jones Hannah (Sydney, Australia) Paget Simon, Webster Richard, Kothur Kavitha, Troedson Christopher, Dale Russell, Mohammad Shekeeb

OBJECTIVE: Dominant mutations in the adenosine deaminases acting on RNA (*ADAR)* gene are classically associated with the pigmentary skin condition dyschromatosis symmetrica hereditaria (DSH), while biallelic mutations characteristically cause Aicardi-Goutieres syndrome (AGS).
METHODS: We report three cases which highlight the unique, autosomal dominant c.3019G>A, p.Gly1007Arg *ADAR* mutation presenting with the Hereditary Spastic Paraplegia (HSP) AGS phenotype or late infantile motor regression with variable manifesting features in the transmitting parent (1-3).
RESULTS: The three children described range in age from 2-13 years and have diverse ethnic backgrounds. Two presented with toe walking in the second year of life and one presented with motor regression associated with Salmonella bacteraemia at 11 months of age. The cerebrospinal neopterin was elevated in each case (68.4-173.85nmol/L). The MRI changes range from subtle to more diffuse susceptibility artefact in the basal ganglia with or without associated atrophy, and are a useful clinical clue to support initial suspicion for this disease (Figure 1).
CONCLUSIONS: Autosomal dominant *ADAR* mutations are an important differential diagnosis for HSP and cerebral palsy, and genetic testing should be pursued in potential cases.
KEYWORDS: Infections/Neuroimmunology, Movement Disorders (including Cerebral Palsy), Rare Diseases

365. Partial Exchange blood transfusion in the Management of Guillian Barre Syndrome in a Developing Country

Offiong Uduak (Abuja, Nigeria) Sanni Usman

OBJECTIVE: Guillian Barre is an acute inflammatory disease of the CNS which may occur following a viral illness. It may rapidly progress leading to respiratory failure and death. In developing countries plasmapheresis or immunoglobulins are not available in most medical facilities. Other lifesaving methods of treatment are considered. This is a presentation of the outcome of treatment of a child with rapidly ascending paralysis with a partial exchange blood transfusion.
METHODS: The clinical chart of the patient was reviewed
RESULTS: A 5year old girl presented to the emergency paediatric unit with a 2 weeks history of weakness of the lower limbs. Parents had sought both traditional and orthodox. On physical examination there was no fever or signs of respiratory distress. The central nervous system, normal slow gait, depressed tones and reflexes in the lower limbs with grade 4. Upper limb power was grade 5 and tone and reflexes were normal. There were no cranial nerve deficits. The cardiovascular, respiratory and gastrointestinal systems were all normal. A diagnosis of Guillian Barre Syndrome(GBS) was made. Cerebrospinal fluid analysis was suggestive. She was commenced on oral Prednisolone. There was progressive ascending deterioration in motor abilities with involvement of cranial nerves. At this point the anesthetists were invited and the plan for a partial exchange transfusion (PEBT) was initiated. Recovery occurred following 2 sessions of PEBT.
CONCLUSIONS: Partial exchange blood transfusion is an available alternative form of treatment of Guillian Barre Syndrome in resource poor countries.
KEYWORDS: Infections/Neuroimmunology, Critical Care

366. A case of juvenile-onset systemic lupus erythematosus complicated with various neurological disorders
Ota Kento (Yonago, Japan) Kitamoto Koichi, Maegaki Yoshihiro

OBJECTIVE: We describe a clinical course of neurological complications observed in a patient with juvenile-onset systemic lupus erythematosus (jSLE).
METHODS: We report a case of a 9-year-old with jSLE and reviewed magnetic resonance imaging (MRI) of the patients.
RESULTS: The patient presented with fever, seizure, exanthema, abdominal pain, and acute renal insufficiency at 7 years of age and was diagnosed with jSLE. Neuropsychiatric SLE (NPSLE) was suspected, and brain MRI revealed multiple infarction and white matter lesions. During the initial treatment with plasma exchange, intravenous methylprednisolone pulse therapy, intravenous cyclophosphamide therapy, and hemodialysis followed by peritoneal dialysis, the patient showed headache. Brain MRI revealed wide-spread subcortical white matter T2/FLAIR hyperintensities were diagnosed as posterior reversible encephalopathy syndrome, and showed right occipital lobe hemorrhage. Although the patient was in remission by immunosuppressant treatments, the patient presented with seizure and showed cytopenia and hypocomplementemia at 8 years of age, and was diagnosed with a relapse of SLE. The patient also presented clusters of focal motor seizure secondarily generalized four months after relapse with no new lesions on brain MRI. Levetiracetam was administered with good effect on seizure remission.
CONCLUSIONS: The patient presented with seizures and headache as neurological findings. Brain MRI showed multiple stroke, hemorrhage, white matter lesion, and cerebral atrophy. In

addition to NPSLE, other etiologies should be considered such as cerebrovascular diseases, infections, and psychiatric diseases, in the differential diagnosis of SLE patients who present with neuropsychiatric symptoms.
KEYWORDS: Infections/Neuroimmunology, Neuroimaging, Stroke (including other Vascular Disorders)

367. A unique case of Anterior Mediastinal mature teratoma-associated NMDAR encephalitis resistant to treatment in the presence of incomplete resection and elevated CA125
Ahsan Nusrat (Los Angeles, CA, United States) Santoro Jonathan

OBJECTIVE: A17 yr old Asian female admitted with new onset seizure and one week of altered mental status, visual hallucinations, fever, headache, anxiety, decreased eye contact and hypophonia.
METHODS: Her MRI brain revealed bilateral cerebellar T2 hyperintense lesions. EEG with diffuse and left focal slowing with bilateral temporal epileptiform discharges. Lumbar puncture revealed RBC 24, WBC 60 (94% lymphocytes), glucose 50, protein 40 and >5 unique oligoclonal bands with elevated IgG Index. CSF anti-NMDA receptor antibody was positive with titer 1:128 although serum titer1:10. She received IVIg (2 g/kg), IV methylprednisolone x5 days for anti-NMDAr encephalitis. Screening pelvic ultrasound was normal, CT Chest/Abdomen/Pelvis with IV/oral contrast showed a right anterior mediastinal mass. On day 7, mass resection revealed, mature teratoma of 6.7cm arising in an involuting thymus. Despite resection, encephalopathy, autonomic dysautonomia, choreoathetoid and dystonic movements continued, requiring Plasmapheresis and Rituximab.
RESULTS: In the absence of improvement, CSF was re-evaluated with NMDA Ab titer of 1:128. CA125 elevated at 122. AFP, B-HCG, LDH were normal. CSF NMDA titer on Day 62 had decreased down to 1:16 without improvement. She was initiated on weekly IVIg and pulse steroids. Pathology of the resected mass was questioned and was found to have margins with focal involvement. She underwent radical thymectomy on hospital day 74 showing minute foci of residual mature teratoma. Two weeks following resection, patient began displaying clinical improvement.
CONCLUSIONS: Interestingly NMDAR Ab titers 10 days prior to repeat resection had decreased down to 1:16 without clinical improvement and only improvement was noticed after radical resection.
KEYWORDS: Infections/Neuroimmunology, Demyelinating Disorders, Teaching of Child Neurology

368. ANTI-NMDA ENCEPHALITIS RELAPSE IN A 9-YEAR-OLD SAUDI BOY: A CASE REPORT AND REVIEW
Bamaga Ahmed (Jeddah, Saudi Arabia) Alghamdi Nora, Balto Huda, Elhoussiny Alaa

OBJECTIVE: Anti-N-methyl-D-aspartate receptors (NMDAR) encephalitis was first described by Dalmua in 2007; this study reported young women with mature or immature teratoma with characteristic encephalitis including psychosis, language disturbance, behavioral changes, and motor deficit; in addition, it was determined that these women had antibodies against NR1/NR2B heteromers of the NMDA receptor (1). Later, several reports on anti-NMDA encephalitis have

been published. The largest case series to date described 577 patients with this disease (2). Subsequent studies reported partial or full recovery in up 80% of the cases. The risk of relapses was identified to be 12–24%. The reported cases of anti-NMDAR encephalitis from the Middle East are extremely rare (3) The first reported case in the Middle East was a 4-year-old Lebanese girl (4) .
METHODS: CASE report
RESULTS: we report a 9-year-old Saudi boy with anti-NMDA encephalitis, who exhibited a neurological relapse 4 years after his first diagnosis.
CONCLUSIONS: Anti-NMDA is increasingly diagnosed in the pediatric age group. Corticosteroids and IVIG remain valuable first-line treatments. However, rituximab is an appealing treatment option, especially in patients who do not tolerate or respond to immunosuppressive therapy with corticosteroids or IVIG. Further research is needed to study the potential benefits of using rituximab at an earlier stage during the treatment to improve symptoms and prevent relapses in patients with anti-NMDAR encephalitis.
KEYWORDS: Infections/Neuroimmunology

369. The Natural History of Lyme-Related Facial Nerve Palsy and Bell's Palsy, and Effects of Steroid Use in Children
Barber Danielle (Philadelphia, PA, United States) Swami Sanjeev, Harrison Jacqueline, McGuire Jennifer

OBJECTIVE: Describe the natural history of Lyme-related facial palsy (LRFP) and Bell's palsy in a large cohort of children. Compare the proportion of children who fully recover facial strength between those who did and did not receive corticosteroids.
METHODS: Retrospective cohort study of children 1.0-18.0 years old who received care at our institution over five years for unilateral acute-onset peripheral FP. Children were identified by electronic medical record query for FP ICD-10 codes; cases were confirmed by chart review.
RESULTS: The charts of 306 children (median 10.3 years, range 1.1-17.9) were reviewed. Twenty-six percent (81/306) had LRFP, 71% (217/306) had Bell's palsy, and 3% (8/306) had another cause of FP. Children with LRFP typically presented between June and November (93%), and more often had an infectious prodrome (≥3 of the following: fever, malaise, headache, myalgias and/or arthralgias in the six weeks prior to FP onset) (54% vs 6%, $p<0.001$). The FP resolved in 234/235 children with LRFP or Bell's palsy who had documented follow up. Ultimate recovery was not different between those that did and did not receive corticosteroids in the first week after symptom onset.
CONCLUSIONS: LRFP and Bell's palsy are common causes of FP in Philadelphia-area children; infectious prodrome may help clinicians distinguish children with LRFP from those with Bell's palsy at symptom onset. Steroid use did not impact ultimate recovery. Future prospective studies may define subtle or temporal differences in treatment effects.
KEYWORDS: Infections/Neuroimmunology

370. Neurological Presentations Associated with Infectious Gastroenteritis in Children
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OBJECTIVE: Neurological complications described in association with infectious gastroenteritis have been limited to seizures associated with rotavirus and *Shigella sp.*,

encephalitis in immunocompromised patients with astrovirus, and case reports/series associated with norovirus. We aim to measure the frequency of neurological sequelae in pediatric cases of infectious gastroenteritis at our institution over a 3-year period.
METHODS: This is a retrospective cohort study that included children hospitalized at our institution from 2014-2017 with a viral or bacterial pathogen detected on clinical testing by Filmarray Gastrointestinal Pathogen Panel (GIP), with an ICD-10 diagnosis code suggesting potential neurological sequelae excluding codes indicating chronic neurological disease or neurologic complications related to trauma. We performed chart review using a standardized data collection tool to characterize potential neurological sequelae associated with norovirus, rotavirus, sapovirus, adenovirus, astrovirus, *Shigella*, and Shiga toxin producing *E. coli* (STEC) detections.
RESULTS: Among 1,409 hospitalizations with gastrointestinal pathogens detected on GIP, neurological complications were present in 36 (2.6%). Neurological sequelae were identified in 11/263 (4.2%) with sapovirus, 6/173 (3.5%) with adenovirus, 5/219 (2.3%) with rotavirus, 2/95 (2.1%) with STEC, 9/454 (2.0%) with norovirus, 3/164 (1.8%) with astrovirus, and 0/41 (0%) with *Shigella sp.* The most common clinical presentation overall was seizure, 28/36 (78%). All of the norovirus cases were associated with seizure, and 4/5 rotavirus cases were associated with seizure (80%). A substantial portion, 12/36 (33%), presented in status epilepticus.
CONCLUSIONS: Neurological complications of infectious gastroenteritis are underappreciated, and frequency and clinical characteristics differ by pathogen.
KEYWORDS: Infections/Neuroimmunology

371. Acute Hemorrhagic Encephalitis as a Complication of Severe Diabetic Ketoacidosis with concomitant New-onset Type 1 Diabetes and Influenza B Infection
Oh Ann (Phoenix, AZ, United States) Bassal Frederick, Mangum Tara

OBJECTIVE: Diabetic ketoacidosis (DKA) is a life-threatening complication of type-1 diabetes mellitus. Infection is the most common precipitating factor for DKA. Severe neurologic complications are associated with DKA, including cerebral edema, stroke, hemorrhage, vaso-occlusive disease and seizures.
METHODS: A single-institution case report of two fully vaccinated adolescents who presented with neurologic complications of DKA in the setting of new-onset type 1 diabetes and influenza B infection. Diagnosis was made based on clinical presentation of severe DKA after viral illness with characteristic neuroimaging and CSF pleocytosis that is consistent with acute hemorrhagic encephalitis.
RESULTS: Patient 1: A 17-year-old girl with history of ganglioglioma resection and focal epilepsy presented with severe diabetic ketoacidosis, encephalopathy and status epilepticus after being diagnosed with influenza B. MRI findings showed multifocal parenchymal hemorrhages. After receiving oseltamavir, mannitol and leviteracetam, she was extubated in 4 days, discharged after a week. Patient 2: A previously healthy 14 year-old girl presented with severe diabetic ketoacidosis, new-onset generalized seizures with MRI findings showing multifocal parenchymal hemorrhages and diffuse meningeal enhancement. She received oseltamavir, IVIG and leviteracetam; however, she required trach placement and had a prolonged hospitalization. After 1.5 months, she has been decannulated and convalescing in rehab.
CONCLUSIONS: Diabetic ketoacidosis precipitated by influenza B infection can cause severe neurologic complications, including acute hemorrhagic encephalitis. Despite receiving the flu

vaccination, both our patients contracted influenza B and had severe neurologic complications with fulminant type 1 diabetes. Our case report highlights the importance of neuro-imaging to identify intracerebral hemorrhage in order to provide early intervention.
KEYWORDS: Infections/Neuroimmunology, Critical Care, Neuroimaging

372. Acute necrotizing encephalopathy of childhood: A multicenter experience in Saudi Arabia

Bashiri Fahad (Riyadh, Saudi Arabia) Al Johani Sultan, Hamad Muddathir, Kentab Amal, Al Wadei Ali, Hundallah Khalid, Hasan Hamdi, Alshuaibi Walaa, Jad Lamyaa, Alrifai Muhammad, Alharthi Nawaf, Abdelmagid Tayseer, Ba-Armah Duaa, Salih Mustafa, Tabarki Brahim

OBJECTIVE: Acute necrotizing encephalopathy of childhood (ANEC) is a rapidly progressing encephalopathy usually characterized by fever, depressed level of consciousness, and seizures. Diagnosis depends mainly on clinical presentation and characteristic neuroimaging findings.Treatment modalities are not well established; empirical treatment with antibiotics and antiviral agents, followed by steroids and immunoglobulin.Patients with ANEC have a variable prognosis, but mortality is very high. we aimed to present the clinical and radiological features, as well as treatment modalities and outcomes, of 12 children with ANEC in five tertiary care centers in Saudi Arabia.
METHODS: A retrospective chart review of patients diagnosed with ANEC in five tertiary centers from January 2015 to October 2018 was performed.Clinical and radiological findings, as well as the therapeutic approach and outcomes, were described.Statistical Analysis was done by using SPSS IBM Statistics.
RESULTS: Twelve children were included ranging in age from 10 months to 6 years. All patients presented with preceding febrile illness, altered level of consciousness, and seizure. Radiological features showed abnormal signals in the thalami and around half of the patients had brainstem involvement. All patients received empirical treatment with antibiotics and antiviral agents; the majority received intravenous immunoglobulin (IVIG) and IV Methylprednisolone therapy. Outcomes were variable ranging from good outcomes with minimal neurological deficits to poor outcomes and death in 25% of cases.
CONCLUSIONS: ANEC is rare but underdiagnosed in children. The treatment is challenging, Early interventions with use of IVIG and IV Methylprednisolone may change the outcome however, further studies are needed to establish a consensus guideline for the management.
KEYWORDS: Infections/Neuroimmunology, Neuroimaging, Genetics

373. Clinical Outcome of Pediatric Anti-NMDA Receptor Encephalitis Evaluated by Clinical Assessment Scale in Autoimmune Encephalitis.

Lim ByungChan (Seoul, Republic of Korea)

OBJECTIVE: This study was aimed to investigate clinical features and long-term outcome of pediatric Anti-N-methyl-D-aspartate receptor (NMDAR) encephalitis.
METHODS: Twenty-eight anti-NMDAR encephalitis patients with positive results for anti-NMDAR antibody test were recruited. The clinical outcome was evaluated by Clinical Assessment Scale in Autoimmune Encephalitis (CASE) and modified Rankin Scale (mRS).
RESULTS: Among 28 total enrolled patients, 21 patients were female (75.0 %). The median onset age was 8.7 years (range, 0.7-17.1 years). All patients received first-line immunotherapy

including intravenous immunoglobulin and/or steroid therapy. The second-line immunotherapy was administered to 18 patients (64.3%). The clinical outcome was evaluated in 25 patients who were followed for more than 6 months from onset. The median follow-up duration of the 25 patients were 30.7 months (range, 6.3-82.9 months). The proportion of patients with less than two points of mRS at 12 months follow-up was 81.8% (18/22).The CASE scores of these 18 patients ranged from 0 to 6, which deficits in language and memory area accounted for the majority of disability. When the outcome was assessed according to the onset age (<12 years and 12-18 years), the younger onset age group tended to show lower maximum severity socre at onset and slower recovery over the clinical course.
CONCLUSIONS: Despite overall favorable clinical outcome, mild cognitive problem including language and memory area could persist in pediatric anti-NMDAR encephalitis patients. A specific outcome measure such as CASE needs to be adopted to delineate the clinical outcome, which will contribute to making an individualized treatment plan.
KEYWORDS: Infections/Neuroimmunology, Neuroscience, Rare Diseases

374. Clinical spectrum and outcome of autoimmune encephalitis in an Argentinian pediatric cohort.
Paz Maria (Buenos Aires, Argentina) Crespo Agustina, Savransky Andrea, Reyes Gabriela, Caraballo Roberto, Calvo Agustin, Tenembaum Silvia

OBJECTIVE: To describe clinical features and outcome of autoimmune encephalitis (AIE) in a pediatric cohort diagnosed and followed at our hospital.
METHODS: This study cohort (2008-2019) consists of two patient categories: 1) Children with definite anti-NMDAR encephalitis); 2) Children with probable AIE (according to Graus diagnostic criteria) who were tested negative. Serum and CSF were tested using live and commercial CBA. Clinical data of the two groups were compared.
RESULTS: Sixty-six children (56% girls) with probable AIE were identified, mean age of 6.8 years (range 0.9-16.8) at presentation. Anti-NMDAR antibody could be assessed in 52/66 children and was positive in 32 (61%).
Presenting symptoms included seizures (50/66), insomnia (43/66), abnormal movements (20/66), psychiatric behavior (19/66). Critical care was necessary in 13 children. Three patients with definite AIE had recently had HSV encephalitis. One girl had ovarian teratoma. Comparison of presenting features revealed that abnormal behavior (40% vs 16%) and dyskinesias (35% vs 22%) were more frequently identified in children with antibody negative AIE. Conversely, plasmapheresis (43% vs 25%) and second-line immunotherapy (rituximab) (28% vs 15%) were more frequently required in children with definite NMDAR encephalitis. Full clinical recovery (mRS score 1) was observed in 16/66 children (24%) at 30 days, in 17 (26%) at 6 months, and in 45 (68%) at 12 months after immunotherapy. Relapses were observed in 5/32 children with definite NMDAR encephalitis.
CONCLUSIONS: Our study extends clinical knowledge on pediatric definite and probable AIE in our region
KEYWORDS: Infections/Neuroimmunology

375. Eculizumab Treated Anti-AQP4 Negative, Anti-MOG Positive Neuromyelitis Optica Spectrum Disorder in a 10-year-old Girl

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OBJECTIVE: Case of a 10 yo girl presenting with first event of severe neuromyelitis optica spectrum disorder (NMOSD) with high levels of anti-MOG antibodies treated with eculizumab.
METHODS: Case Report
RESULTS: 10 yo girl presented with a one day history of bilateral itchy eyes progressing to painful, complete bilateral vision loss and a one day history of diffuse papular, erythematous rash. Pupils were nonreactive to light. Fundoscopic examination revealed abnormal vessels and papilledema bilaterally. Gait was ataxic. MRI showed bilateral optic nerve thickening, T2 hyperintensity, and diffuse enhancement throughout the orbits extending to the optic chiasm. There was intramedullary signal abnormality from the odontoid synchondrosis to mid C6 and within the right side of the spinal cord at T6-7. CSF was negative for anti-AQP4 antibodies and showed 21.6 WBC, normal glucose and protein. Blood serology was positive for very high anti-MOG IgG (1:10,000) but negative for anti-AQP-4 antibodies. The patient received 3 days of IV methylprednisolone and plasmapheresis. As no benefit was seen after 2 rounds, eculizumab was initiated as per pediatric aHUS protocol. Her visual acuity improved within 10 days to 20/20 in her right eye, 20/400 in her left. Eculizumab was continued after discharge with 1200 mg q2 weeks. Three weeks from discharge, the patient's visual acuity improved to 20/20 in the right eye, 20/30 in the left, and only mild ataxia on tandem.
CONCLUSIONS: This case demonstrates a role for eculizumab in severe acute presentation of Anti-MOG Associated Disease (MOGAD).
KEYWORDS: Infections/Neuroimmunology

376. Anti-NMDA receptor encephalitis in a patient with juvenile idiopathic arthritis (JIA) on abatacept

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OBJECTIVE: To describe a case of anti-NMDA receptor encephalitis in a patient with JIA on the immunosuppressant abatacept
METHODS: Case report
RESULTS: An 8-year-old boy with JIA and uveitis in remission presented with 1.5 months of emesis, weight loss, sleepiness, irritability and confusional episodes, 2.5 years after starting abatacept. Neurological exam was notable for difficulties with memory and following complex commands. MRI Brain demonstrated multifocal non-enhancing T2/FLAIR white matter hyperintensities. CSF analysis showed 4 WBC (65% lymphocytes) and 3 CSF-restricted oligoclonal bands. EEG showed asymmetric sleep features and lack of well-formed spindles. Anti-NMDAR antibodies returned positive in CSF (1:128) and serum (1:240). He received methylprednisolone 30mg/kg/day IV for five days and mental status significantly improved. He was discharged on a prednisone taper. Abatacept was discontinued and he transitioned to mycophenolate mofetil for treatment of all his autoimmune conditions. Repeat serum testing four months after presentation was negative for anti-NMDAR antibodies. At follow-up five months after presentation, he was near baseline.
CONCLUSIONS: The development of anti-NMDA receptor encephalitis in this patient with JIA and uveitis while being treated with abatacept may reflect: 1) genetic predisposition to

autoimmunity and/or 2) an adverse effect of abatacept, a CTLA4-fusion protein that stimulates CTLA inhibitory signaling in T cells, including regulatory T cells. Patients with JIA and/or those being treated with abatacept who develop new-onset neurological symptoms should be evaluated for anti-NMDA receptor encephalitis.
KEYWORDS: Infections/Neuroimmunology

MOVEMENT DISORDERS (INCLUDING CEREBRAL PALSY)

377. Surgical options for treatment of spasticity in children with hereditary spastic paraplegia

Pol Laura (Amsterdam, Netherlands) Schie Petra, Slot Mariam, Buizer Annemieke

OBJECTIVE: To provide an overview of outcome and complications of selective dorsal rhizotomy (SDR) and intrathecal baclofen pump implantation (ITB) for spasticity treatment in children with hereditary spastic paraplegia (HSP), to improve walking pattern, prevent contractures or improve comfort and personal care.
METHODS: Retrospective study including subjects with HSP, who had undergone SDR or ITB. For SDR, walking children had to meet strict selection criteria (strength, selectivity, no dystonia, motivation for a rehabilitation program, strong social support system). Gross motor function measure (GMFM) scores and level of spasticity (modified Tardieu scale) were assessed.
RESULTS: Ten patients (5 males) were included (most frequent mutations were in *ATL1* (n=3) or *SPAST* (n=3) genes). Four patients walked without and two with walking aids. Four were non-walking children. Seven patients underwent SDR, two patients ITB and one patient both. Six of the SDR patients were walking patients. Mean age at surgery was 7.8±5.1 years, with a mean follow-up of 3.4±1.6 years. Postoperatively spasticity in the legs was reduced in all patients. The change in GMFM score was +8.0 (0-19.7 min-max). The three ITB patients (*SPAST (n=2)* and *PNPLA6 (n=1)* gene mutation) were non-walking children with a progressive disease course. No complications of surgery occurred.
CONCLUSIONS: SDR is a feasible treatment option in carefully selected children with, HSP, especially in walking patients. The majority of patients benefit with respect to gross motor function and complication risk is low. ITB was mainly used in children with more severe and progressive disease.
KEYWORDS: Movement Disorders (including Cerebral Palsy), Neurorehabilitation

378. Abnormal Prefrontal Cortical-Striatal Functional Connectivity in Children with Primary Complex Motor Stereotypies

Nebel Mary-Beth (Baltimore, MD, United States) Mostofsky Stewart, Mahone E, Singer Harvey

OBJECTIVE: Complex motor stereotypies (CMS) are rhythmic, repetitive, prolonged, predictable, and purposeless movements that stop with distraction (e.g., hand/arm flapping, waving, wiggling). They occur in developmentally normal children (primary) or are associated with underlying neurological conditions (secondary). CMS are believed to be habitual behaviors, although little is known about their underlying neurobiology. In this study, we examined

functional connectivity within frontal-striatal circuits associated with goal-directed (pre-frontal to striatum) and habitual (premotor/SMA to striatum) pathways.
METHODS: Resting state functional magnetic resonance imaging was obtained on 24 children with CMS (mean age 10.7 ± 1.4) and 24 typically developing children – balanced for age, gender, handedness, intellectual ability, socioeconomic status, and imaging quality. Connectivity was evaluated between the striatum [executive, limbic, and sensorimotor regions] and frontal lobe including dorsolateral prefrontal (dlPFC), medial prefrontal (mPFC), orbitofrontal (OFC), premotor (PMC) and supplementary motor (SMA) areas.
RESULTS: Children with CMS showed significantly reduced frontal-striatal functional connectivity between: a) the executive striatum and the OFC and dlPFC and b) the limbic striatum and the OFC, dlPFC, and mPFC. In contrast, no differences were observed in functional connectivity between the sensorimotor striatum and any frontal lobe region.
CONCLUSIONS: Results emphasize the concept of a required optimal balance between goal-directed and habitual pathways in the pathophysiology of motor stereotypies. Specifically, findings suggest that the early appearance and persistence of stereotypies may reflect reduced development within the prefrontal-striatal networks underlying establishment of mature goal-directed behavior, rather than enhanced connectivity within premotor/motor to striatal pathways associated with habitual, patterned behaviors.
KEYWORDS: Movement Disorders (including Cerebral Palsy)

379. Clinically-feasible and objective method to use MRI to predict dystonic cerebral palsy
Chintalapati Keerthana (St. Louis, MO, United States) Miao Ben, Aravamuthan Bhooma

OBJECTIVE: To determine a quantitative and clinically-feasible method to predict dystonic cerebral palsy (CP) based on MRI injury severity following neonatal hypoxic-ischemic encephalopathy.
METHODS: The injury patterns predisposing to dystonic CP are unclear. Existing studies often lack standardized MRI injury quantification, expert dystonia phenotyping, or subjects with comparable CP etiologies. Available MRI assessment scales typically require subjective review by expert consensus, precluding widespread clinical implementation. To address these issues, we examined brain MRIs at day of life 4-5 in neonates who underwent therapeutic hypothermia at a single tertiary care center for hypoxic-ischemic encephalopathy at term gestation. Minimum apparent diffusion coefficient (ADC) values in the striatum and thalamus were normalized to ADC values of cerebrospinal fluid using clinically-available software (IBM iConnect Access). Medical records were screened through 5 years of age for pediatric neonatal neurology or movement disorders specialist documentation of tone abnormalities.
RESULTS: Normalized ADC values in the striatum and thalamus were significant classifiers of children who developed expert-identified dystonia with receiver operator characteristic areas under the curve of 1.0 (95% CI 1.0-1.0, P<0.01, N=21). A normalized ADC cutoff of 0.7 provided 100% specificity and sensitivity for dystonia.
CONCLUSIONS: MRI analysis requiring only basic neuroanatomical knowledge and clinically-available imaging software may predict who will go on to develop dystonia following neonatal hypoxic-ischemic encephalopathy in a small subset of children followed from birth at a single tertiary care center. This measure may be a useful prognostication adjunct and help establish appropriate vigilance for dystonia following neonatal brain injury.
KEYWORDS: Movement Disorders (including Cerebral Palsy), Neonatal & Fetal Neurology

380. Clinical diagnostic yield of whole exome sequencing in cerebral palsy

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OBJECTIVE: Cerebral palsy (CP) is a major neurodevelopmental disorder affecting motor function. Accumulating evidence suggests that genetic contributions to CP may be significant. We assessed the diagnostic yield of whole exome sequencing (WES) in three cohorts of individuals with CP (n=1,777 cases).
METHODS: We performed whole exome sequencing (WES) in three cohorts and aggregated data. Gene-positive cases harbored a pathogenic or likely pathogenic by ACMG criteria in a known disease gene previously described in association with a cerebral palsy phenotype.
RESULTS: The diagnostic yield of WES was 27.5% (488/1,777 cases). Pathogenic or likely pathogenic variants were identified in 238 different genes; 90 genes had recurrent variants and five genes were identified in all three cohorts. Linear modeling indicated that the likelihood of harboring a pathogenic variant was higher in those with multiple comorbid developmental brain disorders (autism, intellectual disability, and epilepsy) (OR =1.63; 95% CI 1.95-27.02; p=0.0023) vs. those with CP alone. Cases lacking CP risk factors were 8-fold more likely to be gene-positive (95% CI = 2.27-51.03; p = 0.0058). ~5% of gene-positive cases had findings that would prompt a change in management.
CONCLUSIONS: Cerebral palsy (CP) is a major neurodevelopmental disorder affecting motor function. Accumulating evidence suggests that genetic contributions to CP may be significant. We assessed the diagnostic yield of whole exome sequencing (WES) in three cohorts of individuals with CP (n=1,777 cases).
KEYWORDS: Movement Disorders (including Cerebral Palsy), Genetics

381. DEEP BRAIN STIMULATION (DBS) AS TREATMENT OF CHILDHOOD ONSET DYSTONIA: EXPERIENCE OF 13 CHILEAN PATIENTS

Munoz Daniela (Santiago, Chile) Troncoso Monica, Balut Fernanda, Aguirre David, Zambrano Emilia, Zepeda Ramiro, Monsalves Sebastian, Mendez David, Catalan Rodrigo, de la Cerda Andrés, Benavides Olga, Villagra Roque, Naranjo Valentina, Hidalgo Maria Jose, Ruiz Isadora

OBJECTIVE: The aim of this study is to evaluate outcome of DBS treatment in patient with chilhood onset dystonia
METHODS: We study chilhood onset dystonia patients treated with DBS. Dystonia severity was meassured pre-DBS and 1, 3, and 6 months after DBS. We used Burke-Fahn-Mardsen Dystonia Scale (BFMDRS), applying its 2 subscales: motor and disability.
RESULTS: 13 patients with bilateral Gpi DBS. 8 men. Average age dystonia onset was 8.5 years. Etiologies: Primary dystonia 5 patients (1 DYT1, 1 DYT 5, 1 DYT 24, 1 mutation SLC6A3 gene, 1 mutation KMT2B gene); 5 Secondary dystonia (2 PKAN, 1 Kernicterus, 2 late dystonia); 3 unknown etiology. Each patient was evaluated with BFMDRS scale pre-DBS and in controls of 1, 3 and 6 months. The average pre-DBS BFMDRS score was 71.4 / 21.5pts on motor / disability scales respectively. The average score in controls of 1, 3 and 6 months was 35.2 / 15.2pts, 29.5 / 12.2pts and 29.2 / 11.9pts respectively. The average improvement percentage was 61.2% on motor scales and 52.3% on disability scales. The percentages of improvement in each

group were: 63.4% / 66.6% primary dystonia, 58.6% / 53.65% secondary dystonia and 55.2% / 41% in dystonia of non-precise etiology. 3 patients achieved 100% improvement of dystonic symptoms, all of them were patients with primary dystonia.
CONCLUSIONS: Our study confirms the efficacy of this therapy, especially in patients with primary dystonia of genetic origin. This is the first Chilean series that describes the response of pediatric patients with dystonia to DBS.
KEYWORDS: Movement Disorders (including Cerebral Palsy)

382. Natural History of GNAO1 Associated Neurologic Disease: Results from Annual Research Clinic
Gilbert Laura (St. Louis, MO, United States) Novak Olga, Balk Karen, Patterson Jacqueline, Smith Erin, Fox Alice, Bell Emily, Goodkin Howard, Robichaux-Viehoever Amy

OBJECTIVE: To define the clinical phenotype of GNAO1 associated neurologic disease, generate initial best practice recommendations, and establish target features for biomarker development.
METHODS: We prospectively examined disease progression and outcomes in a dedicated research clinic. We evaluated 22 participants with confirmed GNAO1 mutation, aged 1 to 23 years. Subjects had a complete history, physical and neurologic exam performed as well as assessments of gross and fine motor skills, quality of life, and caregiver burden.
RESULTS: We verified that there seems to be a genotype-phenotype correlation for epilepsy versus movement disorder only subjects. There was significant variability in disability and movement disorders within genotypes. All subjects initially presented with hypotonia, and seizure onset occurred within the first weeks of life. Majority of subjects have chorea and dystonia with 52% (11/21) having chorea "storms." 10% (2/21) of subjects have intractable epilepsy with another 10% (2/21) with well-controlled epilepsy on monotherapy. The most common associated symptoms were temperature instability (57%, 12/21), sleep abnormalities (43%, 9/21), and GI motility issues (43%, 9/21). Deep Brain Stimulation (DBS) is effective in treating chorea "storms" (4/4 patients) and 2 of those cases also had improvement in dystonia. GMFM scores ranged from 8% to 85% of normal. Other than the GMFM for motor disability, currently available scales (Peabody, BFMDS, AMS, MAS) do not appropriately measure the level of ability and disability nor the quality and quantity of abnormal movements.
CONCLUSIONS: This study has broadened the understanding of the phenotypic spectrum and helps to define the natural history of the disorder.
KEYWORDS: Movement Disorders (including Cerebral Palsy), Genetics

383. A Caregiver Home Video Examination Tool for Complex Movements Associated with NGLY1 Deficiency
Revanur Anjali (Palo Alto, CA, United States) Ruzhnikov Maura, Brimble Elise, O'Malley Jennifer, Mackenzie Katherine

OBJECTIVE: To develop a standardized caregiver-obtained home video examination tool enabling remote evaluation of the complex movement disorder associated with NGLY1 deficiency.
METHODS: As part of an ongoing prospective natural history study, 26 international participants completed remote video assessments in 4-month intervals over the course of one

year. Detailed instructions were provided to caregivers and videos were recorded by a personal smartphone or tablet (Fig 1). Completed recordings were securely uploaded for expert review. A questionnaire exploring feasibility of completing home videos was also completed by 15 participants.
RESULTS: The mean age of participants was 10.0 years (range 1.9-21.0). The majority of caregivers completed videos in the requested time frame (n=22/26, 85%). On average, videos were 6.33 minutes long (range 3.02-12.15) and of adequate quality for expert review. Participants who responded to the questionnaire (n=15) generally found the instructions easy or neutral to understand (14/15, 93%) and 11/15 (73%) were able to use the secure online uploader without difficulty. Five (33%) caregivers found it challenging to complete the videos within the required 2 week time frame of each video due date. Only one participant would have preferred a video conference over the secure uploader.
CONCLUSIONS: Standardized caregiver-obtained home videos were successfully generated, allowing for remote expert characterization of the NGLY1 deficiency movement disorder phenotype. This examination tool will be used to validate a novel movement disorder rating scale, and may also be useful for home examination of other complex childhood movement disorders.
KEYWORDS: Movement Disorders (including Cerebral Palsy), Neurometabolic Disorders, Rare Diseases

384. Clinical characterization of dystonia in children with periventricular leukomalacia
Ueda Keisuke (St. Louis, MO, United States) Aravamuthan Bhoomas, Pearson Toni

OBJECTIVE: Periventricular leukomalacia (PVL) is commonly associated with spasticity, but we often encounter children with PVL who demonstrate dystonia. Our objective was to estimate the true prevalence of dystonia in children with PVL and spastic cerebral palsy (CP) based on expert review of clinical examination videos.
METHODS: A retrospective study. Inclusion criteria: Children with a diagnosis of spastic CP and PVL on MRI. Exclusion criteria: Insufficient clinical information in the medical record; lack of video; co-existing central nervous system disorders, or metabolic/genetic diseases. Their videos were blindly reviewed for dystonia by three pediatric movement disorders and CP neurologists. Dystonia was defined as intermittent, involuntary, and inappropriate muscle activation causing abnormal movements, abnormal trajectory during the activity, and change in speed and duration of the movement. MRI images and/or radiology reports were examined to classify the severity of PVL as grade 1) punctate T1/T2 signal change in periventricular white matter, 2) extensive lesions along the wall of lateral ventricles associated with ventricular enlargement, or 3) the presence of cystic lesions.
RESULTS: Of 1514 children, 135 children (75 boys, 2-30 years old at the time of the video recording) met inclusion and exclusion criteria. Overall, dystonia was observed in 92 children (68%). The presence of dystonia was not affected by gestational age or PVL grade.
CONCLUSIONS: Dystonia was a common symptom in children with spastic CP and PVL. Since dystonia may be underdiagnosed or misdiagnosed as spasticity, our findings suggest there should be increased vigilance for dystonia in children with PVL.
KEYWORDS: Movement Disorders (including Cerebral Palsy)

385. Management practices and long-term follow up of pediatric functional (psychogenic) movement disorder at a tertiary care center

Hull Mariam (Houston, TX, United States) Maldonado-Duran Jesus-Martin, Parnes Mered

OBJECTIVE: Current recommendations of managing FMD revolve around a multidisciplinary approach without clear evidence for which interventions are more successful for remission. We evaluated management practices and compared efficacy of specific interventions on remission of symptoms of functional movement disorder (FMD) in our pediatric population.
METHODS: A retrospective cohort study includes patients ≤21 years old with a diagnosis of FMD (based on ICD9/10 codes and/or documentation) evaluated at Texas Children's Hospital from 2011-2018. Demographics, diagnostic studies, medical history, and medical reports reviewed. Patients and/or caregivers subsequently underwent phone surveys.
RESULTS: A total of 203 charts were queried, 173 patients (73.4% female) met inclusion criteria. Mean age of symptom onset was 13.1 years. History and exam were adequate to make the diagnosis on initial presentation in 45 patients (26%). A precipitating event was identified in 35.3% of patients. Pre-existing movement disorders occurred in 11% of patients; majority being Tourette/tourettism (63.1%). The most common type of involuntary movement was tremor (46.8%). According to clinicians, a frank discussion of the diagnosis contributed the most to improvement in 19.6% of patients that achieved symptom remission, followed by meeting with a psychologist familiar with the diagnosis (15.7%). Patients with symptom remission were more likely to have been receptive to the diagnosis (p-value 0.03).
CONCLUSIONS: Substantial practice variation exists at a single institution regarding management of FMD. Psychology referral was the most common intervention, however according to providers caring for patients with FMD, the most helpful intervention was an open discussion of the diagnosis with the family and patient.
KEYWORDS: Movement Disorders (including Cerebral Palsy)

386. Utility of VMAT2 inhibitors in management of stereotypy in children: a series of six patients

Hull Mariam (Houston, TX, United States) Parnes Mered

OBJECTIVE: Stereotypies are continual, rhythmic, patterned movements that can occur in typically-developing children, and are more common in those with cognitive deficits. Particularly in the latter population, the movements can result in inadvertent and devastating self-injury, or interfere with the ability to be present in social settings. In patients with typical cognition, behavioral retraining has been effective; however, for patients with intellectual disability ,other avenues are explored. VMAT2 inhibitors have been effective in the treatment of several movement disorders. We aim to evaluate the effectiveness of VMAT2 inhibitors in the treatment of stereotypy.
METHODS: A retrospective review included patients under 18 years with stereotypy requiring treatment (due to either self-injurious behaviors or inhibiting socialization/therapy) who were evaluated at Texas Children's pediatric movement disorders clinic from 2014-2019 and underwent a trial of tetrabenazine.

RESULTS: Six patients met inclusion criteria. All patients had severe or profound intellectual disability. The ages of patients ranged from 4 to 15 years. Three patients were treated for self-injurious motor stereotypy that placed them at risk for cervical spine injury or retinal detachment. Of these patients, two had 50% reduction of the concerning movements. One was discontinued due to agitation. Three patients had near-constant vocal stereotypy preventing meaningful social interactions. Of these patients, two demonstrated a notable decrease in the frequency of the vocalizations. One was later discontinued in the setting of acute dystonic reactions (which recurred after switching to deutetrabenazine).
CONCLUSIONS: Of six patients with impairing stereotypy, four demonstrated meaningful benefit when treated with tetrabenazine.
KEYWORDS: Movement Disorders (including Cerebral Palsy)

387. Free automated dystonia identification using smartphone-quality videos acquired in outpatient clinic
Aravamuthan Bhooma (St. Louis, MO, United States) Ueda Keisuke, Pearson Toni

OBJECTIVE: To determine whether automated video analysis can discriminate dystonia identified by subspecialists in children with cerebral palsy (CP)
METHODS: Dystonia can be difficult to identify particularly when co-morbid with spasticity in children with CP. We analyzed 12 videos (1080 pixel resolution, 30 frames/second) acquired during routine outpatient care of children with spastic diplegic CP in plain clothes without additional skin/surface markers walking straight towards the camera. Subjects were 12-18 years old and had periventricular leukomalacia on MRI. Three pediatric movement disorders specialists reviewed videos for dystonia in the upper or lower limbs (6 with, 6 without). Limb position over time was calculated blindly using open-source deep neural network-guided pose estimation (DeepLabCut) allowing assessment of two key gait variables chosen *a priori*: knee and foot position variance.
RESULTS: Knee position variance was a significant classifier of dystonia with receiver operator characteristic area under the curve (AUC) of 1.0 (95% CI 1.0-1.0, P=0.004). A variance cutoff of 27 pixels provided 100% specificity and sensitivity for classifying dystonia in this 12 video set (with higher variances suggestive of dystonia). Foot position variance was not a significant classifier (AUC=0.81, 95% CI 0.54-1.0, P=0.08).
CONCLUSIONS: Video analysis of a small subset of children matched for age, diagnosis, and injury pattern reveals that free and automated video gait analysis can identify patients determined by experts to have dystonia. Techniques like this may be useful screening tools for identifying dystonia in children with CP in areas where specialists or formal gait labs are unavailable.
KEYWORDS: Movement Disorders (including Cerebral Palsy)

388. Emergency deep brain stimulation in a girl with dystonic storm due to GNAO1-associated hyperkinetic-dystonic movement disorder
Schoene-Bake Jan-Christoph (Hannover, Germany) Saryyeva Assel, Krauss Joachim, Jack Thomas, Bueltmann Eva, Chaib Hind, Hartmann Hans

OBJECTIVE: Mutations in the *GNAO1* gene, encoding for a G-protein-subunit, are associated with a hyperkinetic-dystonic movement disorder and mental retardation as well as an epileptic-encephalopathy. Patients with the movement disorder show continuous hyperkinetic movements

of variable degree with frequent exacerbations during minor illness, pain or surgery resulting in life-threatening dystonic storms. Various medications such as clonidine and tetrabenazine are used both to prevent exacerbations and as options in the acute treatment of dystonic storms. Sedation, analgesia and relaxation may be required to terminate the crisis. DBS has shown to be effective in preventing exacerbations. We report the case of an adolescent girl with refractory dystonic storm and emergency implantation of DBS.
METHODS: Case report.
RESULTS: The 16-year old teenager presented repeatedly with dystonic states and rhabdomyolysis (max.CK 100.000 U/ml) requiring ICU treatment. In most events, balanced sedation with continuous hydromorphone, clonidine infusions, midazolam-bolus plus oral clobazam and tetrabenazine was sufficient to control the hyperkinetic movements. During the last episode, even maximum doses of this combination were insufficient to control the symptoms. As the patient developed impaired bowel passage and hemorrhagic colitis due to the prolonged dystonic storm, emergency stereotactic implantation of DBS-electrodes in the globus pallidus internus (GPi) was performed. Shortly after activating the implantable pulse-generator, symptoms resolved and the medication could be tapered to zero over three weeks without recurrence of symptoms. Only low dose dronabinol was added to reduce spasticity.
CONCLUSIONS: Emergency implantation of DBS-electrodes in the GPi in dystonic storm due to a *GNAO1* mutation is an effective therapeutic option.
KEYWORDS: Movement Disorders (including Cerebral Palsy), Critical Care

389. Validity of neuropathic and nociceptive pain ratings in adults with cerebral palsy
Chin Eric (Baltimore, MD, United States) Hoon Alexander, Lenz Colleen, Johnson Jennifer, Jantzie Lauren, Campbell Claudia, Caterina Michael, Stashinko Elaine, Ye Xiaobu, Robinson Shenandoah

OBJECTIVE: Assess validity of neuropathic and nociceptive pain measurement in adults with cerebral palsy (CP) using established pain questionnaires. Cognitive and communicative challenges are common in individuals with CP, and validity cannot be assumed.
METHODS: Eighteen adults with CP able to independently answer questions completed standardized interviews (PROMIS Pain Quality Short Forms, PainDETECT neuropathic pain questionnaire). We assess validity of pain qualities:
1) by determining whether different questionnaires assessing the same concept (neuropathic pain) agree and 2) by identifying clusters in ratings of pain descriptors and comparing these clusters to typical descriptions of neuropathic or nociceptive pain. 1)Measures of neuropathic pain (PROMIS neuropathic T-scores and PainDETECT scores) were compared using non-parametric Spearman's correlation coefficient ρ. 2)PROMIS neuropathic and nociceptive questionnaire items were pooled, and principal component analysis was performed on each item's raw scores. A component was retained if eigenvalues exceeded the median of its corresponding component in 1000 iterations of a permutative null model.
RESULTS: Measures of neuropathic pain (PROMIS neuropathic T-scores and PainDETECT scores) shared ρ^2=48% of variance (p=0.002). Two factors (accounting for 49% and 20% of PROMIS pain quality variance, respectively) survived cutoff criteria. Factor 1 loadings were dominated (loadings > 0.2) by neuropathic qualities (pain that is "numb", "electrical", "stinging", "tingly", "like pins and needles") as well as "tender" pain. Factor 2 loadings were dominated by nociceptive qualities ("steady", "deep", "achy", "sore") except for "tender" pain.

CONCLUSIONS: Measures of neuropathic pain show convergent validity in communicative adults with CP. Endorsed pain descriptors largely cluster along typically-described neuropathic and nociceptive lines.
KEYWORDS: Movement Disorders (including Cerebral Palsy), Neurorehabilitation, Cognitive/Behavioral Disorders (including Autism)

390. From cerebral palsy to hereditary spastic paraplegia
Amrom Dina (Brussels, Belgium) Monier Anne, Soblet Julie, Vilain Catheline, Smits Guillaume

OBJECTIVE: Cerebral palsy (CP) is a clinically and etiologically heterogeneous condition. The observation of little change in CP prevalence despite progress of medical interventions suggests individual predisposing causes are playing a role. We aimed to update the etiologic work-up of our CP patients to allow specific treatment and appropriate genetic counseling.
METHODS: We studied our cohort of 270 CP patients and selected patients of the diplegic spastic type. We carried out detailed review of medical records, phenotyping of their specific clinical and neuroimaging features. We explored a potential constitutional cause by genotyping with comparative genomic hybridization (CGH) array, targeted gene sequencing and/or next generation sequencing with mendeliome.
RESULTS: One family encompassed two siblings with intracranial calcifications conferring them a pseudo-TORCH phenotype but without lymphocytosis; CGH array and mendeliome were negative, additional next generation sequencing is ongoing. All other patients were sporadic. Single gene pathogenic or likely pathogenic variants included *L1CAM* (SPG1, X-linked), *SPG11* (SPG11, autosomal recessive), *KIF1A* (SPG30, autosomal recessive), *KIF1A* (de novo, autosomal dominant), *ERLIN1* (SPG62, autosomal recessive), *RNASEH2B* (type 1 interferonopathy / Aicardi-Goutières Syndrome 2 (AGS2), autosomal recessive).
CONCLUSIONS: Cerebral palsy is a clinical description. Among inherited factors, hereditary spastic paraplegia (HSP) can be difficult to distinguish from CP, especially if there is only one affected patient in the family and/or a suggestive pre/perinatal history. We characterized a number of HSP types as the final diagnosis of diplegic spastic CP, and one patient with a type 1 interferonopathy (AGS2). Next generation sequencing is still carried out in the unsolved patients.
KEYWORDS: Movement Disorders (including Cerebral Palsy), Genetics

391. Benign Infantile Tremor Syndrome (BITS): a new movement disorder.
Hull Mariam (Houston, TX, United States) Parnes Mered

OBJECTIVE: Several benign movement disorders in infancy have been described including neonatal jitteriness, benign neonatal sleep myoclonus, shuddering spells, and others. We present infants at our institution presented with action tremor with onset weeks to months later after birth and otherwise similar to neonatal jitteriness.
METHODS: A retrospective chart review included three patients of interest and phone survey was completed to evaluate patient's long-term progress. We also reviewed the charts of and phoned two patients with similar tremor noted in the first hours to days of life, consistent with neonatal jitteriness.
RESULTS: Five patients presented to the pediatric movement disorders clinic at Texas Children's Hospital with similar episodic, proximal, irregular, large-amplitude tremor, with onset between the first hours of life and two months of age with episodes lasting seconds up to 30

minutes while awake, without association with feeding/sleeping. Body parts involved usually included the arms but sometimes legs and jaw. Average length of follow-up has been 32.8 months. All patients demonstrated typical development, and resolved between 4 and 10 months of age without recurrence.
CONCLUSIONS: We propose that the three patients with episodic tremor onset weeks to months after birth represent an expansion of the phenotype previously referred to as neonatal jitteriness, as demonstrated by the near-identical tremor characteristics seen in the two patients with tremor seen hours to days after birth. We suggest the term benign infantile tremor syndrome is more appropriate to describe this common benign movement disorder that presents in infancy and resolves within one year in typically developing children.
KEYWORDS: Movement Disorders (including Cerebral Palsy), Neonatal & Fetal Neurology

392. Tremor Presenting in Infants and Children Under Age 2 years
Doja Asif (Ottawa, Ontario, Canada) Wilson Mitch, Healy Sarah

OBJECTIVE: To examine the clinical features, course, and treatment of infants and children under age 2 with very early onset tremor.
METHODS: Retrospective chart review of all patients under age 2 presenting to a tertiary care movement disorders clinic between 2005-2019. Descriptive statistics were used to describe and summarize key features of the population and inferential statistics were used to make comparisons among different variables within the sample.
RESULTS: We identified 33 children with tremor presenting under age 2 (14 females). Three patients (9%) had a positive family history of tremor. The mean age at onset of tremor was 3.43 months (SD 3.79), with a mean age at diagnosis of 6.78 months (SD 5.30). In 11 patients (33%) the tremor occurred multiple times daily versus weekly or less frequently. The tremor did not interfere with functioning in any patient and no patients required treatment for their tremor. Tremor was found to be more noticeable when eating (7 patients), prior to or immediately after sleeping (6 patients) or when upset or excited (4 patients). Mean age at follow up was 10.36 months (SD 5.17, range 2-21 months). At follow up, 10 patients (30%) had complete resolution of their tremor with the rest being stable or improved. Patients with resolved tremors tended to have a younger age of diagnosis ($F=4.994$, $p= .013$).
CONCLUSIONS: Tremor with onset under age 2 follows a benign course, with no patients in our study requiring treatment and many eventually outgrowing the disorder.
KEYWORDS: Movement Disorders (including Cerebral Palsy)

393. PEDiDBS 2020: update on the international registry of pediatric patients undergoing deep brain stimulation
Marks Warren (Fort Worth, TX, United States) Bailey Laurie, Sankpal Umesh, Sanger Terrence, Mink Jonathan, Lin Jean, Kruer Michael, Koy Anne, Timmerman Lars

OBJECTIVE: In 2003, Deep brain stimulation was first approved dystonia in the United States under a Humanitarian Device Exemption. Indications for and surgical techniques have evolved nonetheless questions remain regarding the role of DBS in pediatric patients. These can best be addressed by multicenter collaborative data sharing.
METHODS: An international collaborative of investigators met several times between 2013 and 2016 to develop a mechanism for data sharing in order to help guide understanding of the role of

DBS in children and adolescents resulting in the formation PEDiDBS. This is international registry available to all centers implanting DBS in children. of children undergoing DBS.
RESULTS: Subjects are entered utilizing a de-identified limited data set stored on a secure REDCap cloud server. There are data fields for demographics including genetic information when available and surgical implant information. Follow-up information including therapeutic response and complications entered over time. Once a page is reviewed for completeness and consistency that part of the data will be locked to further changes in order to preserve the integrity of source information used in analysis. Each site, identified by number maintains access to its own data. Aggregate data for analysis by participating sites can be requested through the data sharing committee.
CONCLUSIONS: There is an expanding role for DBS that now includes movement disorders, epilepsy and neuropsychiatric syndromes. PEDiDBS represents an important method of further elucidating the role of deep brain stimulation in pediatrics. PEDiDBS is now open for participation. Full information is available at www.PEDiDBS.org.
KEYWORDS: Movement Disorders (including Cerebral Palsy), Genetics, Neurometabolic Disorders

394. Anti-NMDAR encephalitis induced super-refractory status dystonicus: response to pallidal deep brain stimulation
Luke Rebecca (Fort Worth, TX, United States) Acord Stephanie, Honeycutt John, Marks Warren

OBJECTIVE: Anti-NMDA receptor encephalitis can present with refractory neurologic symptoms, including movement disorders, which can be difficult to manage with medical treatment. When not responsive to traditional medication approaches, deep brain stimulation may ameliorate dystonia and hyperkinesis.
METHODS: We present a case of anti-NMDA receptor encephalitis with an ovarian teratoma who was refractory to traditional medical management for her movement disorder. Subsequently she had a deep brain stimulator placed which allowed her to be weaned off her intravenous medications and demonstrate clinical improvement.
RESULTS: A fourteen year old female presented with fever, altered mental status, and an isolated seizure. She progressed to orofacial and limb dyskinesias with worsening encephalitis requiring intubation and eventual tracheostomy. Anti-NMDAR antibodies were positive in her spinal fluid and an ovarian teratoma was removed early in her course. Other management included high dose steroids, intravenous immunoglobulin, plasma exchange, Rituximab, and Cyclophosphamide. She developed super-refractory status dystonicus with associated hyperkinesis and dysautonomia required continuous sedation with Propofol, Dexmedetomidine, Ketamine and Phenobarbital among other non-intravenous medications. After sixty-four days in the ICU including sixty-two requiring general anesthesia infusions, DBS was placed. Fifteen days after activation of the system, all of her general anesthesia had been discontinued and she was successfully transitioned out of the ICU for medication weaning and rehabilitation.
CONCLUSIONS: Pallidal DBS was used to successfully ameliorate anti-NMDA receptor encephalitis induced super-refractory status dystonicus. DBS should be considered earlier in the course of medically refractory status dystonicus and may limit the need for long-tern sedation and protracted ICU care.
KEYWORDS: Movement Disorders (including Cerebral Palsy), Infections/Neuroimmunology

395. Efficacy and safety of abobotulinumtoxinA in pediatric lower limb spasticity (PLLS): 2nd interim results from a phase IV, prospective, observational, multicenter study

Gormley Mark (St. Paul, MN, United States) Dabrowski Edward, Tilton Ann, Christian Asare, Evans Sarah, Maisonobe Pascal, Wietek Stefan

OBJECTIVE: The primary objective was to assess subject-centered, function-related goal attainment (T-Score) after repeated abobotulinumtoxinA (aboBoNT-A) injections. Long-term safety (up to 18 months) was also assessed.
METHODS: This phase IV study was designed to collect real-world data on the clinical use of aboBoNT-A in patients with PLLS (aged 2-17 years). Prescription decisions were made prior to, and independent from, study enrollment. Functional goals (utilizing the T-score) were identified at baseline by patient/parent/caregiver in consultation with investigators. Adverse events were reported.
RESULTS: This second interim analysis included N=201 patients, of which 78.1% were botulinum neurotoxin (BoNT)–non-naïve, and 69.2% were aged 2-9 years. The cumulative T-score for the total population was 51.6 (SD 9.69). By the last treatment assessment, mean T-score for the total population was 48.1 (8.08); BoNT-naïve (N=44) had a T-score of 52.1 (3.58) versus 47.5 (8.47) in BoNT–non-naïve; in patients aged 2-9 years, T-score was 46.7 (8.31) versus 52.1 (6.41), respectively, in patients aged 10-17 years. In the safety population (N=243), 44 TEAEs were reported in 26 patients (10.7%); most were mild to moderate, with 1 reported as severe. Pain in extremity, limb discomfort, muscle swelling, and myalgia reported in 3 patients were deemed treatment-related. No reported TEAEs led to study drug withdrawal or death.
CONCLUSIONS: Goal attainment outcomes reflect overachievement (T-score slightly larger than at 50.0) for the overall PLLS population as well as for BoNT-naïve patients and the 10-17 age subgroup. AboBoNT-A was well tolerated, with a low incidence of TEAEs.
KEYWORDS: Movement Disorders (including Cerebral Palsy)

396. A Randomized Controlled Trial comparing Vitamin B12 monotherapy versus combination multi-nutrient therapy with Vitamin B12 for efficacy in treatment of Infantile Tremor Syndrome

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OBJECTIVE: Infantile Tremor Syndrome is a clinical syndrome of delayed developmental milestones, tremors, anemia and hyper pigmentation of skin, prevalent in Indian children. Though it is strongly believed to be a nutritional deficiency disorder, the exact etiology is not clearly defined.
To compare mean Caregiver impression of change (Likert) scores, CAPUTE (Developmental Quotient, DQ) and VSMS scores (Social Quotient, SQ) at one week and one month in children with Infantile Tremor Syndrome treated with daily injectable Vitamin B-12 *versus* injectable Vitamin B-12 with other multi-nutrients.
METHODS: The study design was an open-label randomized active-controlled non-inferiority clinical trial. Seventy-two (N=72) children aged 3 months to 2 years were enrolled and randomized to receive either 1 mg of daily injectable Vitamin B-12 (B12-only, n=37) *versus* 1 mg of daily injectable Vitamin B-12 with other multi-nutrients (B12+MV, n= 30). Baseline

CAPUTE and VSMS scores were taken and assessments were repeated at 1 week (Likert, CAPUTE) and 1 month (Likert, CAPUTE and VSMS) of therapy.
RESULTS: Primary outcome was assessed in 67 of the 72 enrolled children. Mean (SD) Likert score in the B12-only group was 16.1 (3.7) and in the B12+MV group was 14.9 (3.7); p=0.237. Mean change in DQ (CAT/CLAMS) and SQ (VSMS) at 1 month in the groups were not significantly different.
CONCLUSIONS: Injectable vitamin B12 monotherapy is non-inferior to combination multinutrient therapy with vitamin B12 in improving neurological outcomes at 1 week of therapy and establishes the central etiological role of Vitamin B12 in Infantile Tremor Syndrome.
KEYWORDS: Movement Disorders (including Cerebral Palsy), Neurometabolic Disorders

397. Efficacy of Parent-Delivered Home-based Therapy for Tics
Singer Harvey (Baltimore, MD, United States) McDermott Shelley, Ferenc Lisa, Specht Mathew, Mahone E

OBJECTIVE: Although behavioral therapy is an effective approach to reduce tics in children and adults, there is insufficient availability and accessibility of behavioral therapy in the community. The goal of the study was to test the clinical efficacy of home-based, parent-provided behavioral therapy in children with Tourette syndrome, ages 7-13 years.
METHODS: An instructional habit reversal training (HRT)-based video and guide was developed for use by parents. Eligible families, in this 10-week study, were enrolled in either a home-based therapy (DVD) group (received disk and written instructions) or an in-person therapist (IPT) group (scheduled visits with the therapist). Outcome scales included the Yale Global Tic Severity Scale (YGTSS) - both the total Tic Severity Score (TSS) and total Global Severity Score (GSS), and the parent report of Clinical Global Improvement (CGI-I).
RESULTS: Forty-four children (mean age =10.21+1.69 years) were enrolled into either the DVD (n=33) or IPT (n=11) groups. Eighteen completed the study; 8 in the DVD and 10 in the IPT group. Outcome measures showed significant reductions in YGTSS change ratios: mean improvement on the TSS was DVD 32.4% (p<.001) and IPT 26.6% (p=.01); and for the GSS, DVD 33.7% (p<.001) and IPT 26.7% (p<.001). In individuals completing the study, a parent CGI-I ranking of “very much” or “much better” was for the DVD group 50%; and IPT group 40%.
CONCLUSIONS: Home-based, parent-administered HRT behavioral therapy is efficacious for reducing tics in children. Required brief telephone contacts early in the DVD treatment course, might reduce the number of dropouts.
KEYWORDS: Movement Disorders (including Cerebral Palsy)

398. Profile of children with movements disorders (metabolic and genetic causes): single center study
Ali Elsayed (Dhahran, Saudi Arabia)

OBJECTIVE: To determine the metabolic and genetic causes among children presenting with movement disorders in single center study over a period of 20 years.
METHODS: We retrospectively reviewed the medical records of 135 patients presenting to the outpatient clinic, Dhahran, Saudi Arabia with movement disorders between 1999-2019. Metabolic screening done at the central laboratory in KFSH& RC, Riyadh. The genetic testing is

done outside laboratory (Bioscientia, Germany). The types of genetic testing requested are; either targeted gene test, NGS gene panel, or whole exome sequencing (WES). WES interpenetrated as pathogenic, likely pathogenic or VUS.
RESULTS: 55 children (40%), found to have genetic and metabolic causes for their movement disorder. Ataxia in 15 patients with different mutations,like VLDR, GEM1N4, DARS2, WWOX, SACS, KIF1A, COQ8A.. 7 Joubert syndrome. 8 cases Neuronal Ceroid Lipofusinosis. 7 with Glutaric aciduria type1. 4 with Organic academias and 3 NK Hyperglycinemia. 5 Parkinsonism (PLA2G6, ATP13A2, SLC6A3, and 2 sibs with SLC18A2 mutations. Mitochondrial diseases 6 (2 Leigh disease LRPPRC, PET100, POLG). Rett syndrome; 4;.7 Children masquerading as cerebral palsy (CP mimics), l2 withTUBB4A-related leukodystrophy,2 sibs with Aicardi-Goutieres syndrome, 1 torsion dystonia
CONCLUSIONS: Due to high prevalence of consanguineous marriage in Arabia, movement disorders due to genetic and metabolic diseases are common and now possible to be diagnosed earlier due availability of genetic testing. So management with special diets and cofactor supplementation can cure or alter the prognosis of metabolic diseases. Early genetic counseling and PGD can be offered to families with incurable diseases.
KEYWORDS: Movement Disorders (including Cerebral Palsy), Neurometabolic Disorders, Genetics

399. Provider Education Programming Boosts Knowledge Around Diagnosing Tourette Syndrome

Tollner Chelsea (Long Beach, NY, United States) Sullivan Angela, Shineman Diana

OBJECTIVE: Tourette Syndrome is a complex neurological disorder characterized by motor and vocal tics, affecting about 1/160 school-aged children. Tourette is a lifelong condition that affects all races, ethnicities, and genders. CDC estimates suggest that 50% of children go undiagnosed. Diagnosis of Tourette can be challenging, particularly for general providers, due to its complexities and heterogeneity of symptoms across individuals. Currently, neurologists are diagnosing Tourette more than other providers. According to a recent web-based survey conducted by the Tourette Association of America (TAA), approximately 70% of children and 60% of adult respondents with Tourette were diagnosed by a neurologist. When asked about time to diagnosis, 71% of parents of children with Tourette reported diagnosis within 2 years of symptoms, while 50% of adults were diagnosed after 6+ years. Additional provider education is necessary to increase diagnosis and provide effective evidence-based treatment.
METHODS: TAA offers nationwide Tourette Syndrome provider education trainings for physicians and allied health professionals working in pediatrics, neurology, psychiatry, and related disciplines through a 16-year partnership with the CDC. Trainings provide an overview of Tourette and other Tic Disorders, co-occurring conditions, differential diagnosis, effective treatments, and case management strategies.
RESULTS: Between 2015-2019, TAA reached 1,982 providers through 41 trainings. 96% of professionals reported improved skills in diagnosing/recognizing Tourette. 88% reported they intended to add Tourette Syndrome education to their practice.
CONCLUSIONS: Provider education can increase awareness and understanding of Tourette Syndrome diagnosis and is a step toward decreasing time to diagnosis and ensuring better healthcare across the lifespan.
KEYWORDS: Movement Disorders (including Cerebral Palsy)

400. Improved Motor Function in Children With AADC Deficiency Treated with Eladocagene Exuparvovec (PTC-AADC): Interim Findings From a Phase 1/2 Study

Wuh-Liang Hwu Paul (Taipei City, Taiwan) Chien Yin-Hsiu, Lee Ni-Chung, Tseng Sheng-Hong, Conway Anne Marie, Pykett Mark, Tai Chun-Hwei

OBJECTIVE: AADC deficiency is caused by mutations in the gene encoding the enzyme AADC, resulting in dopamine deficiency and movement disorders. Current treatments fail to restore dopamine levels and improve motor function. We report interim findings from a study evaluating efficacy and safety of PTC-AADC, a recombinant adeno-associated virus vector containing human cDNA encoding AADC.
METHODS: This is a 2-year interim analysis from a 5-year, phase 1/2, prospective, open-label trial in AADC deficiency using bilateral intraputaminal injections of $1.8x10^{11}$ vg PTC-AADC. Endpoints and assessments are shown (table). Mean follow-up was 39.9 months.
RESULTS: Of 10 patients (median age 34.0 months) treated, 1 withdrew at 11 months (influenza B encephalopathy leading to death). All others completed follow-up through year 2. Motor function scales significantly improved over 4 years (figure). Mean body weight increased in year 1 (P=0.0011). Hypotonia, oculogyric crises, limb dystonia, and stimulus provoked dystonia decreased. Mean putaminal ^{18}F-DOPA uptake increased by year 1 and through year 2. No viral shedding was detected. All patients experienced ≥1 TEAE (mostly mild or moderate); none were considered definitely treatment-related. 27/131 TEAEs were possibly treatment-related, including 18 dyskinesia episodes; most resolved within 6 months. Seven patients experienced 18 serious AEs; all resolved except influenza B encephalopathy in 1 patient resulting in death. All were considered unrelated to treatment.
CONCLUSIONS: Children with AADC deficiency achieved improvements in motor function after intraputaminal PTC-AADC therapy. No new safety signals were identified. These findings support the efficacy and safety of PTC-AADC in AADC deficiency.
KEYWORDS: Movement Disorders (including Cerebral Palsy), Neuromuscular Disorders

401. The effect of one year intrathecal baclofen treatment in children and adolescents with dyskinetic cerebral palsy

Bonouvrie Laura (Amsterdam, Netherlands) Haberfehlner Helga, Becher Jules, Vles Johan, Vermeulen R, Buizer Annemieke

OBJECTIVE: Previously reported results (IDYS trial) showed better attainment of personal treatment goals in patients with severe dyskinetic cerebral palsy (CP) with intrathecal baclofen treatment (ITB) compared to placebo after three months of blinded treatment. The primary aim of this study was to describe the effect of ITB after one year treatment.
METHODS: This study was a prospective cohort study. Patient previously included in the IDYS trial were followed up 12 months after pump implantation. Patients with severe dyskinetic CP aged 4 to 24 years (Gross Motor Functioning Classification System level IV and V), effectively receiving ITB were included. The primary outcome was goal attainment scaling of individual treatment goals (GAS T-score). Dystonia was measured with the Barry Albright Dystonia Scale (BADS) and the Dyskinesia Impairment Scale (DIS).
RESULTS: Twenty-seven out of thirty-eight patients (71.1%) achieved at least one treatment goal after 9-12 months of ITB treatment. GAS T-scores increased on average with 19.12 (95%

confidence interval=14.49-23.74; p<0.001; Effect size Cohen's *d*: 1.39). Change in pain scores is a predictor for poor outcome on the GAS. Complications occur frequently. The BADS score and the DIS dystonia score during rest showed a small but significant decrease after 12 months of treatment compared to baseline.
CONCLUSIONS: Goals are well attained after 12 months ITB treatment. The overall decrease in dystonia is significant but small and the clinical relevance is still unknown. To benefit outcome of ITB adequate pain management should be provided and management to avoid complications should be optimized.
KEYWORDS: Movement Disorders (including Cerebral Palsy), Translational/Experimental Therapeutics

402. Puerto Rican family cohort presenting with rapid-onset dystonia-parkinsonism due to an ATP1A3 Pathogenic Variant
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OBJECTIVE: To describe a Puerto Rican family with three affected members with an ATP1A3 pathogenic variant that presented with the rapid-onset dystonia-parkinsonism phenotype.
METHODS: We describe a family with three affected members with the ATP1A3 c.2267G>A(R756H) pathogenic variant who presented with the rapid-onset dystonia-parkinsonism phenotype.
RESULTS: Retrospective review of a family with ATP1A3 pathogenic variant (n=3). In all of the three affected members, same pathogenic variant found(c.2267G>A(R756H). Age of onset of all patients during childhood. Patient IIa and IIb were ten years old and five years old respectively. All patients presented rapid onset of symptoms triggered by fever. Bulbar symptoms were the most prominent symptom with dysarthria, mutism, and dysphonia. A rostrocaudal gradient of dystonia and parkinsonism were observed in 100% of the patients. Trial of levodopa-carbidopa was given to 75% of patients(IIa and IIb) without response. Symptomatic relief of dystonia seen with benzodiazepine trial.
CONCLUSIONS: Rapid-onset dystonia-parkinsonism phenotype is well described in the literature by the abrupt onset of bulbar symptoms and rostrocaudal gradient of dystonia and parkinsonism. We report a family with ATP1A3 pathogenic variant. To our knowledge this is the first family reported in Puerto Rico. It is imperative to create awareness to consider genetic testing in a patient with abrupt onset, rostrocaudal gradient dystonia, and prominent bulbar findings.
KEYWORDS: Movement Disorders (including Cerebral Palsy), Genetics, Rare Diseases

403. Near-infrared spectroscopy (NIRS) based neurofeedback training in children with Tourette syndrome
Cheong Pou-Leng (Hsinchu, Taiwan) Sun Chia-Wei

OBJECTIVE: Our goal is to develop a wearable wireless non-invasive NIRS device for checking prefrontal activation and developing and effective neurofeedback program at out-patient clinic settings to provide a treatment alternative in TS patients.

METHODS: 6-15 years old Tourette syndrome subjects were included, excluding those with intelligent quotient <70, developmental disabilities or other neurological diseases like epilepsy. After the Tourette severity evaluation (YGTSS) and neuropsychiatric tests, they received the NIRS examination with the Posner paradigm and then 8-week NIRS-based neurofeedback training with real-time oxy-Hb monitor of degree of prefrontal activation. Tourette severity evaluation and the NIRS examination (Posner paradigm for attention) were followed up at a 3-month interval for 1 year after the neurofeedback training.
RESULTS: 11 TS children with persistent tics and tic impairment score ³30 in the Yale Global Tic Severity Scale (YGTSS)children were recruited for neurofeedback training. (male: female= 9:2, mean age: 10.18 years old, mean YGTSS score: 59.45). During the neurofeedback training, their tics disappear on increased oxygenated hemoglobin (oxy-Hb) level and 10 succeeded in reducing or stopping the initial drug use after one-year follow-up.
CONCLUSIONS: Our light wireless wearable NIRS device with this neurofeedback training protocol was shown to be well performed at out-patient clinic setting. NIRS based neurofeedback training needs patients to be able to be focused during the training and thus more interesting game-based neurofeedback protocol which can let subjects be more attended and personalized would be an important future development prospect.
KEYWORDS: Movement Disorders (including Cerebral Palsy), Neuroimaging

404. High practice variability in cerebral palsy diagnosis: a need for clarification of the consensus definitions?
Gilbert Laura (Saint Louis, MO, United States) Fehlings Darcy, Shetty Sheetal, Fahey Michael, Tilton Ann, Kruer Michael, Aravamuthan

OBJECTIVE: To determine whether practice variability exists within cerebral palsy (CP) diagnosis. We sought to characterize diagnostic variability between practitioners given possible heterogeneous practice styles between specialties, newly discovered CP etiologies (e.g. genetic), and contrasting European and Australian CP registry guidelines regarding the inclusion of hypotonia.
METHODS: We surveyed physician members of the American Academy of Cerebral Palsy and Developmental Medicine or the Child Neurology Society Neonatal Neurology, Movement Disorders, or Neurodevelopmental Disabilities Special Interest Groups. After providing the 2007 international consensus definition of CP, the online survey probed physician views on CP diagnosis in four hypothetical case scenarios.
RESULTS: Of 695 physicians contacted, 330 (47%) completed the survey. Two scenarios yielded consensus: 1) non-progressive spastic diplegia associated with prematurity and periventricular leukomalacia (96% would diagnose CP), and 2) progressive spastic diplegia (92% would not diagnose CP). However, diagnostic variability was revealed when presented with a non-progressive motor disability of a genetic etiology. 67% would diagnose CP in the setting of spastic diplegia, and 46% would diagnose CP in the setting of generalized hypotonia. Of those surveyed, neurologists were more likely than other specialists to diagnose CP in the setting of non-progressive generalized hypotonia with a genetic etiology.
CONCLUSIONS: Physicians demonstrated CP diagnostic variability in the setting of genetic etiologies or generalized hypotonia, despite the provision of the 2007 international consensus definition of CP. This variability between practitioners could result in distress for patients and

families and limit access to necessary treatments. These concerning results may warrant clarification of the international consensus definition.
KEYWORDS: Movement Disorders (including Cerebral Palsy)

405. Selective loss of parvalbumin expressing GABAergic neurons in the globus pallidus of an animal model of dystonic kernicterus
Yang Fu-Chen (Kansas City, MO, United States) Traxler Catherine, Stopperan Julia, Riordan Sean, Stanford John, Shapiro Steven

OBJECTIVE: Our animal model of kernicterus, jaundiced Gunn rat pups model given sulfonamide (jj-sulfa) to displace bilirubin from blood into brain tissue, is remarkably similar to human kernicterus. In both, globus pallidus (GP) is affected and associated with secondary dystonia. We hypothesize that selective loss of GP parvalbumin positive (PV+) GABAergic neurons is the primary cause of dystonic kernicterus, and if so, replacing these cells would be a suitable target for cell-based therapies.
METHODS: At postnatal day 17 (P17) jjs and littermate non-jaundiced (Nj) controls who were then injected with either sulfonamide 100mg/kg or saline. At P21, rats were perfused, their brains sectioned, and GP analyzed immunohistochemically for PV and the neuronal marker NeuN. PV+ neurons and total neurons (NeuN) were counted by two individuals blinded to the experimental groups in 10 GP sections per animal.
RESULTS: At sacrifice, jj-sulfa rats were severely dystonic while jj-saline and Nj-sulfa were unaffected. Our results showed: 1) The number of PV+ neurons in the GP was significantly lower in jj-sulfa rats (600±52(mean±sem);n=6) versus Nj-sulfa (2303±75;n=6) (p<0.0001) and jj-saline (1896±53;n=4) (p<0.0001). The number of neurons NeuN+ but not PV+ did not differ significantly between the groups.
CONCLUSIONS: There is a striking preferential loss of PV+ neurons compared to non-PV+ neurons in GP in our experimental jj-sulfa model of kernicteric secondary dystonia. We hypothesize that loss of PV+GABAergic GP neurons is a cause of this dystonia and suggest that replacing these cells would be a suitable target for cell-based therapies.
KEYWORDS: Movement Disorders (including Cerebral Palsy), Rare Diseases

406. Brain structural and microstructural alterations in Children with Spastic diplegic cerebral palsy
Ogura Kaeko (Tokyo, Japan) Abe Nobuhito, Arai Hiroshi

OBJECTIVE: Spastic diplegic cerebral palsy (SDCP) due to periventricular leukomalacia is a common type of cerebral palsy, which associated with both motor and nonmotor symptoms. We applied voxel-wise tract-based spatial statistics (TBSS) of diffusion-tensor imaging (DTI) including measurements of fractional anisotropy, a parameter of neuronal fiber integrity, as well as cortical thickness to identify structural changes of brain in children with SDCP.
METHODS: Twenty-six patients (mean age, 10.2 years) and 18 healthy children (mean age, 9.9 years) underwent DTI and three-dimensional spoiled gradient echo imaging for cortical thickness. Clinical metrics included the Gross Motor Function Classification System, the Manual Ability Classification System, and intelligence quotient. The study was approved by the Institutional Review Board of Bobatn Hospital. All of the subjects gave written informed consent

to participate in the study after its nature and possible consequences had been explained to them. There is no conflict of interest.
RESULTS: Compared with controls, SDCP children showed decreased FA in the splenium of the corpus callosum, posterior limb of internal capsule, midbrain, and corona radiata diffusively. SDCP children also showed decreased cortical thickness was found in the right superior parietal cortices.
CONCLUSIONS: The results confirmed previous neuroimaging findings and identified new cortical region, and they could help explain the symptoms in SDCP with periventricular leukomalacia.
KEYWORDS: Movement Disorders (including Cerebral Palsy), Neuroimaging

407. Gross Motor and Intellectual Functioning Among Children with Cerebral Palsy: Is There Any Association?
Saad Tania (Dhaka, Bangladesh) Akhter Shaheen

OBJECTIVE: To assess the relationship between gross motor and intellectual functions among the children with Cerebral Palsy.
METHODS: This cross sectional study was carried out in the Institute of Paediatric Neurodisorder and Autism (IPNA), BSMMU, Dhaka, during Oct. 2017 to May 2018. A total of 82 children, under 12 years of age, diagnosed as CP (according to the current definition) were enrolled in this study. The gross motor function of all children was evaluated using GMFCS. Psychological assessment of all the patients was done by professional psychologist using age specific psychometric tools. Statistical analyses was obtained by SPSS-23.
RESULTS: One third of the patients (39.0%) belonged to age 2-4 years.More than three fourths of the patients (85.4%) were of term gestational age. Perinatal asphyxia was associated in 92.7% patients, 30.5% had neonatal seizure and 12.2% patients had epilepsy. Spastic quadriplegic CP constituted 57.4% of population. Almost half of the patients (48.8%) GMFCS level was II, 28.0% patients were of GMFCS level III. Nearly a half (48.8%) patient was with mild intellectual impairment and 22.0% patients were with moderate intellectual impairment. There is a significant negative Spearman's correlation (r=-0.639; p=0.001) between GMFCS and intellectual levels.
CONCLUSIONS: There is a significant correlation found between gross motor and intellectual functioning among children with CP. This finding indicates that more severe motor impairments are associated with higher intellectual dysfunction. Therefore, it may help in a quick assessment of the spectrum of illness, planning for early intervention and communicating more effectively with the parents of children with CP.
KEYWORDS: Movement Disorders (including Cerebral Palsy)

408. Rapid improvement of Sydenham chorea (SC) after concurrent single dose of high dose steroids and IVIG
Osman Mohaned (Cambridge, MA, United States) Luo Yancheng, BudhuJB Joshua, Chu Catherine, Swoboda Kathryn

OBJECTIVE: SC is the most common form of acquired chorea in childhood. This acquired movement disorder is characterized by chorea (involuntary brief, random and irregular movements of the limbs and face), emotional lability, and hypotonia. Although SC is one of the

most well-characterized post-infectious immune-mediated neurologic disorders, first-line treatments, target basal ganglia symptoms rather than the understood pathophysiology. Comparable immune-mediated neurologic disorders are treated with a combination of rapid and chronic immunosuppression. We propose that a similar mechanistically principle approach should be considered in SC.
METHODS: We report a case of a 13 year old Male with PMH of ADHD who presented to the Neurology clinic with abnormal movements for 3 weeks and recent emotional liability.
RESULTS: Neurological evaluation was remarkable for significant motor impersistence, continuous random, purposeless, non-rhythmic jerking movements. Throat culture was positive for GAS, ESR slightly elevated to 15, work-up otherwise unremarkable including, EKG, Cardiac echocardiogram and MRI Brain. A diagnosis of SC was made. Patient was treated concurrently with high dose methylprednisolone and IVIG with marked improvement of his movements after 1 dose of each.
CONCLUSIONS: We chose to treat our case like other discrete CNS immune mediated conditions, from a pathophysiologic viewpoint, the available data suggest involvement of the basal ganglia and cortical structures[1]. Our treatment approach was directed at decreasing antibody production (steroids) and rapidly removing the circulating antibodies (IVIG) simultaneously. To our knowledge we are not aware of similar cases of SC treated concurrently with steroids and IVIG, with marked improvement in this short period.
KEYWORDS: Movement Disorders (including Cerebral Palsy), Infections/Neuroimmunology, Rare Diseases

409. Idiopathic Moyamoya Disease Presenting as Isolated Hemichorea
Abdul Hamid Omer (Memphis, TN, United States) Klimo Jr. Paul, Choudhri Asim, Elijovich Lucas, Shah Namrata

OBJECTIVE: To describe a case of a 7 year-old Caucasian girl who developed isolated chorea in her right upper and lower extremities progressively increasing over 2 years.
METHODS: Literature review of children presenting with chorea as the only manifestation in Moyamoya disease.
RESULTS: 7 year old right-handed Caucasian girl presented with progressively worsening choreiform movements in her right upper and lower extremities affecting her fine motor skills and gait impairment. There was no motor weakness, hyperreflexia or spasticity on her neurological exam. Neuroimaging studies showed 'Ivy sign'- asymmetric prominence of vessels within the subarachnoid spaces overlying the left cerebral hemisphere with corresponding serpiginous T2 FLAIR abnormality but no parenchymal volume loss or diffusion restriction. MRA showed focal moderate to severe stenosis at the junction of the paraophthalmic and supraclinoid segments of the left ICA, with post-stenotic dilatation. Angiography demonstrated focal stenosis involving the ophthalmic segment of the left internal carotid artery with 50% stenosis. There was compensation through a medium sized left posterior communicating artery as well as PCA to MCA and ACA collateralization. Brain SPECT scan showed no evidence of perfusion defects in the cerebral hemispheres, basal ganglia or thalami. She underwent successful revascularization procedure (left pial synangiosis) with resolution of her choreiform movements and normalization of her gait. Neuroimaging studies will be presented with poster.
CONCLUSIONS: Our case demonstrates that Moyamoya disease should be suspected when evaluating children with hemichorea and describes resolution of these movements after

revascularization surgery. Neuroimaging and vascular studies should be obtained in children with unilateral movement disorder.
KEYWORDS: Movement Disorders (including Cerebral Palsy), Stroke (including other Vascular Disorders), Neuroimaging

410. Inter-relation between quality of life, hand functioning and cognitive abilities of CP children: prospective randomized study.
Voloshyn Taras (Truskavets, Ukraine)

OBJECTIVE: It is not cost-efficient to involve all medical staff and use wide variety of diagnostic and intervention tools for every single patient with cerebral palsy (CP). We should treat primarity related to quality of life manifestation instead of treatment of all symptoms.
METHODS: 606 children aged 2 to 17 years(mean 6years6months) with CP(G80): examined by 3 independent doctors. 56,2%males, 43,8%females. Randomized blinded assessment. Fine hand function assessed by "9-hole peg"test, "Box and Blocks"test, dynamometry. Intellectual functioning assessment done using Raven Matrices. Quality of life (QoL) assessment according to Caregiver Priorities and Child Health Index of Life with Disabilities(CPCHILD).
RESULTS: The mean QoL score for children GMFCS levels I and II was 58.5(SD 16.6), for GMFCS III, IV and V children – 22.4(SD 13.3). QoL was more related to fine hand functioning(r=0,344) than to cognition(r=0,294). There was a strong correlation bond between fine hand functioning and cognition(r=0,663). In case fine hand function improved positive changes in cognition were observed in 73% of subjects($p<0,05$). Correlation between grasp power and IQ was weak(r=0,183). Also grasp power improvement was slightly related to QoL(r=0,099).
CONCLUSIONS: Most important part of the research was the benefit from finding out inter-relation between hand functioning, cognition and quality of life. Study allowed to understand what is better to work on (hand speed, accuracy but not muscle power) for improvement of cognitive functioning. Positive changes in fine hand functioning improve QoL even more than changes in cognition. So in cases of limited rehabilitation resources training of fine motor skills should be prioritised.
KEYWORDS: Movement Disorders (including Cerebral Palsy), Neurorehabilitation, Teaching of Child Neurology

411. Hypodontia and Developmental Regression as Diagnostic Clues in POLR3A-related Hypomyelinating Leukodystrophy: A Case Report
Cay-Martinez Karla (New York, NY, United States) Heshmati Arezou

OBJECTIVE: POLR3A-related hypomyelinating leukodystrophy (POLR3A-HLD) is a neurodegenerative disorder characterized by a spectrum of neurologic and systemic anomalies. Developmental delay, cognitive decline, and progressive motor and cerebellar dysfunction are hallmarks. Uncommon findings include seizures, optic atrophy, and gaze-evoked nystagmus. Systemic findings often include abnormal dentition, endocrinopathies, and oculopathies in the form of myopia. We describe a patient with POLR3A-HLD, found to have a homozygous mutation in c.2547C>G, in which hypodontia and developmental regression were key for diagnosis.

METHODS: We conducted an evaluation of the pertinent history and results in the EMR along with a literature review in order to assess current understanding on POLR3A-HLD.
RESULTS: A 5 year-old full-term Hispanic girl with a repaired cardiac defect developed normally until age 2 years when she experienced gait and speech difficulties. Symptoms insidiously progressed to include ocular movement anomalies, cerebellar and motor dysfunction, loss of ambulation, dysphagia, hyper-salivation, and cognitive regression. After a first-of-life clinical seizure, the patient was evaluated by inpatient neurology. Initial exam revealed severe cerebellar and motor symptoms (cerebellar dysarthria, gaze-evoked nystagmus, as well as abnormal smooth pursuits, vertical gaze limitations, UMN signs, and tremors), optic nerve atrophy and hypodontia. Brain MRI showed significant global hypomyelination, and an EEG demonstrated focal right parietal slowing. Clinical suspicion of POLR3A-HLD was confirmed with a genetic assay positive for homozygous mutation in c.2547C>G.
CONCLUSIONS: POLR3A-HLD represents a diagnostic and treatment challenge that requires a multidisciplinary approach to address symptoms. Subtle clinical features such as hypodontia can aid in early diagnosis and ascertain extent of disease.
KEYWORDS: Movement Disorders (including Cerebral Palsy), Genetics

412. Incidence and risk factors for cerebral palsy and hypotonia in children with congenital heart disease
Ghosh Suman (Gainesville, FL, United States) Co-Vu Jennifer, Bleiweis Mark

OBJECTIVE: Children with congenital heart disease (CHD) are at an increased risk for neurodevelopmental delay, epilepsy and learning disabilities from brain injury such as stroke, hypoxic ischemic encephalopathy and white matter injury. This studies aims to determined the incidence and risk factors associated with cerebral palsy and hypotonia in this population.
METHODS: We conducted a retrospective chart review of infants who underwent congenital heart surgery at our institution from 2006 till 2017. Children with follow up for at least two years after surgery were included in our analysis. Diagnosis of cerebral palsy or hypotonia was made by a pediatric neurologist or developmental pediatrician.
RESULTS: Of the 250 patients who met study criteria, 18.8% were found to have cerebral palsy with the majority with spastic hemiplegic cerebral palsy and 44.7% of the study population were diagnosed with hypotonia.
CONCLUSIONS: Most common etiology for cerebral palsy were stroke and white matter injury. Risk of cerebral palsy increased with risk of mortality associated with corrective congenital heart surgery, STAT score. This study provides information that may be used to identify and monitor CHD infants at risk for cerebral palsy and hypotonia.
KEYWORDS: Movement Disorders (including Cerebral Palsy), Neurorehabilitation, Stroke (including other Vascular Disorders)

413. Neonatal Bilirubin Encephalopathy as a Complication of HSV Skin, Eye, and Mouth Disease (SEM)
Kasischke Karl (Tampa, FL, United States) Morgan Bethanie, Cuffel Kelly, Avallone Jennifer, Geller Thomas

OBJECTIVE: Skin, Eye and Mouth disease (SEM) is a frequent neonatal herpes simplex virus (HSV) infection characterized by external lesions to the skin, eye, and mouth without internal

organ involvement. It accounts for 45% of neonatal HSV cases. Even without CNS involvement, there is an underappreciated risk for severe neurological sequelae as exemplified by the case presented here.
METHODS: Case report
RESULTS: A boy born at 38 weeks via normal spontaneous vaginal delivery was discharged home after 24 hours. He presented to the hospital after 4 days for lethargy, decreased PO, and lack of crying. Bilirubin was found to be 37 mg/dl. Mucocutaneous PCR was positive for HSV. CSF studies were normal and without pleocytosis. Both serum and CSF HSV PCR were negative. Brain MRI showed acute bilirubin encephalopathy with bilaterally elevated T2 and FLAIR signal in the globus pallidus and ischemic changes in the splenium and hippocampus. He had neonatal seizures, developmental delay, and failure to thrive (FTT) in early life. At 7 months old, he re-presented with abnormal involuntary movements including stiffening of both arms, hypertonia, dystonia, opisthotonus, and retrocollis. His exam was remarkable for setting sun sign with bilateral tonic downward gaze and limited upgaze without signs of increased intracranial pressure on neuroimaging. FTT was attributed to the increased metabolic demand from frequent abnormal involuntary movements related to dystonia. Hypertonicity and dystonia improved with oral diazepam treatment.
CONCLUSIONS: Kernicterus is an underappreciated risk associated with SEM disease. Severe neurological complications may arise from this systemic infection even without primary CNS involvement.
KEYWORDS: Movement Disorders (including Cerebral Palsy), Neonatal & Fetal Neurology, Neuroimaging

414. Efficacy and safety of low dose penicillamine therapy of neurologic Wilson disease–A prospective observational study.
Kundu Gopen (Dhaka, Bangladesh) Islam Rumana, Akhter Shaheen

OBJECTIVE: To assess the safety & the clinical outcome of treatment with low dose penicillamine, in Wilson disease presented with neurological manifestations
METHODS: A Prospective observational study was conducted at Bangabandhu Sheikh Mujib Medical University (BSMMU), Dhaka. Thirty nine (39) patients of Neurologicwilson disease wereevaluated at paediatric neurology ward during the period of January 2012 to December 2019. Follow up was done after treatment with low dose penicillamine (250mg) therapy of 39 Neurologic Wilson disease to see the outcome.
RESULTS: Total number of studied children were 39. Mean age was 10.2 ± 3.1 year and male to female ratio was 2:1. Among them 20.51% had history of consanguineous mating parents .Progressive deterioration of school performance (89.74%), gait disturbance (92.31%), dysarthria (92.31%) and dystonia (41.03%) was found. KF ring found in 83.33% of patient. Neuroimaging study showed basal ganglia hyperintensity in 53.85.% , white matter hyper intense signal changes 15.38% cases and ischemic change in grey matter in 15.38 % cases. Majority of the children (74.36%) were improved with pencillamine therapy. KF ring disappeared in 5.12% cases after therapy in follow up. Commonest side effects were worsening of neurological symptomsin 25.64 % and rash & fever in 5.1% cases after penicillamine therapy.
CONCLUSIONS: In our study about three forth cases of Neurologic Wilson diseases were improved with low dose penicillamine therapy. One fourth cases of Neurologic Wilson diseases

were deteriorated with this therapy that is lower, compared to previously reported high dose therapy.
KEYWORDS: Movement Disorders (including Cerebral Palsy)

415. Dystonia - Different Prospects
Rizk Tamer (Saint John, New Brunswick, Canada)

OBJECTIVE: Movement disorders are considered one of the most controversial diseases when it comes to diagnosis, classification, and evidence-based lines of management, each case is different, and it can be quite challenging to get these movements under control. Dystonia may result from either diffuse or localized pathology of the cerebral cortex, brain stem, or spinal cord. Management of dystonia is challenging, and specific goals should be identified. We aim to discuss dystonia from a new perspective.
METHODS: This book covers: 1. Orofacial Dystonia and Other Oromandibular Movement Disorders 2. Non-Motor Symptoms in Patients with Primary Dystonia
3. Tardive Dystonia due to D2 Antagonists and Other Agents
RESULTS: Dystonia is considered one of the most disabling conditions in the pediatric age group, which may remain until adulthood; treatment is usually unsatisfactory.
CONCLUSIONS: Movement Disorders continue to be a serious burden that call for better understanding, prompt recognition, prevention, and better treatment.
KEYWORDS: Movement Disorders (including Cerebral Palsy)

416. Status Dystonicus: A case of Deep Brain Stimulation as a Diagnostic Tool
Turek Grant (Louisville, IN, United States) Schuster Catherine, Barton Christopher

OBJECTIVE: Describe a case of Status Dystonicus managed with Deep Brain Stimulation (DBS) that re-initiated the diagnostic journey.
METHODS: Status Dystonicus, the severe emergency of movement disorders, has varied etiologies. Difficult to treat, rare, often interventions are pursued before defining an etiology.
RESULTS: 14-year-old male with Spastic Quadriplegic Cerebral Palsy, developmental delay, and sensorineural hearing loss with cochlear implants presented in Status Dystonicus. This affected respirations, vital signs, and acute care. Drastic enough to cause significant rhabdomyolysis, therapies were maximized and exhausted. Further management necessitated a DBS. After removal of cochlear implants, an MRI was obtained for surgical planning. Results lacked white matter injury from the presumed etiology of prematurity. Further investigation included genetic testing. Though various mutations of unknown significance were present, one mutation affected a gene consistent with his presentation and course: KMT2B - Dystonia 28. Though a variant, the deleterious effects of this mutation fit the clinical course including sensorineural hearing loss, early onset dystonia, and intellectual/developmental delay.
CONCLUSIONS: The implantation of cochlear implants delayed delineating the source of the patient's symptoms, but management of the patient's dystonia required placement of DBS that restarted the diagnostic. As more genetic treatments develop and a deeper understanding of minor changes in the human genome is gained, it only becomes more important to elucidate etiology. It is our hope that this serves as a sentinel event encouraging physicians to continue with diagnostic evaluations where question remains and thus further our collective understanding of patient's and ourselves.

KEYWORDS: Movement Disorders (including Cerebral Palsy), Genetics, Rare Diseases

417. Whole exome analysis in pediatric movement disorders

Wong Leechin (Taipei, Taiwan) Lee Wang-Tso

OBJECTIVE: To identify the underlying genetic etiology in children with movement disorders by whole exome sequencing.
METHODS: This prospective study was performed in a childhood movement disorder clinic of National Taiwan University Children Hospital, a tertiary referral hospital in Taiwan. Eligible patients were recruited in the clinic or referred with a diagnosis of childhood movement disorders through collaborating physicians. We collected phenotype data, including movement disorders, developmental history, brain imaging reports, and prior clinical genetic testing reports. DNA samples were collected and performed whole exome sequencing. All variants were classified according to American College of Medical Genetics and Genomics guidelines.
RESULTS: Sixty-two patients were recruited. There were 40 patients had dystonia, 23 patients had chorea/athetosis, 8 patients had myoclonus, 5 patients had tremor, 13 patients had ataxia ,10 patients had paroxysmal movements disorder and 8 patients had parkinsonism. Pathogenic variants were found in 34 patients, leading to a diagnostic yield of 55%. There were 27 different causative genes identified, with FOXG1, GCH1, TBC1D24, NPC1, ATP1A3 being the most common. Of note, disease-specific treatment were administered following genetic diagnosis in some patients.
CONCLUSIONS: We report a satisfying genetic diagnostic yield (55%) in a cohort of pediatric movement disorders. The yield rate is higher than that of the gene panels (11-28%). In addition, the genetic diagnosis led to disease-specific treatments in some patients. In summary, our study show that whole exome sequencing has important implication in both diagnosis and treatment in pediatric movement disorders.
KEYWORDS: Movement Disorders (including Cerebral Palsy), Genetics

418. Assessing quality of life (QoL) in a cohort of children with Cerebral Palsy (CP)

Samia Pauline (Nairobi, Kenya) Tirkha Melissa, Kassam Amina-Inaara, Muindi Richard, Wamithi Susan, Orwa James, Shevell Michael

OBJECTIVE: There is a paucity of data on the quality of life (QoL) of children with cerebral palsy (CP) in Africa. In addition to QoL determination, this study aims to describe clinical characteristics of Kenyan children with CP.
METHODS: This was a cross-sectional study where QoL was assessed by parent proxy-reports using CPQoL-child (n=72) and CPQoL-adolescents (n=15) questionnaires. Clinical data was compiled from medical records. QoL was measured using Likert scales and results were summarized descriptively.
RESULTS: Eighty-seven child–parent dyads receiving treatment for CP were recruited. Majority of the children were male (66%) and the median age was 7 years (IQR=5). The mean age at diagnosis was 10 months (SD=13.2). Although majority of the children (97%) were delivered in hospital, 10% did not obtain any antenatal care and approximately two-thirds (63%) reported complications during delivery. These included birth asphyxia (67.8%), prematurity (10.3%), jaundice (5.7%) and sepsis (5.7%). The mean overall CP-QoL-child score was 60.0 (SD=32.4). For the domain feelings about functioning, the mean was 56.3 (SD=31.9, α=0.82)

and for access to services, the mean was 52.4 (SD=33.1, α=0.78). The mean overall CP-QoL-adolescent score was 68.9 (SD=27.5). For the domain feelings about functioning, the mean score was 69.7 (SD=26.0, α=0.84), and for access to services, the mean score was 47.7 (SD=32.5, α=0.83).
CONCLUSIONS: The overall QoL was more compromised for younger children, compared to that of adolescents. Critically, both groups reported poor QoL in relation to access to services. Preventive and facilitative efforts in healthcare would improve QoL for Kenyan children with CP.
KEYWORDS: Movement Disorders (including Cerebral Palsy)

419. Movement Disorder Phenotypes in SCN8A Encephalopathy
Tochen Laura (Washington, DC, United States) Pierce Emily, Bumbut Adrian, Schreiber John

OBJECTIVE: *SCN8A* encodes Nav1.6, a voltage-gated sodium channel; mutations in *SCN8A* are associated with a spectrum of developmental disorders and epilepsy. The clinical features of genetic developmental and epileptic encephalopathies (DEEs) continue to expand, and many genetic DEEs have been associated with complex movement disorders. We sought to characterize the spectrum of movement disorder phenotypes in individuals with SCN8A –related epilepsy.
METHODS: Subjects with epilepsy due to SCN8A pathogenic variants were recruited through patient advocacy groups, SCN8A.net, and at Children's National Hospital, to participate in a multidisciplinary evaluation. Epilepsy phenotypes were assigned as mild, intermediate, moderate DEE, or severe DEE. Consent/assent was obtained for movement specific interview and video recording. Movement disorder phenotypes were evaluated by direct observation or by history. Additional clinical features of the first 17 subjects were reported previously with limited attention to the movement phenotype.
RESULTS: 22 subjects were included (12 M, 10 F). The most common feature was hypotonia in 18 individuals (82%). 12 subjects were ambulatory (55%), 4 required support (18%), and 6 were non-ambulatory (27%). 11/16 who were ambulatory independently or with assistance had ataxia. Stereotypy was the next most common movement feature in 10 subjects (45%) and was more common in mild-moderate phenotypes. Dystonia was present in 8 individuals (36%), and tremor was present in 5 individuals (23%). Chorea/complex dyskinesia occurred in 3subjects (14%), and was more commonly present in those classified as moderate-severe DEE.
CONCLUSIONS: A wide spectrum of movement disorder phenotypes exist within this SCN8A cohort. Some movement characterizations align with other phenotypic features.
KEYWORDS: Movement Disorders (including Cerebral Palsy), Genetics, Epilepsy

420. Interrater Agreement for Movement Disorder Classification in Children with Mixed Movement Disorders
Masten Margaux (Rochester, NY, United States) Vermilion Jennifer, Dean Shannon, Pourdeyhimi Roxana, Mink Jonathan, Yilmaz Sanem

OBJECTIVE: The Movement Disorders-Childhood Rating Scale (MD-CRS) consists of three parts: classification, general assessment, and movement disorder severity. We tested the classification component to determine the interrater agreement among five pediatric neurologists with training in childhood movement disorders.

METHODS: 112 videos of 66 children with hyperkinetic movement disorders were reviewed independently by five assessors, including a senior pediatric movement disorders neurologist (Rater 1) and 4 individuals trained by him. The raters answered three questions: 1) Is more than one movement disorder present? 2) What is the [prominent] movement disorder? 3) What other movement disorders are present? Fleiss' Kappa scores were computed to evaluate agreement and Cohen's Kappa scores were used to determine the agreement between Rater 1 and the other raters.
RESULTS: The most frequent movement disorders in the sample were dystonia/athetosis (~30%) and chorea/ballism (~30%). Highest agreement for a specific movement disorder was for dystonia. Final agreement on number of movement disorders was 58%. For prominent movement disorder, the highest interrater agreement between any 2 investigators was 89% and the lowest was 76%, but agreement among all five raters was only 42%. For other movement disorders, agreement ranged from 65% to 82% among any 2 investigators.
CONCLUSIONS: Interrater agreement ranged from poor to good, with highest agreement for the prominent movement disorder and the lowest for other movement disorders. Our results suggest that even with formal training, there is substantial disagreement among pediatric movement disorder's experts. We suggest formal training to reliability on the MD-CRS prior to use in research studies.
KEYWORDS: Movement Disorders (including Cerebral Palsy)

421. Normal Motor Organization in Children and Youth with Functional Motor Disorder
Gibbs Savannah (Memphis, TN, United States) Patterson Amy, Weatherspoon Sarah, Wheless James, Narayana Shalini

OBJECTIVE: Functional motor disorders (FMD) represents 4% of pediatric motor disorders and result in debilitating symptoms, stigma, and risk of misdiagnosis, and potential lifelong morbidity. We examined whether the motor organization in children and youth with FMD was altered using transcranial magnetic stimulation (TMS) as a diagnostic technique.
METHODS: We retrospectively identified 5 individuals diagnosed with FMD who underwent upper and lower extremity motor mapping with TMS (see Table 1). The location of the primary motor cortex, the motor threshold and corticomotor latency in the two hemispheres for upper and lower extremities were measured.
RESULTS: In all patients, TMS applied to bilateral primary motor cortices elicited motor evoked potentials in contralateral abductor pollicis brevis (APB) and tibialis anterior (TA) muscles. The location, extent and the corticomotor latencies were found to be within normal limits (Table 1, Figure 1 for examples).
CONCLUSIONS: The primary motor cortices were successfully localized and were found to be normal in all patients with FMD. TMS was found to be a useful diagnostic tool to rule out organic motor disorders by demonstrating normal output from primary motor cortices to the periphery. Additionally, by demonstrating an intact motor network to the individual experiencing FMD, TMS can also be an useful treatment option. Further studies are needed to establish further the diagnostic utility of TMS in elucidating the physiological changes in the motor network in FMD as well as its therapeutic efficacy.
KEYWORDS: Movement Disorders (including Cerebral Palsy), Cognitive/Behavioral Disorders (including Autism), Neuroimaging

422. KMT2B related dystonia – A pediatric case with progressive course

Aksoy Ayşe (Samsun, Turkey) Yayıcı Köken Özlem, Ceylan Ahmet, Toptaş Dedeoğlu Özge

OBJECTIVE: To report a case diagnosed as KMT2B-related dystonia (DYT-KMT2B) which is a complex childhood-onset movement disorder described to date in few patients.
METHODS: A 9 years old male patient presented with his clinical findings and genetic results
RESULTS: A 9 years old male was admitted complaining of involuntary movement of arm, shoulder, forearm and hands. He was born from non-consanguineous parents. He had feeding difficulties (breastfeeding and swallowing) since birth and growth retardation since he was a toddler. He had a nasonated dysarthritic speech in addition to involuntary movements such as twisting, torsion and rotation in bilateral upper and lower extremities which were more prominent on the right and caused postural dysfunction. Muscle strength was 5/5 on the right and 4-/5 on the left. Neuroimaging results were within normal limits. In the follow-up, the movement disorder which was only right sided became bilateral on the whole body and repetitive intermittent generalized dystonia and myoclonus causing oromandibular and bulbar dysfunction was noted in a three-years period. While he was able to live a normal life with the help of haloperidol and trihexyphenidyl treatment, he gradually deteriorated secondary to progressive dystonia in the three-years follow up. Whole exome sequencing revealed a novel nonsense mutation c.2453dupT (p.M818fs*28) on KMT2B (NM_014727.2) (pathogenic according to ACMG).
CONCLUSIONS: The characteristic clinical findings of the DYT-KMT2B was seen in our patient such as developmental delay and progressive disease course evolving commonly from lower-limb focal dystonia into generalized dystonia with prominent cervical, cranial, and laryngeal involvement and bulbar dysfunction.
KEYWORDS: Movement Disorders (including Cerebral Palsy), Genetics

423. Lacosamide for Children with Paroxysmal Kinesigenic Dyskinesia

Furukawa Gen (Toyokawa, Japan) Negishi Yutaka, Takeuchi Tomoya, Ishihara Naoko, Okumura Akihisa

OBJECTIVE: The present This study was performed to evaluate the efficacy and tolerability of lacosamide (LCM) for paroxysmal kinesigenic dyskinesia (PKD) in children.
METHODS: We retrospectively reviewed the medical charts of pediatric PKD patients (aged < 16 years) treated with LCM. Data regarding demographic characteristics, proline-rich transmembrane protein 2 (*PRRT2*) gene variant, clinical features of PKD, dose of LCM, efficacy, and adverse events were recorded. The study was approved by the ethics committee of Toyokawa City Hospital.
RESULTS: Four eligible patients (3 males, 1 female) were identified, with an age of onset ranging from 8.3 to 14.7 years. *PRRT2*variant was evaluated in three children and a c.649dupC variant was identified in one child with a positive family history. Attacks were bilateral in three children and left-sided in one. Two children had a family history of PKD and one child had a family history of benign infantile epilepsy. Treatment with carbamazepine failed in two children due to drowsiness with or withoutand auditory disturbance. The initial dose of LCM was 50 mg/day in three children and 100 mg/day in one. All patients were attack-free within a few days. The maintenance dose was mostly similar to the initial dose. No adverse events related to LCM were reported during follow-up.

CONCLUSIONS: LCM is an effective and well-tolerated treatment for PKD in children, and low-dose treatment may be viable.
KEYWORDS: Movement Disorders (including Cerebral Palsy), Rare Diseases

424. Comparison of Dystonia Rating Scales in Children with Primary (Isolated) Dystonia
Masten Margaux (Rochester, NY, United States) Mink Jonathan

OBJECTIVE: To test an age-independent video protocol in children with primary dystonia and to test the validity and utility of the Burke-Fahn-Marsden Dystonia Rating Scale (BFMDRS), the Barry-Albright Dystonia Scale (BADS), and the Global Dystonia Rating Scale (GDRS).
METHODS: We developed a pediatric video examination protocol and tested the protocol in 16 individuals with dystonia and normal cognition, age 4-16 years. Dystonia etiologies included genetic (DYT1, DYT4, DYT5, DYT6, or DYT11), putamen infarction, or idiopathic. 10 indivdiuals had "isolated dystonia". The others had co-existing ataxia (DYT4), myoclonus (DYT11), chorea (idiopathic), or parkinsonism (DYT5) that prevented precise scoring of dystonia separate from co-existing movement disorders.
RESULTS: Severity ranges in the sample were: BFMDRS 4-80 (Median 24.5); BADS 4-19 (Median 11); GDRS 11-78 (Median 39). The BADS had an apparent ceiling effect. A preliminary correlation analysis was performed to explore cross-validation (Figure). There was a significant positive correlation between all paired comparisons. Based on these, the BADS is unlikely to be superior to the other two scales. Ease of use was highest for the GDRS, which is consistent with prior studies in adult-onset primary dystonia.
CONCLUSIONS: With recent advances in diagnostics, it is apparent that there is both substantial genetic heterogeneity and substantial genetic pleiotropy in childhood-onset dystonia. Furthermore, only a minority of children with dystonia that have truly isolated dystonia. Future natural history studies in childhood dystonia should focus on specific entities and will need to include tools that assess multiple movement disorders, discriminate among coexisting movement disorders, or a combination.
KEYWORDS: Movement Disorders (including Cerebral Palsy), Rare Diseases

425. Transient Segmental Myoclonus Following Combined Liver-Kidney Transplant: A Case Report
McLaughlin Aaron (Dallas, TX, United States) Khan Tuba, Lauritsen Jonathan, Batley Kaitlin, Sabo Tonia, Waugh Jeff

OBJECTIVE: To describe the evaluation and management of acute-onset segmental myoclonus
METHODS: Case Description: A 16 yo Hispanic girl with methylmalonic acidemia, chronic kidney disease, and history of functional neurological disorder manifesting as prolonged blindness underwent combined liver/kidney transplantation with excellent post-operative course. 1.5 weeks after transplant she developed intermittent "jerking" about her abdominal incision site. Soon afterward she was observed to slump, developed rightward head version, right face/eyelid twitching, and generalized tremulousness and unresponsiveness for 2 minutes. Initial Emergency Room workup included normal head CT, normal post-transplant kidney and liver functions, low serum magnesium and elevated serum tacrolimus. The patient received one-time doses of levetiracetam and magnesium with resolution of her jerking movements. Our initial differential

diagnosis included seizure, myoclonus secondary to tacrolimus-induced hypomagnesemia, and functional neurological disorder.
RESULTS: Clinical Course: Her abdominal jerking resumed one day following admission, and she had a second episode of shaking and unresponsiveness. EEG was normal, and abdominal jerking movements did not have an electrographic correlate. On exam, the jerking was non-rhythmic, constant amplitude, resolved in deep sleep, involved the paraspinals (right > left), right peri-scapular muscles, and interrupted her speech but did not vary with breaths. MRI of brain, cervical and thoracic spine was normal. Ultrasound confirmed bilateral diaphragmatic myoclonus.
CONCLUSIONS: While myoclonus has been reported as a side effect of tacrolimus, prior descriptions were limited to generalized or nocturnal myoclonus. The segmental myoclonus in our patient was exquisitely responsive to levetiracetam, which was successfully weaned two months after onset without recurrence to date.
KEYWORDS: Movement Disorders (including Cerebral Palsy)

426. A novel case of opsoclonus-myoclonus
Sweat Marie (San Diego, CA, United States) Sahagian Michelle

OBJECTIVE: To report a case of opsoclonus-myoclonus in a 2 year old male with a MeCP2 mutation
METHODS: A 2 year old male with MeCP2 mutation resulting in global developmental delay, severe hypotonia, central hypoventilation and swallowing dysfunction who presented with severe dysautonomia shortly after a hospitalization for fundoplication complicated by Strep viridans bacteremia. His presenting symptoms included hypotensive shock, respiratory failure and hyperpyrexia to 42.7C. Once sedation was withdrawn the patient was no longer at his neurological baseline and had developed impressive opsoclonus-myoclonus.
RESULTS: MRI brain revealed cytotoxic edema in the basal ganglia. There was no evidence of a focal abnormality in the brainstem or cerebellum. Infectious and metabolic workup was unremarkable. Abdominal ultrasound and urine VMA/HVA completed as part of a neuroblastoma evaluation were negative. Due to medical fragility it was determined the patient would not safely tolerate ACTH. He ultimately received a short course of high dose steroids without improvement of his symptoms.
CONCLUSIONS: Our current understanding of opsoclonus-myoclonus is that it is an immune driven process, either paraneoplastic or parainfectious. This case report suggests an alternative mechanism including sequelae from hypoxia and hyperpyrexia.
KEYWORDS: Movement Disorders (including Cerebral Palsy), Genetics

427. Flying under the radar: the diagnostic dilemma for low excretor Glutaric Aciduria Type 1 with insidious presentation
Foran Jason (Cork, Ireland) Crushnell Ellen, Knerr Ina, Moore Michael, McSweeney Niamh

OBJECTIVE: A 4-year-old girl was referred for assessment of dyskinetic cerebral palsy. Initial investigations in her country of birth, India had not yielded a diagnosis. Her dyskinesia was persistent and intermittently became florid involving all 4 limbs and significant drooling. Motor and speech development were most affected with a preservation of cognitive development. Her

symptoms were not subsequent to an acute encephalopathic crisis in the context of intercurrent illness or an episode of status dystonicus.
METHODS: She was previously found to have bilateral putamen hyper-intensity on MRI.Initial urine organic acids were normal however a dystonia genetic panel showed 2 potentially pathogenic variants on the GCDH gene consistent with a diagnosis of Glutaric Aciduria Type 1 (alternatively Glutaric academia Type 1) (GA1). Repeat urine organic acids showed isolated increased 3-hydroxy glutarate excretion consistent with the diagnosis and characterising the patient as a "low excretor" a group where diagnosis is more difficult but prognosis is similar. Repeat MRI Brain at age 4-showed volume loss and symmetric T2 hyperintensity in the posterior putamina bilaterally.
RESULTS: This case is significant as it highlights the diagnostic dilemma of GA1 where differing clinical courses, genetic mutations, radiological findings and excretion patterns may lead to a later diagnosis than optimal.
CONCLUSIONS: The presence of newborn screening for GA1 should not dull the clinician's suspicion of the possibility that GA1 may be underlying complex movement disorders. Timely diagnosis is essential as neurological sequelae are largely irreversible.
KEYWORDS: Movement Disorders (including Cerebral Palsy), Neurometabolic Disorders

428. Randomized Controlled Trial of Probiotics PS128 in Children with Tourette syndrome
Wu Chang-Chun (Taipei, Taiwan) Wong Lee-Chin, Hsu Chia-Jui, Tsai Ying-Chieh, Lee Wang-Tso

OBJECTIVE: Tourette syndrome is thought to result from a complex interaction between social-environmental factors, multiple genetic abnormalities and neurotransmitter disturbances. Probiotics PS128 has been demonstrated in animal studies to be a psychobiotic strain and to modulate levels of neurotransmitter in the brain. Therefore, we conducted a double-blinded randomized-controlled trial to examine if probiotics improve symptoms of children with Tourette syndrome.
METHODS: This is a double-blinded, randomized controlled trial using Lactobacillus plantarum PS128® as intervention, a Lactobacillus plantarum probiotics. All patients enrolled fulfilled DSM-V diagnostic criteria for Tourette syndrome, and were within 6-18 years-old. Patients were randomly assigned to placebo group or PS128 group for 2 months, followed by open-label trial for 2 months. Patients were assessed before initiating trial, 1 and 2 months after randomization, and a last time after the open label. The primary outcome is evaluated by YGTSS and our secondary outcome studies the possible comorbidities in these children, including ADHD, OCD, migraine, and depression. Stool was also collected at 0, 2, 4 months for microbiota analysis.
RESULTS: Fifty-eight patients were enrolled in our trial. Preliminary data showed that both placebo and PS128 group revealed improvement in YGTSS. It suggested a placebo effect for the control group. However, there was no significant difference in improvement between control group and PS128 group. Secondary outcomes are still under analysis.
CONCLUSIONS: Although probiotics may not have better positive effects in children with Tourette syndrome, further studies are needed to clarify the effects of probiotics on the comorbidities of Tourette syndrome.
KEYWORDS: Movement Disorders (including Cerebral Palsy)

NEONATAL & FETAL NEUROLOGY

429. Long term cognitive outcome of term infants with neonatal encephalopathy
Lee Bo Lyun (Busan, Republic of Korea) Gano Dawn, Rogers Elizabeth, Xu Duan, Lundy Shannon, Christopher Lauren, Barkovich A. James, Ferriero Donna, Glass Hannah

OBJECTIVE: Previously, we reported survivors of neonatal encephalopathy demonstrated watershed distribution injury on neonatal MRI and local changes in perisylvian gray and white matter at 6-month MRI, which were associated with adverse language outcomes in early childhood. However, little is known about later time point outcomes. Our objective is to describe the adolescent cognitive profile of term infants with neonatal encephalopathy.
METHODS: Term neonates with encephalopathy were prospectively enrolled and imaged using 1.5 or 3.0T MRI from 1999-2008. They underwent a brief neurocognitive assessment using various Wechsler Scales of Intelligence (WISC-IV, WISC-V, or WASI-II). Infants were not treated with therapeutic hypothermia (TH).
RESULTS: 23 adolescents were evaluated at 13 ± 2 years (range, 10-16). Neonatal characteristics and MRI findings are presented in Table 1. At follow-up, two children had cerebral palsy and epilepsy; one had attention deficient hyperactivity disorder (ADHD). Neonatal encephalopathy severity score and watershed injury score correlated with worse overall estimated cognitive ability ($P<0.05$). Children with neonatal watershed pattern injury had lower estimated overall cognitive ability, perceptual reasoning skills, and auditory working memory; they demonstrated no significant difference in verbal comprehension skills (Table 2) as compared to a normal neonatal imaging group.
CONCLUSIONS: Severity of encephalopathy and watershed injury are associated with lower overall estimated cognitive ability, especially with regard to nonverbal reasoning skills and auditory working memory in adolescents with a history of neonatal encephalopathy not treated with TH. Differences in these cognitive areas may underlie early language difficulties seen in children with neonatal encephalopathy and watershed pattern injury.
KEYWORDS: Neonatal & Fetal Neurology

430. Neonatal seizure profile in the Neonatal Intensive Care Unit (NICU) at St. Paul's Hospital Millennium Medical College (SPHMMC) in Addis Ababa, Ethiopia
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OBJECTIVE: Neonatal seizures are common in high risk infants, challenging to recognize clinically, and contribute to high morbidity. Hypoxic Ischemic Encephalopathy (HIE), the most common cause of neonatal seizures in the US, is more prevalent in low-middle income countries (LMICs). Neonatal seizure data are limited in LMICs. We aimed to assess the incidence and common etiologies of neonatal seizures at SPHMMC in Addis Ababa, Ethiopia, and how they are recognized and treated.
METHODS: Neonates receiving antiseizure medication over one year were identified from the SPHMMC NICU logbook; available patient records were reviewed.
RESULTS: 159/3090 (5.15%) patients were treated for neonatal seizures. Seizure semiology was described in 54 neonates. 92/159 had HIE; 68/159 had sepsis. 54/159 died. The majority of

patients (115/159) received phenobarbital (Table 1). 9 received outpatient follow-up, 3/9 were on phenobarbital 1 month after discharge. EEG data were available for 5 patients. 55 patients had cranial ultrasounds; two also had a brain MRI. 21/55 were lesional.
CONCLUSIONS: Approximately 5% of neonates in the SPHMMC NICU were treated for neonatal seizures. Seizure semiology documentation was limited and variable, diagnostic studies were obtained infrequently; outpatient follow up was scarce. Common etiologies were HIE and infection. In order to better identify high risk neonates, it is necessary to improve documentation of seizure semiology, rate of head imaging, and access to EEG diagnostics. Through an ongoing quality improvement project, we aim to obtain sustainable, feasible methods of better identifying neonatal seizures in LMICs, which may include amplitude integrated EEG and standardization of seizure documentation (Figure 1).
KEYWORDS: Neonatal & Fetal Neurology, Epilepsy, Critical Care

431. Early BNDF Levels Are Elevated in Very Low Birth Weight (VLBW) Neonates with Abnormal EEGs

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OBJECTIVE: VLBW newborns are at significant risk for poor long-term outcomes, including cerebral palsy. The availability of reliable methods for predicting long-term outcomes after premature birth is lacking. Neonatal EEG is an objective method for early assessment of brain function. The relationship between blood biomarkers and neonatal EEG has not been evaluated.
METHODS: Data were drawn from a retrospective sample of neonates admitted to the Johns Hopkins NICU (2009-2015). Cord blood and serum biomarker levels were measured from banked blood samples by ELISA and included several inflammatory markers (GFAP, IL6, IL8, IL10) and BDNF. An "averaged" biomarker level was calculated for patients who underwent multiple blood draws between days of life 0-4. EEGs were categorized broadly as normal or abnormal (Table 1) and were compared with biomarker levels.
RESULTS: VLBW premature patients (n=335) with no evidence of intracranial pathology were included in this study. EEGs were completed on 16 neonates during their NICU admission (7 normal, 9 abnormal). There were no significant differences in birth weight, gestational age at birth, postconceptional age when EEG was obtained, or gender between the normal and abnormal EEG groups ($p > 0.05$). The abnormal EEG group had significantly elevated BDNF levels compared to the normal EEG group (Figure 1). No other biomarker levels segregated with EEG findings; correlations with specific EEG abnormalities are being evaluated.
CONCLUSIONS: These data demonstrate an association between higher postnatal serum BDNF levels and brain dysfunction as evidenced by abnormal EEG findings. Why elevated BDNF levels correlate with cerebral electrical abnormalities deserves further investigation.
KEYWORDS: Neonatal & Fetal Neurology, Neuroscience

432. Neonatal Neurodevelopmental Impairments at Nursery: Early Identification and effective Interventions in Bangladesh

Salwa Zeena (Dhaka, Bangladesh) Shilpi Asma, Raj Aftab, Ahmed Nizam

OBJECTIVE: This study was carried out at nursery for early identification of neonatal neurodevelopmental impairments and providing early interventions for better outcome.

METHODS: Facility-based cross-sectional study was conducted by Physician and Development Therapist at Square Child Development Center (CDC), Square Hospitals Limited in Bangladesh from April, 2019 to December, 2019 to all neonates of nursery between age15-28 days. A total of 818 neonates were underwent for Neonatal Rapid Neurodevelopmental Assessment (RNDA)[1,2], an assessment instrument was applied to all neonates for early identification of any neurodevelopmental impairments (NDI) with early interventions.
RESULTS: Analysis of the study population revealed the following basic data: 818 neonates were discharged from nursery over this study period and we found male female ratio- 1.14:1, Preterm-170 (20.78%), LBW- 138 (16.87%), Impairment-59 (7.21%). Among 59 newborn, domain wise impairments were detected in primitive reflexes (35.6%), gross motor (71.2%), fine motor (0%), vision 5.08%, hearing (8.5%), speech (3.4%), cognition (0), behavior (0) and seizure was found in 1 (1.7%). Neonates at nursery were born either by normal vaginal delivery or cesarean section, expected to be healthy but we found the above mentioned impairments among 7.21% neonates.
CONCLUSIONS: Neonatal screening (n-RNDA) for the first time is incorporated for all newborn at Square Hospitals Ltd, a private tertiary care hospitals in Bangladesh. All neonates should be assessed for any neurodevelopmental impairments which will provide a functional profile for early interventions. It will also produce a basis for appropriate and early referral for their functional limitations towards an improve quality of life.
KEYWORDS: Neonatal & Fetal Neurology, Cognitive & Behavioral Disorders (including Autism), Neurorehabiliation

433. Feasibility of using plasma extracellular vesicles as a tool to discover novel biomarkers of brain injury and development in very preterm infants: a pilot study
Elitt Christopher (Boston, MA, United States) Ross Madeline, Wang Lan, Balaj Leonora, Rosenberg Paul, Belfort Mandy

OBJECTIVE: Preterm infants are at high risk for brain injury, but the pathogenesis remains unclear due in part to a lack of biomarkers. We piloted sequencing RNA from plasma extracellular vesicles (EVs). As a first approach, we compared EV gene expression in a preterm cohort with an established adult cohort, and compared gene expression in female to male infants. We hypothesized that the gene expression profile in preterm infants would differ from adults, and would be different in infants of different sex.
METHODS: From 8 very preterm infants (gestational age, 23-30 weeks), we collected 0.5-1 mL of whole blood at term equivalent age. We isolated EV RNA from plasma with the Qiagen exoRNeasy kit and sequenced/analyzed RNA using the QIAseq Ultraplex RNA secondary analysis package.
RESULTS: Mean infant plasma EV RNA concentration was 326 pg/uL (range, 79-1,175). The mean number of unique genes identifiable in preterm infant samples was 6,217 (range, 559-14,165). The number of identifiable genes highly correlated with RNA concentration ($r=0.91$). More genes were detectable in infant EVs compared to healthy adult EVs. Comparing gene expression between infant and adult cohorts, 56 genes had significant differences in expression ($p<0.05$). There was also differential expression of 16 genes between female and male infants ($p<0.05$).
CONCLUSIONS: We successfully performed RNAseq on plasma EV RNA isolated from <1 mL blood from preterm infants. Significant differences in gene expression between preterm

infants and adults, and between male and female infants supports the validity of this approach to study brain development and injury in preterm infants.
KEYWORDS: Neonatal & Fetal Neurology, Neuroscience

434. Kernicterus Spectrum Disorders Diagnostic Toolkit: validation using retrospective chart review
Dasari Vijaya (Kansas City, MO, United States) Shapiro Steven, Gelineau-Morel Rose

OBJECTIVE: Kernicterus Spectrum Disorders (KSDs) result from hyperbilirubinemia-induced brain injury. Families of children with undiagnosed neurodevelopmental disorders and a history of neonatal hyperbilirubinemia often question this potential diagnosis. We developed a Toolkit (KSD-TK) questionnaire to predict the likelihood of KSDs. This study compares the accuracy of the KSD-TK to clinical diagnoses made by our Children's Mercy Hospital Kernicterus Center of Excellence (KCOE).
METHODS: We retrospectively reviewed charts of 37 patients evaluated between 2011-2019 at the KCOE. We completed a KSD-TK for each patient using data including highest bilirubin, newborn risk factors, neonatal exam, follow-up exam, auditory testing, and MRI results. KSD-TK diagnostic prediction was compared to "gold standard" clinical diagnoses given after KCOE evaluation and used to calculate positive and negative predictive values, sensitivity, and specificity.
RESULTS: Of the 37 patients, 29 were clinically diagnosed with and 8 without kernicterus. All 14 patients with KSD-TK "definite" kernicterus and 14 of 15 patients with KSD-TK "probable" kernicterus were clinically diagnosed with kernicterus. One of 2 patients with KSD-TK "possible" kernicterus was diagnosed with kernicterus. None of 6 patients with KSD-TK "not kernicterus" were clinically diagnosed with kernicterus. When KSD-TK "definite" and "probable" are combined, the positive predictive value (PPV) and sensitivity of the KSD-TK are 96.6%, while the negative predictive value and specificity are 87.5%.
CONCLUSIONS: The KSD-TK is a promising tool for diagnosing kernicterus with a PPV and sensitivity of 96.6%. Future studies will attempt to replicate these results using KSD-TK's completed by families and referring providers.
KEYWORDS: Neonatal & Fetal Neurology, Movement Disorders (including Cerebral Palsy), Rare Diseases

435. Restricted diffusion in the splenium of the corpus callosum is specific and predictive for seizure in neonates with hypoxic ischemic encephalopathy: a retrospective chart review
Nguyen Linda (San Diego, CA, United States) Chen Dillon, Gold Jeffrey

OBJECTIVE: Restricted diffusion in the splenium predicts recent seizures in adults. We investigated splenium restriction in neonates with hypoxic ischemic encephalopathy (HIE), where diagnosing seizures is difficult because the clinical manifestation is often very subtle.
METHODS: We performed a retrospective chart review of 144 neonates with HIE who underwent MRI within the first 10 days of life. The areas examined for injury include splenium, other corpus callosum, gray matter, deep gray matter, and subcortical white matter. Neurodevelopmental outcomes were assessed using the Bayley Scales of Infant Development at 12-18 months of age. APGAR scores and pH were also analyzed in relation to MRI changes.

RESULTS: Approximately 50% of neonates had at least one abnormal MRI area, and 18% had splenium abnormality. Confirmed electrographic seizures were documented in 38%. Changes in the splenium had sensitivity = 42%, specificity = 97%, positive predictive value = 88% for seizure. Seizure was associated with changes in all brain regions examined and poorer developmental outcomes. APGAR scores and pH were not associated with MRI abnormalities (except that APGAR at 10 minutes was associated with changes in gray matter).
CONCLUSIONS: Restricted diffusion in the splenium is specific and predictive for seizures in neonates with HIE. Seizures represent a risk factor for brain injury and worse neurodevelopmental outcomes. Child neurologists and neonatologists should consider splenium restriction in their treatment of neonates at risk for seizures and counsel families about likely outcomes accordingly.
KEYWORDS: Neonatal & Fetal Neurology, Neuroimaging, Epilepsy

436. Feasibility Data from the Boston Bumetanide Trial: Implications for Neonatal Seizure Trial Design
Singh Avantika (Boston, MA, United States) Rofeberg Valerie, Landers Jessica, Bergin Ann, Hayes Breda, Fortuno Carmen, O'Reilly Deirdre, Krishnamoorthy Kalpathy, Jensen Frances, Wypij David, Staley Kevin, Soul Janet

OBJECTIVE: Neonatal seizure treatment trials are desperately needed as anti-seizure drugs are <50% effective. We sought to determine the feasibility of early enrollment, cvEEG and randomization in a multicenter, double-blind RCT of bumetanide as add-on therapy to phenobarbital to treat refractory EEG-confirmed seizures.
METHODS: For all screened neonates, we recorded and analyzed seizure etiology, and timing of NICU admission, consent, initiation of cvEEG, seizure onset, first EEG-proven seizure after phenobarbital (PB) load administration (i.e., 'qualifying seizure'), and study drug administration (SDA). Chi-Square and Kruskal-Wallis tests were used as appropriate to compare neonatal characteristics, etiologies and study sites.
RESULTS: We screened 539 neonates at risk for/with seizures (Figure), enrolled 111 of 191 (58%) eligible neonates whose parents were approached, and randomized 43 (Figure). Most screened (56%) and enrolled (42%) neonates had HIE, but seizures occurred least frequently in HIE compared with other diagnoses ((Table, $p<0.001$). Seizure onset occurred earliest in HIE (13.4hr) compared with stroke (29.1hr), ICH (25.2hr) and other diagnoses (64.3hr, $p<0.001$), but rate of seizures post-PB load, time to qualifying seizure and SDA did not differ significantly by etiology. The qualifying seizure occurred median 15.1hr after seizure onset, and SDA was achieved at median 2.5hr after qualifying seizure.
CONCLUSIONS: Data from a double-blind RCT demonstrate that it is feasible to obtain consent, initiate and review the cvEEG rapidly to test a drug early in the course of neonatal seizures. These and additional data to be presented illustrate the strengths of an add-on therapy design and inform design of future RCTs for neonatal seizures.
KEYWORDS: Neonatal & Fetal Neurology, Epilepsy

437. High BNDF is Associated with Low White Matter Microstructure in Very Low Birth Weight (VLBW) Newborns with no IVH
Carrasco Melisa (Baltimore, MD, United States) Catenaccio Eva, Stafstrom Carl, Parkinson Charla, Everett Allen, Graham Ernest, Tekes Aylin, Northington Frances

OBJECTIVE: VLBW children (birth weight <1500g, gestational age at birth <28 weeks) are at significant risk for cerebral palsy, developmental delay, and learning disabilities. There is a limited availability of reliable and cost-effective methods for predicting brain injury and long-term outcomes in this population. Serum BDNF protein may serve as a potential early biomarker of brain injury in VLBW neonates. Our objective is to understand the relationship between white matter microstructure and BDNF in VLBW patients.
METHODS: Data were drawn from a retrospective sample of neonates (2009-2016). Cord blood BDNF levels were measured from blood samples by ELISA. MRI and diffusion tensor imaging data were obtained near term (post-conceptional ages 36-44 weeks). We pursued an Atlas-Based analysis which parcellated the patient's images into 122 anatomic regions, for which fractional anisotropy (FA) measures were calculated. Low FA is a marker of decreased white matter integrity.
RESULTS: N=335 VLBW premature patients with no evidence of intraventricular hemorrhage were recruited to this study. MRI and cord BDNF levels were available for 10 patients. Outlier biomarker values were removed from subsequent analyses if higher/lower than 2 standard deviations of the estimated median; one patient's data was not usable in this context. Patient demographics are summarized in Table 1; additional results are summarized in Table 2.
CONCLUSIONS: In VLBW neonates, greater BDNF in the cord blood is associated with low FA values in DTI near term, which points to impaired white matter integrity. The relationship between BDNF levels and long-term prognosis needs to be further explored in large cohorts.
KEYWORDS: Neonatal & Fetal Neurology, Neuroimaging, Neuroscience

438. Long-term developmental and seizure outcomes in neonates with acute perinatal brain injury

Trowbridge Sara (Boston, MA, United States) Condie Lois, Singh Avantika, Rofeberg Valerie, Landers Jessica, Bergin Ann, Hayes Breda, Fortuno Carmen, Krishnamoorthy Kalpathy, Jensen Frances, Wypij David, Staley Kevin, Soul Janet

OBJECTIVE: Seizures in neonates are commonly caused by acute perinatal brain injury, and EEG monitoring is recommended by ACNS guidelines. However, questions remain regarding the relationship of neonatal seizures to long-term neurologic outcome. We addressed these questions in neonates enrolled in a randomized, controlled trial of bumetanide to treat neonatal seizures.
METHODS: Continuous video-EEG data (cvEEG) were collected for all enrolled neonates, and neuropsychological testing, including the Bayley-III, was administered at 18-24 months of age by a single neuropsychologist. Retrospective chart review determined postneonatal epilepsy occurrence and type. Statistical analysis was performed with SPSS Statistics.
RESULTS: Of 111 enrolled neonates, 57 (31 male) were included in the current analysis, with median gestational age 39 weeks. Other neonates were excluded by seizure etiology, neonatal death, or loss to follow-up. Thirty-four neonates had hypoxic-ischemic encephalopathy (60%), while 16 had ischemic stroke (28%) and 7 intracranial hemorrhage (12%). Most neonates (79%) had clinical and/or EEG-confirmed seizures. Neuropsychological testing was performed at a median age of 19 months. The mean Bayley-III composite scores were below expected for age, with cognitive 93 (SD 13), language 90 (SD 20), and motor 92 (SD 18). Ten (18%) had epilepsy

at follow-up. Initial analysis did not show significant correlations between either seizure etiology or presence of neonatal seizures with later diagnosis of epilepsy or Bayley-III composite scores.
CONCLUSIONS: Presence or etiology of neonatal seizures did not correlate with subsequent neurodevelopmental outcome or post-neonatal epilepsy. Further analysis of neonatal seizure burden and other EEG characteristics may yield novel findings.
KEYWORDS: Neonatal & Fetal Neurology, Epilepsy

439. Efficacy and Safety of First Line Levetiracetam Use in Seizures after Neonatal Congenital Heart Defect Repair
Keene Jennifer (Seattle, WA, United States) Wainwright Mark, Morgan Lindsey, Mietzsch Ulrike, Musa Ndidi, Bozarth Xiuhua, Natarajan Nina

OBJECTIVE: Levetiracetam (LEV) is used for neonatal seizures, however its efficacy remains uncertain. Retrospective studies demonstrate non-inferiority of LEV relative to phenobarbital (PHB), however recent prospective studies suggest LEV is less effective than phenobarbital (PHB). The aim of this study was to evaluate the efficacy and safety of LEV as a first line anti-seizure medicine (ASM) following neonatal congenital heart defect (CHD) repair.
METHODS: A single center retrospective chart review was conducted of neonates with seizures during continuous EEG monitoring following CHD repair from 2015 to present. Ten neonates were identified and nine received LEV as a first line ASM and were included in subsequent analysis. Primary outcomes were number requiring treatment with a second ASM and adverse events following LEV administration.
RESULTS: Eight of nine neonates were successfully treated with LEV monotherapy. Five neonates had no seizures after first LEV dose. Four neonates had hypotension, agitation or respiratory worsening requiring escalation of care in the hour after LEV administration; however, three neonates had similar findings independent of LEV administration (Table 1).
CONCLUSIONS: The majority of neonates post CHD repair treated with LEV at our institution did not require additional ASMs to achieve seizure cessation. Adverse events observed were not clearly attributable to LEV given the baseline frequency of events. Neonates with seizures after CHD repair would benefit from a prospective evaluation of ASM efficacy and safety as these patients likely have divergent pathophysiology, adverse effect vulnerability and response to ASM administration in comparison to the non-CHD population.
KEYWORDS: Neonatal & Fetal Neurology, Epilepsy, Critical Care

440. Brain Injury and Early Neurodevelopmental Outcomes in Patients with Heterogeneous Neonatal Congenital Heart Diseases
Vassar Rachel (San Francisco, CA, United States) Peyvandi Shabnam, Miller Steven, Gano Dawn, Zetino Yensy, McQuillen Patrick

OBJECTIVE: Brain injury rates and neurodevelopmental (ND) outcomes have been reported in patients with transposition of the great arteries (TGA) and hypoplastic left heart syndrome (HLHS), but little is known about patients with other critical congenital heart disease (CHD). This study aims to characterize brain injury patterns and ND outcomes in patients with Other lesions beyond TGA and HLHS.
METHODS: This prospective cohort study included infants with TGA, HLHS, and Other lesions that underwent pre- and post-operative brain MRI and were followed for ND outcomes.

Other lesions included left- and right-ventricle-outlet-tract obstruction or truncus arteriosus. Neurodevelopment at 30-months-of-age was measured using Bayley-II cognitive (MDI) and motor (PDI) scores and was compared between groups.
RESULTS: A total of 228 subjects were included (TGA=124; HLHS=62; Other=42, including 8 with genetic syndromes). Pre- and post-operative overall brain injury rates were not significantly different (Table 1). Incidence of pre-operative stroke was lower in the Other group (3%) compared to the TGA group (20%) and HLHS group (16%), (p=0.036, Table 1). At 30 months (n= 86), subjects with TGA had higher mean ND (MDI= 95.0, PDI= 92.3), compared to those with HLHS (MDI= 87.9, PDI= 75.5) and Other lesions (MDI= 80.6, PDI= 80.0), (p<0.01).
CONCLUSIONS: Along with similarly high brain injury rates compared to patients with TGA or HLHS, patients with Other CHD lesions have impaired motor and cognitive development at 30 months, most similar to the HLHS group. Patients with all types of critical CHD are at risk for impaired ND outcomes and developmental screening is suggested.
KEYWORDS: Neonatal & Fetal Neurology, Neuroimaging, Critical Care

441. Long term prophylactic anticonvulsant uses on neurodevelopmental and neurophysiological outcome in asphyxiated neonate with encephalopathy
Saha Dipa (Dhaka, Bangladesh) Saha Narayan, Haque Azimul, Saha Chinmoy

OBJECTIVE: to assess the neuro developmental morbidity in asphyxiated neonates with long term anticonvulsant.
METHODS: A total of 70 asphyxiated neonates with HIE-II/ III, gestational age ≥ 35 completed weeks were enrolled from January 2017-january 2018 in this randomized clinical trial where cases were categorized into three groups by lottery method. Group A and B received PHB 5mg/kg/day twice daily and PHB 2.5mg/kg/day once daily respectively while Group C didn't receive any anti-seizure medication. Neurodevelopmental assessment as well as electrophysiological study was done at 1month, 3month, 6 months and finally at 1 years of age in every cases. Data were analyzed by Chi-square & logistic regression test to find out the outcome.
RESULTS: Among 70 cases mean gestational age was 37.74±0.98 weeks, M: F was 3:2 and most of them were inborn (51.4%). At 6 months 33 cases were analyzed, 11 were in each group. Cognitive impairment was found more in group A (50%) followed by group B (33.3%) and group C (16.67%) (p= 0.05). Significant motor delay was observed in Group A (42.8%) and group B (42.8%) in comparison to group C (14.28%) (p=0.04). Electrophysiological abnormality was also predominant in group A (44.4%) than group B (22.2%) and group C (11%) but not statistically significant. At 1 years significant cognitive impairment were found among group A then B and C.
CONCLUSIONS: Long term use of phenobarbital may impair psychomotor development.
KEYWORDS: Neonatal & Fetal Neurology

442. Quantitative assessment of electroencephalograms from preterm infants aged 24–25 postmenstrual weeks
Fukasawa Tatsuya (Aichi, Japan) Kubota Tetsuo, Narahara Sho, Negoro Tamiko, Okumura Akihisa, Kidokoro Hiroyuki

OBJECTIVE: To describe electroencephalogram (EEG) findings quantitatively in infants aged 24–25 postmenstrual weeks.

METHODS: We evaluated the occurrence (/30 min) of brushes, frontal sharp bursts, temporal high-amplitude theta bursts and occipital sharp bursts by infant clinical status, and compared the data with those of controls aged 26–27 and 28–29 postmenstrual weeks.
RESULTS: We recorded 27 EEGs; three were recorded under sedation, seven were from infants with intracranial hemorrhages (IVHs) (of Grade III or IV in three), three were from infants who later developed periventricular leukomalacia (PVL), and one showed a disorganized pattern. We compared the remaining 13 EEGs to 19 control EEGs taken at weeks 26–27 and 15 at 28–29 weeks postmenstrually to those of infants receiving sedatives, and to the EEGs of those with PVL or IVH. In infants aged 24–25, 26–27, and 28–29 postmenstrual weeks, the median occurrences of brushes were 13.3, 19.6, and 39.5, respectively, thus increasing significantly at later postmenstrual age. The respective median occurrences of frontal sharp bursts were 5.45, 3.87, and 0; of temporal high-amplitude theta bursts 0, 0.968, and 4.86; and of occipital sharp bursts 3.16, 6.15, and 3.85, The occurrence of temporal high-amplitude theta bursts increased significantly at later postmenstrual age. The EEGs of infants receiving sedatives or with IVH (Grade III or IV) tended to exhibit lower frequencies of all components.
CONCLUSIONS: The frequencies of various EEG components depend on infant clinical status and postmenstrual age, even in infants aged 24–25 postmenstrual weeks.
KEYWORDS: Neonatal & Fetal Neurology

443. Mimicker of Hypoxic Ischemic Encephalopathy In a Neonate
Lin Jenny (Atlanta, GA, United States) Dutt Monideep

OBJECTIVE: Case report of a virus mimicking hypoxic-ischemic encephalopathy (HIE).
METHODS: Chart review.
RESULTS: Three-day-old girl was born at 37 weeks via vaginal delivery, complicated by umbilical cord "true knot." Apgar scores were 8/9. At birth, she had decreased left arm movement and was suspected to have a brachial plexus injury. On day of life (DOL) 2, she had focal twitching. EEG showed subclinical seizures, treated with phenobarbital. CSF showed 69 WBCs, 41,550 RBCs, 38 glucose, 166 protein. MRI brain on DOL 6 showed symmetric restricted diffusion in white matter, splenium, posterior limbs of the internal capsules, thalami. MRI on DOL 13 showed improved white matter signal and normal MR spectroscopy. Genetic/metabolic work-up was normal. MRI at 8 weeks showed resolution of abnormalities without volume loss. At six months, development was normal. Given history and radiological normalization, diagnosis was presumed to be parechovirus leucoencephalitis.
CONCLUSIONS: In neonatal encephalopathy and white matter abnormality, a broad differential diagnosis is necessary in absence of perinatal hypoxia. Human parechovirus is an important less known cause of neonatal leucoencephalitis with characteristic radiological symmetric diffusion restriction of periventricular and subcortical white matter, corpus callosum, external and internal capsules, sparing basal ganglia and infratentorial regions. Unlike HIE, this patient had a late presentation and improving course, characteristic imaging and disappearance of white matter abnormality and no volume loss. It is important to identify this infection early, as its treatment is primarily supportive with variable outcomes. This would avoid expensive investigations for other causes of white matter injury.
KEYWORDS: Neonatal & Fetal Neurology, Infection/Neuroimmunology, Neuroimaging

444. Antenatally Diagnosed Fetal Intraventricular Hemorrhage: Systematic Review and Meta-Analysis

Dunbar Mary (Calgary, Alberta, Canada) Woodward Kristine, Leijser Lara, Kirton Adam

OBJECTIVE: Intraventricular germinal matrix hemorrhage (IVH) is a condition unique to the immature brain that carries significant morbidity and mortality. IVH is well studied in infants born preterm, however little known about the risk factors and outcomes when IVH occurs in the fetus. In this systematic review and individual patient data meta-analysis, we sought to explore potential risk factors and determine whether grade of fetal IVH predicted outcome.
METHODS: Systematic review and individual patient data meta-analysis included studies of human fetuses with antenatal diagnosis by ultrasound or MRI of primary intraventricular hemorrhage. The outcomes were co-occurring clinical factors and motor, shunt, and epilepsy outcomes. Logistic regression was used to evaluate relationships, expressed as odds ratios (OR) with 95% confidence intervals (CI).
RESULTS: There were 284 cases included for analysis (Figure 1). The most common co-occurring conditions were twins (19%), intrauterine growth restriction (11%), and congenital anomalies (10%). Survival was significantly lower in grade IV than grades I/II (56.3% versus 80.8%; OR 0.24, 95% CI 0.08-0.73). Shunts were required in 54% of infants with fetal hydrocephalus (Figure 2A). Motor impairment was significantly more common in grade IV than grade I/II (75% vs. 8%, OR 58.9, 95% CI 5.9-582). For grade III IVH, motor impairment was confounded by gestational age at birth (Figure 2B). Epilepsy affected 26% of grade IV (Figure 2C).
CONCLUSIONS: Fetal IVH grade related to survival, VP shunt, motor outcome, and epilepsy. In 40% of cases fetal IVH occurred in an otherwise healthy pregnancy, emphasizing the need for prospective epidemiologic studies.
KEYWORDS: Neonatal & Fetal Neurology, Stroke (including other Vascular Disorders), Neuroimaging

445. Fetal-onset Leukoencephalopathy with Vanishing White Matter Disease

Yeo Tong (Singapore, Singapore) Baral Vjiaydedra, Ng Zhi, Tan Ling, Thomas Terrence

OBJECTIVE: Vanishing white matter disease (VWMD) is an autosomal recessive leukoencephalopthy caused by *eIF2B* gene mutations. These genes encode the eukaryocytic initiation factor *eIF2B* protein which initiates and regulates production of cellular proteins, particularly during periods of increased demands and stress. Here, we report a severe rapidly progressive fetal-onset VWMD. Subsequent exacerbations led to an inexorable neurodevelopmental and physical decline.
METHODS: Case presentations and literature review
RESULTS: A 2.7kg male was born at 37 week-gestation by normal vaginal delivery. Parents were first cousins. He had meconium aspiration syndrome at birth and required respiratory support. He had episodes of unexplained hypoglycemia. Initial neurological examination showed axial hypotonia.
MRI brain showed marked bilateral symmetrical cerebral white matter abnormalities. Abnormal cortical gyrations, thin corpus callosum, hypoplastic cerebellum and vermis, intracranial arachnoid cyst were noted. Extensive routine and metabolic investigation were unrevealing. Whole exome sequencing revealed homozygous variant in EIF2B5(c.1022A>G;p.Asn341Ser)

consistent with VWMD. His subsequent clinical course was dominated by feeding difficulties, failure to thrive, axial hypotonia, long tract signs with spasticity and hyperreflexia of his extremities, status epilepticus and recurrent apneic events following trivial viral infections with fever.
CONCLUSIONS: Previous literature has described a wide clinical spectrum, from a rare congenital form to an adult form with slow neurological progression. Fetal VWM disease is less frequently described. Our report described the fulminant course of *EIF2B5*-related *fetal onset* VWMD, and highlighted the need to consider this devastating disease in the differential diagnosis of early onset encephalopathy with bilateral symmetrical white matter abnormalities.
KEYWORDS: Neonatal & Fetal Neurology, Rare Diseases, Neuroimaging

446. Improving Detection of Neonatal Seizures Associated with Hypoxic Ischemic Encephalopathy During Therapeutic Hypothermia: A Quality Improvement (QI) Initiative
Rosati Justin (Rochester, NY, United States) Nguyen Jennifer

OBJECTIVE: Hypoxic Ischemic Encephalopathy (HIE) is the most common cause of neonatal seizures (Glass et al., 2009). Higher seizure burden is associated with more severe brain injury and worse neurodevelopmental outcomes (Srinivasakumar et al., 2015). Our institutional Therapeutic Hypothermia (TH) protocol includes conventional EEG (cEEG) within 6 hours of TH initiation with repeat at 12-24 hours of normothermia. However, we hypothesize that despite a protocol, cEEG timing and duration is variable, leading to nonstandardized management and delayed seizure treatment.
METHODS: At a tertiary care academic center between January 2018-October 2019, 46 neonates were diagnosed with HIE, 42 were considered for TH, and 32 were treated with TH. Adherence to institutional TH protocol was defined as cEEG within 6 hours of TH initiation with repeat at 12-24 hours of normothermia. Neurology consultation was tracked.
RESULTS: In this cohort, 0 neonates adhered exactly to institutional TH protocol. 2 had cEEG within 6 hours of TH initiation. Mean time to initial cEEG was 20 hours; median time was 11 hours. 26 had Neurology consultation.
CONCLUSIONS: Our data verified low compliance to institutional TH protocol and suboptimal seizure management. A cEEG was universally obtained, although timing was delayed. Neurology consultation was not routinely established. To improve early detection of neonatal seizures associated with HIE during TH and minimize time to seizure treatment, we propose a multidisciplinary approach (Child Neurology, Epilepsy, and Neonatology) to identify and reduce barriers such as cEEG accessibility and Neurology consultation to improve compliance to 50% in 6 months through 2 PDSA cycles.
KEYWORDS: Neonatal & Fetal Neurology, Critical Care

447. A case of prenatal presentation of Wieacker-Wolff syndrome
Wiegand Sarah (Los Angeles, CA, United States) Tamrazi Benita, Ho Eugenia

OBJECTIVE: Arthrogryposis multiplex congenita is a physical exam finding characterized by multiple joint contractures affecting two or more areas of the body. It is associated with more than 400 diagnostic entities and caused by intrinsic, environmental, and extrinsic etiologies. We describe a case of arthrogryposis secondary to presumed pathogenic mutations in the ZC4H2 gene, associated with Wieacker-Wolff syndrome.

METHODS: A male infant was born at term with prenatal diagnosis of arthrogryposis multiplex congenita. Fetal MRI showed diffuse white matter volume loss, right hemidiaphragm eventration, clenched hands, and fixed extension of the extremities. Postnatally, the infant developed respiratory failure with ventilator dependence. Exam was notable for cleft palate, cortical thumbs, club feet, fixed contractures involving all extremities, and areflexia. Postnatal brain MRI showed diffuse white matter volume loss with a thin corpus callosum and ex vacuo dilatation of the ventricles. MRS was unremarkable.
RESULTS: Trio whole exome sequencing showed a de novo hemizygous pathogenic mutation c.561+1G>Z identified in the ZC4H2 gene. This is a novel canonical splice donor site variant that presumably causes abnormal gene splicing. The ZC4H2 gene encodes for zinc finger proteins involved in neuronal development, neuromuscular junction formation, and interneuron differentiation.
CONCLUSIONS: Wieacker-Wolff syndrome is an X-linked recessive neurodevelopmental disorder associated with fetal akinesia secondary to axonal guidance molecule dysregulation, associated with arthrogryposis multiplex congenital, motor delays, facial and bulbar weakness, dysmorphisms, and skeletal abnormalities.
KEYWORDS: Neonatal & Fetal Neurology, Genetics

448. Autonomic Tone in Preterm Infants Correlates with Morbidity of Prematurity
Schlatterer Sarah (Washington, DC, United States) Reich Daniel, Govindan Rathinaswamy, Al-Shargabi Tareq, Kota Srinivas, Iyer Sneha, Herrera Nicole, Jacobs Marni, Hitchings Laura, Maxwell G. Larry, Baker Robin, du Plessis Adre, Mulkey Sarah

OBJECTIVE: To compare autonomic nervous system (ANS) development in infants without significant morbidity of prematurity (group 1) vs. those with (group 2).
METHODS: We compared ANS tone in 114 preterm infants using heart rate variability (HRV) analysis obtained weekly from NICU admission to discharge. Normalized low frequency (nLF) and alpha 1 characterized sympathetic tone. Normalized high frequency (nHF) characterized parasympathetic tone. Median regression with a group by time interaction term modeled ANS maturation and evaluated differences in maturation rates.
RESULTS: Group 1 (n=68) had a mean (SD) birth GA of 30.5 (2.5) weeks and a NICU stay of 52.4 (29.5) days. Group 2 (n=46) had a birth GA of 27.7 (2.5) weeks and a NICU stay of 93 (60) days. Birth GA did not differ between groups (p=0.08). There was a difference in the slope of the trajectories of alpha 1 (p=0.000), nLF (p=0.02), and nHF (p=0.02) between groups. Alpha 1 was initially lower in group 2 (p=0.000), but values were similar between groups at discharge. Admission nLF was similar between groups, but higher in group 2 at discharge. Group 2 nHF was higher at admission and lower than group 1 at discharge.
CONCLUSIONS: ANS maturity impacts regulation of stress responses and may play a role in neuropsychiatric outcomes. Our data suggest that medically complex infants have lower sympathetic tone at admission and may have less robust parasympathetic development over time. Understanding ANS function may lead to treatments that improve short- and long-term outcomes in preterm infants in the future.
KEYWORDS: Neonatal & Fetal Neurology

449. Neonates and infants with neurological manifestations verified by electroencephalography and neurological imaging: a cohort study, Quito Ecuador. 2014-2018

Moreira Fernanda (Quito, Ecuador) Roman Marcelo, Dueñas Gonzalo, Contreras Guilca, Roman Ana

OBJECTIVE: Determine whether a neonate's or an infant´s manifestation was or was not neurological, using electroencephalography and neuroimaging.
METHODS: This retrospective cohort study analyzed different facts as type of birth, sex, APGAR score, gestational age of neonates and infants with diagnosis of asphyxia, epilepsy or neonatal seizures and compared them with the exam findings of electroencephalography, cranial ultrasonography and/or magnetic resonance imaging.
RESULTS: From 2014 up to 2018, twenty-four (24) neonates and infants needed to be at the Neonatal Intensive Care Unit to find out if their manifestations were mainly neurological. Fifty-eight percent was represented by males and 42% by females. The main type of birth was c-section (71%). Twenty percent of this group had less than 3 for the APGAR score the first minute of life. Term babies were characterized by 83%; just two babies were preterm, one of them had 29 weeks of gestational age. An electroencephalography was performed on 16 of these cases, just 46%, had an abnormal result. The first neuro-image exam performed was a cranial ultrasound with 12.5% having an abnormal result. One of the neonates, despite having the first ultrasound reported as normal, during the next controls leukomalacia was found. Twenty-five percent of the magnetic resonance imaging was abnormal, showing sequelae of ischemic hypoxic injury.
CONCLUSIONS: Most of the patients were hospitalized with a diagnosis of neonatal asphyxia, 20% with an APGAR score less than 3 the first minute of life. Three patients of that group had electroencephalography and magnetic resonance imaging abnormalities.
KEYWORDS: Neonatal & Fetal Neurology, Neuroimaging

450. Neonatal Seizure Burden during Therapeutic Hypothermia

Ojha Kshama (Louisville, KY, United States) Pal Abhinav, Barnes Gregory, Stewart Dan

OBJECTIVE: The Primary aim of this study is to develop quantitative metrics for the use of continuous electroencephalography (cEEG) during Therapeutic Hypothermia (TH). The goal of the metrics is to determine the duration and need for the use of limited EEG resources during TH.
METHODS: A retrospective analysis of the EEG data gathered from neonates undergoing TH, on cEEG at Norton Children's Hospital (NCH) from 2014-2018, to assess the background and timing of recorded EEG abnormalities and seizures.
RESULTS: A total of 136 neonates underwent TH during 2014-2018, 24 were excluded sec to them either being deceased, prematurely removed from TH or having insufficient data. CEEG from 112 neonates were analyzed. Out of the 112 CEEG analyzed, 38 had either severe background or Szs on day 1. 74 remaining neonates' with no sz on day 1 and normal or mildly abnormal background were followed until rewarming on CEEG. Only 1 out of 74 neonates had szs during rewarming, but 98.6% of neonates remained seizure free. Mean number of sz days when background was normal/mildly abnormal were 0.09 as compared to a mean of 1.27 days when background was mod-severely abnormal. Sarnat scoring, EEG background and szs on day

1,2,3 and rewarming had a statistically significant positive correlation. Total number of seizures and MRI abnormalities also demonstrated a statistically sig positive correlation.
CONCLUSIONS: If the CEEG during TH has a normal or a mildly abnormal background with no szs, during the first 24 hrs, EEG can be discontinued after 24hrs.
KEYWORDS: Neonatal & Fetal Neurology, Epilepsy, Teaching of Child Neurology

451. From Womb to Birth: Institutional Experience with Fetal Neurology Consultations
Gumayan Rae Leonor (Columbus, OH, United States) Ream Margie

OBJECTIVE: Summarize clinical characteristics, correlation of prenatal and postnatal diagnoses, and postnatal outcomes of patients referred for fetal neurology consultation.
METHODS: Retrospective review of consultations from 4/2/2009 to 8/8/2019 at Nationwide Children's Hospital, Columbus, OH.
RESULTS: Of the 179 fetal consults received, 126 were completed. The most common prenatal malformations involved posterior fossa abnormalities (25.3%), corpus callosal/septal dysraphism (25.0%), and ventriculomegaly (19.7%). In comparison, postnatal imaging revealed the most common malformations involved the corpus callosal/septal (31.3%), cerebral cortex (27.1%), and posterior fossa (13.7%). Thirty-five percent of the women were carrying their first pregnancy, while only 12% of the women were advanced maternal age and 14% had >1 pregnancy loss. The average gestational age (GA) at prenatal MRI was 26.0 weeks prior to a referral at 27.1 weeks. Average GA at consultation was 30.1 weeks. Of the 127 anticipated fetuses, 5 experienced fetal demise, 7 underwent elective termination, and 10 died postnatally. The majority were admitted to the neonatal ICU, however only 44% required surgical intervention for feeding, breathing, or hydrocephalus. Ten neonates had seizures during their NICU stay. Accuracy of prenatal diagnoses was analyzed on the 110 babies that had a pre- and postnatal imaging. Most prenatal imaging findings were confirmed postnatally, however 8.2% of infants had an unexpectedly normal MRI.
CONCLUSIONS: Our summarized experience can improve perinatal counseling and develop more accurate plans for neonatal care. There is limited literature on fetal neurology consultations, so sharing the above demographics and outcomes can serve as a guide for other institutions.
KEYWORDS: Neonatal & Fetal Neurology, Neuroimaging, Critical Care

452. The use of midazolam for refractory neonatal seizures
Martin Matthew (Columbus, OH, United States) Ream Margie

OBJECTIVE: To identify risk factors and outcomes associated with neonatal seizures not responsive to traditional seizure medications that require treatment with continuous infusion of midazolam.
METHODS: This single center retrospective review included 522 neonatal ICU patients who required EEG monitoring. Data included birth history, seizure prevalence, imaging findings, anti-seizure medications, and the endpoints of cerebral palsy, epilepsy, or death.
RESULTS: From a preliminary analysis of 250 charts, 70 patients had EEG-confirmed seizures, with 33% receiving midazolam infusions for seizure control. Patients who failed two or more medications prior to midazolam had >20% rates of mortality and morbidity. None of the patients whose seizures stopped with only one medication developed epilepsy or cerebral palsy. Of

patients who did not receive midazolam infusions, 34% experienced seizure cessation with monotherapy with phenobarbital or levetiracetam and 43% required two medications. Of the 23% who received three or four medications prior to seizure control, >63% developed epilepsy or cerebral palsy. There was no significant difference between the patients who did not require midazolam and those who did in terms of gestational age, birth weight, or APGAR scores. The sequence of medications used for the midazolam group was less variable, which may reflect application of our institution's neonatal seizure protocol preferentially to patients with status epilepticus.
CONCLUSIONS: Refractory neonatal seizures increase the risk of unfavorable developmental outcomes. Birth characteristics are not predictive of seizure responsiveness. Use of two seizure medications prior to midazolam infusion, or three seizure medications without midazolam was associated with worse outcomes.
KEYWORDS: Neonatal & Fetal Neurology, Epilepsy

453. Targeted Protocols for the Treatment of Neonatal Seizures Improves Short-Term Outcomes

Moeller Ashley (Indianapolis, IN, United States) Boyle Frances, Rose Rebecca, Buss William, Stefanescu Beatrice, Wing Sarah

OBJECTIVE: Seizures occur more frequently in the neonatal period than any other time in life. However, treatment of neonatal seizures is still quite varied. In 2015, our program initiated a standardized protocol for the treatment of status epilepticus in neonates. We revised the protocol in 2019 to be inclusive of any neonate with seizure activity and to provide targeted treatment based on seizure burden. The aim of this study is to determine whether our updated protocol improves short-term patient outcomes.
METHODS: We prospectively collected data from two patient cohorts in our Level IV NICU. The first cohort (n=70) consists of patients admitted during the 12 months prior to the initiation of our new targeted protocol. The second cohort consists of those admitted during the eight months that followed (n=33). All patients with EEG-confirmed seizures during the time of the study were included. In order to compare short-term patient outcomes between cohorts, we evaluated length of stay, duration of EEG monitoring, and requirement for continuous infusion of sedating medication.
RESULTS: Length of stay decreased among surviving neonates from 39 days in the initial protocol to 33 days in the targeted protocol. The duration of EEG monitoring decreased from 5.6 days to 4.6 days and the percentage of neonates who required a continuous infusion of sedating medication decreased from 36% to 21%.
CONCLUSIONS: While we continue to evaluate the effects of our updated protocol, preliminary results indicate that a targeted approach to seizure treatment may improve short-term outcomes in neonates.
KEYWORDS: Neonatal & Fetal Neurology, Epilepsy, Critical Care

454. Phenotypic spectrum of ARID1B: From Nonsyndromic Intellectual Disability to Coffin–Siris Syndrome

Chattopadhyay Arijit (Kolkata, India) Datta Dipanjana, Bhattacharya Anjan, Chatterjee Raghunath, Chakraborty Joyeeta, Guha Roy Priyamvada

OBJECTIVE: Pathogenic variants in ARID1B are one of the most frequent causes of intellectual disability (ID) and also related to neuro-developmental disorders like coffin siris syndrome. We present a case study series, reflecting the genotype and phenotype correlations of mutations identified in two patients with mutations identified in *ARID1B* gene.
METHODS: Case 1 : A 3 yr old child first born to non consanguineous parents with hypotonia severe global developmental delay , distinct facies and a MRI finding for dysgenesis of corpus callosum with mildly dilated ventricles
Case 2: A 10 yr old child second born to non consanguineous parents with hypotonia difficulty in walking, scholastic problems, repetitive speech and frequent school changes. The child was clinically diagnosed with Autism.
Both children were investigated by exome sequencing and mutations were identified in *ARID1B* gene. On basis of the mutation the protein structure was predicted and delta G value calculated to understand the stability.
RESULTS: An intronic c.5025+1del G in *ARID1B* was identified in case 1 leading to truncated protein formation, while a c.1379 C>T missense mutation was identified in exon 1 of ARID1B in heterozygous condition leading to altered protein secondary structures and altered protein stability (*ΔG ARID1B WT : -868Kcal/mol ; and for mutant -831Kcal/mol).* The truncated severe form was attributed to a syndrome disease named as Coffin Sirris syndrome while the milder missense form had clinical manifestations of intellectual disability.
CONCLUSIONS: Thus, genotypic variations in ARID1B gene have implications to the protein structure and function thereby resulting in phenotypic variability.
KEYWORDS: Neonatal & Fetal Neurology, Genetics, Rare Diseases

455. How common is misdiagnosis of neonatal hypoxic-ischaemic encephalopathy (HIE) in babies offered therapeutic hypothermia?
Satodia Prakash (Coventry, United Kingdom) Jarvis Helen

OBJECTIVE: Background: Neonatal HIE outcomes have improved following therapeutic hypothermia treatment. It can be difficult to accurately diagnose HIE and assess brain cooling criteria clinically, as other conditions can mimic HIE. The failure to recognise such "HIE mimic" conditions results in unnecessary therapeutic hypothermia treatment. Objective: To assess the etiology and outcome of "HIE mimic" conditions in neonates admitted in a neonatal intensive care unit.
METHODS: Retrospective review of clinical files of neonates admitted for therapeutic hypothermia during a period of 10 years (Jan 2010 to Dec 2019). Data was collected on antenatal risk factors, labour and delivery complications, sepsis, neurological abnormalities, investigations including neurophysiology and imaging. Admission and final etiology of neonatal encephalopathy was reviewed. Outcome at discharge was recorded.
RESULTS: 93 neonates (36 to 41 weeks gestation) fulfilling cooling criteria as per NICE (UK) guidance underwent passive or active brain cooling treatment for HIE diagnosis on our NICU. HIE was associated in some cases with birth trauma.
6 babies (6.5%) had "HIE mimic" diagnosis - 2 had GBS sepsis, 2 had type 0 Spinomuscular atrophy, 1 had chromosomal severe sensory motor polyneuropathy (MFN2 mutation)and 1 had meningitis.
2 babies with SMA and baby with MFN2 mutation died.

CONCLUSIONS: Neonatal sepsis/ menigitis and fetal onset SMA can mimic HIE after birth. High index of suspicion is required for diagnosis of these conditions. Objective tests (genetic and heartbeat variability markers) may help to diagnose HIE more accurately.
KEYWORDS: Neonatal & Fetal Neurology, Rare Diseases, Critical Care

456. ACTA1 gene mosaicism manifesting as congenital fiber type disproportion with brain white matter lesions
Khan Mahjabeen (Saint Louis, MO, United States) Pinz Hailey, Kirby Amelia

OBJECTIVE: We report a case of a neonate who presented with congenital fiber type disproportion(CFTD), caused by an *ACTA1*gene mutation with white matter lesions on MRI.
METHODS: A male infant was born at 34 weeks of gestation via vaginal delivery. Pregnancy was complicated by large polyhydramnios. Mother had an "uncertain type" of muscular dystrophy with mild non-progressive muscle weakness. Neonate had respiratory distress at birth requiring intubation and mechanical ventilation. Exam revealed profound generalized hypotonia, absent deep tendon reflexes, and no spontaneous movements. On day 2 of life, he developed seizures prompting further workup. EEG showed diffuse cerebral dysfunction with subclinical seizures. MRI brain demonstrated confluent restricted diffusion in almost the entire supratentorial white matter consistent with hypoxic ischemic encephalopathy(HIE). However, this case had no evidence of birth asphyxia. Owing to poor prognosis, life support was withdrawn on day 7 of life.
RESULTS: Post mortem muscle biopsies showed myopathic changes and marked fiber size variation in 30-40% of muscle fibers, pathognomonic of CFTD. Muscular dystrophy panels sent on mother and neonate, identified a mosaic variant of uncertain significance in the *ACTA1*gene in the mother and a germline *ACTA1*mutation in the baby.
CONCLUSIONS: Our case brings three novelties to literature. First, CFTD presenting as severe disease in a neonate is very rarely reported. Secondly, CFTD associated with*ACTA1*gene mosaicism has never been reported. Thirdly, white matter lesions were seen on MRI that are similar to HIE, interestingly without perinatal asphyxia. Similar CNS lesions of uncertain etiology have been reported in association with other congenital neuromuscular disorders.
KEYWORDS: Neonatal & Fetal Neurology, Neuromuscular Disorders, Genetics

457. Effects of Music Based Intervention (MBI) on Neurodevelopment and Pain in Preterm Infants: Study Design and Rationale
Morris Erin (Minneapolis, MN, United States) Silverman Michael, Eberly Lynn, Wang Sonya

OBJECTIVE: Background: Worldwide annual rates of preterm birth continue to rise. While over 90% survive, 50% of these preterms suffer from neurodevelopmental impairments. Furthermore, preterm infants experience repeated painful procedures during their first few weeks of life. What remains unknown is how music impacts preterm brain maturation, neurodevelopment, and pain responses. Research Objectives: Establish a unique multi-disciplinary team of experts in child neurology, music therapy, neonatology, statistics and biomedical engineering to explore the impact of music-based intervention on preterm neurodevelopment and pain responses in a two arm prospective double blinded randomized trial (music-based intervention and control cohorts).

METHODS: Randomized, controlled, double blinded music-based intervention (MBI) trial of 60 preterm newborns born at 30 weeks gestation in the Neonatal Intensive Care Unit. (Clinicaltrials.gov NCT04286269) Each MBI subject will receive 5 music sessions per week with predetermined lullaby playlists through headphones for a total of 6 weeks, while Control subjects will receive no music through headphones. 30 hour EEG recordings performed every two weeks will track brain maturation through awake/sleep cycling analyses. Premature pain infant profile (PIPP) scores during newborn blood screens will measure pain responses. Event Related Potentials (ERPs) will measure neurodevelopment at one month corrected age.
RESULTS: To be determined. This is a study design and rational abstract.
CONCLUSIONS: This research represents a novel approach to explore the potential high impact that music (with minimal risks) can have on brain maturation, neurodevelopment and pain responses using objective and reproducible measures of EEG, ERP, and PIPP.
KEYWORDS: Neonatal & Fetal Neurology

458. The Oddball Paradigm and Child Development – A US/Sri Lankan Collaboration
Kaur Harsheen (Albuquerque, NM, United States) Wanigasinghe Jithangi, Pirrung Christopher, Cavanagh James, Kodituwakku Piyadasa, Umeshka Isuru, Phillips John

OBJECTIVE: Developmental therapies help children at risk for delay, if commenced very early. Therefore, early diagnosis is essential. The auditory oddball evoked potential (EP) may have predictive power for childhood development, and portable technology now allows this to be done in remote locations and cross-cultural settings.
METHODS: In this ongoing study, 2 and 6 months old Sri Lankan infants undergo auditory EP using a portable EEG system. A standard 80/20 oddball paradigm is used with tones presented via speakers close to the infant. After secure transfer from Sri Lanka to the US, data are filtered and preprocessed, and mismatch negativity (MMN) is calculated at Cz and Fz. Developmental testing occurs at 18 months.
RESULTS: To date, of 39 subjects enrolled, 29 provided adequate datasets at 2 months of age (70% female, 24 term, 3 premature, 2 term encephalopathy). A representative waveform at Cz is depicted in Figure 1, showing results for the standard and novel tones, and the MMN. Although, independent sample t tests did not reach statistical significance, there was a consistent reduction of MMN at Cz in subjects with postnatal complications or premature delivery (medium-large effect size; Hedge's $g = 0.72$), and among lower birthweight term children (Figure 2). There was no relationship identified at Fz.
CONCLUSIONS: Using portable technology, it is possible to acquire and analyze auditory oddball data from infants living in remote locations. Furthermore, the MMN at Cz may be sensitive to early brain injury, to be further explored as a biomarker of developmental outcome.
KEYWORDS: Neonatal & Fetal Neurology, Cognitive/Behavioral Disorders (including Autism), Neurorehabilitation

459. Neurodevelopmental clinic for high-risk neonates in a low-resource country.
De la Torre Alejandro (Quito, Ecuador) Jara Veronica, Tafur Cristina

OBJECTIVE: To design a follow up clinic for high-risk neonates at Hospital General San Francisco in Quito, Ecuador. We intent to create a continuum of care, from the neonatal period

through the first few year of life. In this multidisciplinary clinic, we will follow growth, neurodevelopment and screen for comorbidities.
METHODS: We created a protocol that includes inclusion criteria, a multidisciplinary team and a follow up schedule with standardized tests. The clinic will follow up patients from the neonatology unit and will be established at the hospital with the hospital personal.
RESULTS: The multidisciplinary team has been established and it includes a pediatric neurologist, neurodevelopmental specialist, neonatologist, pediatrician, physical therapy, audiology, ophthalmology and social work.
Inclusion criteria includes prematurity, central nervous system dysfunction, bronchopulmonary dysplasia, persistent hypoglycemia and other genetic disorders. For this reason we investigated the prevalence of prematurity in our hospital. (Graphic 1) For each condition, a tentative schedule has been created, with follow up visits for each specialty that will be modifying to accommodate each patient. We will be using standardized neurodevelopmental scales including Battelle® Developmental Inventory.
CONCLUSIONS: In Ecuador there is a high prevalence of neurological conditions including cerebral palsy and intellectual disability, as a consequence of complications that occurred in the neonatal period. This is a novel clinic in the country that will aid the prompt diagnosis and treatment of neurodevelopmental delays, with the goal of improving prognosis and quality of life.
KEYWORDS: Neonatal & Fetal Neurology

460. Long-term neurological outcomes in children who suffered from cerebellar injury as neonates
Seese Ronald (Pittsburgh, PA, United States) Cummings Dana

OBJECTIVE: Acute brain injury is a frequent perinatal neurological complication that sometimes involves the cerebellum. While the short-term outcomes of infants with neonatal cerebellar injury are well-described, neurological sequelae in older children are under reported. Here, we describe long-term neurological outcomes in children who suffered from neonatal cerebellar injuries.
METHODS: In-house automated software identified patients who were evaluated by neurologists at our institution both as neonates (≤ 28 days) and as children (≥ 1 year). Neonatal hospital course, neonatal imaging, and outcome measures related to epilepsy and neurodevelopmental disability during childhood were then systematically extracted from the medical record. Patients were divided into two groups based on neonatal neuroimaging: those with cerebellar involvement and those without cerebellar injury.
RESULTS: Of the 290 neonates followed through childhood over the past 10 years, 33 (12%) experienced neonatal brain injury. All 33 cases involved supratentorial parenchymal injury and 5 (15%) also included cerebellar injury. Rates of developmental delay were similarly high (> 60%) in both groups. However, the development of epilepsy was significantly less in the group with cerebellar involvement (60%) compared to that with cerebellar sparing (100%; $P < 0.001$). In some cases, children with cerebellar sparing required admission for seizure control and developed medically refractory seizures as well as status epilepticus. None of these outcomes emerged in the group with cerebellar involvement.

CONCLUSIONS: Long-term epilepsy-related sequelae occur less frequently when the cerebellum is involved in neonatal brain injury. Further studies are needed to clarify how cerebello-cortical networks impact functional brain connectivity and epilepsy.
KEYWORDS: Neonatal & Fetal Neurology, Stroke (including other Vascular Disorders), Epilepsy

NEUROIMAGING

461. Neuroimaging in Acute Encephalopathy in children: Early, late or repeat?

Aripirala Prasanthi (Hyderabad, India) Mohammed Obaidullah, Bandi Ramya, Juvvadi Sandeep, Konanki Ramesh, Lingappa Lokesh

OBJECTIVE: To know the yield of early (72hours) vs late (>72hrs) neuroimaging and utility of repeat neuroimaging in children with acute encephalopathy.
METHODS: Children (>1month age) presenting with acute encephalopathy and requiring neuroimaging as part of their clinical care over 4 months period were included. Those with encephalopathy due to trauma, toxin/drug exposure and previous structural abnormalities were excluded.
RESULTS: Forty nine eligible children were included: 35(71.4%) were male, mean age was 61 months (2- 161 months). Infections and related complications were the commonest aetiology of acute onset encephalopathy in children accounting for 57% cases (figure 1). Twenty nine of 49 children underwent 2nd imaging of which four were due to inappropriate initial choice of test (CT) or requirement of additional MRI sequences, hence considered as single imaging. Of 25 children who underwent repeat neuroimaging, imaging helped in clinical management (refining diagnosis, better prognostication or change in treatment) in 24 children (96%) (figure 2). Repeat imaging did not help in further management in one child. In 9/49 patients, imaging was not helpful in diagnosis. In these children MRI was normal or had non-specific changes and aetiology was acute symptomatic seizures, unknown clinically progressive disease or autoimmune in nature.
CONCLUSIONS: Early neuroimaging (<72 hours) has a good diagnostic yield (65%) in children with acute encephalopathy. With yield of 64% and management implication in 96%, repeat neuroimaging has definite role in clinical management of these children. Repeat neuroimaging should be considered in clinical situations of diagnostic uncertainty, for better prognostication and refining treatment.
KEYWORDS: Neuroimaging, Infections/Neuroimmunology, Critical Care

462. Unusual unihemispheric brain MRI findings in pediatric Parry-Romberg syndrome and en coup de sabre

Seese Ronald (Pittsburgh, PA, United States) Glaser Daniel, Furtado Adre, Torok Kathryn, Thakkar Kavita

OBJECTIVE: Parry-Romberg syndrome (PRS) and en coup de sabre (ECDS) are subtypes of localized scleroderma. Involvement of the central nervous system (CNS) has been reported, but systematic analyses of CNS imaging findings and their clinical associations in children are

lacking. Here, we aim to characterize neuroimaging findings and associated neurological symptoms in these conditions.
METHODS: Neuroimaging and neurological symptoms of children evaluated at our institution with a diagnosis of PRS or ECDS were retrospectively reviewed. Laterality, location, stability, and number of lesion(s) were evaluated, as was the presence of susceptibility artifact(s) and contrast enhancement. History of seizures or headache was also noted.
RESULTS: Out of 81 patients with PRS or ECDS diagnosed by rheumatologists between 2003-2019, neuroimaging was reviewed in 25 children and found to be abnormal. In 12 (48 %) of these 25 cases, headaches and/or seizures were present. In 22 (88 %) cases, lesions were ipsilateral to skin findings. White matter was involved in 18 (72 %) patients. MRI abnormalities were appreciated before a rheumatological diagnosis in 7 (28 %). Susceptibility artifacts were noted in 11 (46 %) of children, and 9 (82 %) of these patients endorsed a history of headaches. Most lesions were localized to the supratentorial compartment, did not enhance, and were stable at 1-year follow up imaging.
CONCLUSIONS: Neuroimaging findings in pediatric PRS and ECDS are often supratentorial, stable, unilateral, and ipsilateral to skin findings, and they can precede cutaneous findings. Headaches are often associated with the presence of susceptibilities on imaging.
KEYWORDS: Neuroimaging, Infections/Neuroimmunology

463. Pontine Tegmental Cap Dysplasia in a Neonate
Rashid Salman (Birmingham, AL, United States) Thornton Alana, Jones Brittney, Ananth Amitha, Singh Sumit

OBJECTIVE: This report highlights the clinical presentation and brain MRI features of the Pontine Tegmental Cap Dysplasia (PTCD).
METHODS: Neurology was consulted for further evaluation of absent gag and corneal reflexes in a 3-month-old girl who was transferred from an outside hospital for gastric tube placement. She was a product of twin gestation (twin lost at 12 weeks of gestation), and was born at term. The patient was reported to have seizures in the first few days of life (managed with phenobarbital). Neurological examination was significant for absent suck and gag reflexes, failure of blink to threat, hypotonic facial muscles and poor mouth closure. A hearing evaluation, sleep study and electroencephalography were unremarkable.
RESULTS: Magnetic resonance imaging (MRI) including diffusion tensor tractography (DTT), revealed the diagnosis of PTCD. (Figure and legends attached)
CONCLUSIONS: PTCD is a relatively recently discovered disorder of brainstem and cerebellar development, which is thought to result from defective axonal growth and guidance during brain development.[1] Neuro-anatomical features include hypoplasia of the cerebellar vermis and middle cerebellar peduncles, a flattened ventral pons, vaulted pontine tegmentum, molar tooth appearance of the pontomesencephalic junction and an absent inferior olivary prominence.[1] Multiple cranial nerve dysfunctions may result in hearing impairment, swallowing issues, gaze abnormalities, and sensory and motor involvement of the face.[1] Seizures, ataxia, bony abnormalities and involvement of other organ systems of varying severity may be seen. There is a spectrum of phenotypic expressions, and some patients may have favorable long-term outcomes of cognition and speech.[1, 2] Normal cognition has also been reported.[2]
KEYWORDS: Neuroimaging, Neonatal & Fetal Neurology, Neuroscience

464. Novel Data from Multimodal Imaging in Urea Cycle-related Neurological Disease
Gropman Andrea (Washington, DC, United States) Sen Kuntal, Whitehead Matthew

OBJECTIVE: Urea cycle-related brain disease may take on variable neuroimaging manifestations, ranging from normal to abnormal with or without a signature appearance. In the past, we have described the usefulness of multimodal imaging in identifying biomarkers of neuronal injury in UCD patients. In this study, we report unique findings in an adolescent male with neonatal-onset OTC deficiency after an episode of hyperammonemia.
METHODS: Multiplanar, multisequence MR imaging (T1WI, T2WI, T2 FLAIR, diffusion weighted images and gradient echo) of the brain was performed on seven separate occasions over the course following the acute illness; first five exams were performed within 28 days of admission and the final two exams were performed approximately 3 and 5 months later.
RESULTS: 1. The initial MR revealed increased signal on T2WI in the basal ganglia, claustrum and frontoparietal white matter; which remained stable over time. By the 5th exam, signal changes had developed in frontal cortex; reflecting permanent injury. 2. DTI tractography of the corticospinal tracts displayed revealed diminution of the number of projectional and commissural fibers over time. 3. Blood flow measurements demonstrated hypoperfusion on the fifth exam followed by hyperperfusion on the final two studies. 4. MR spectroscopy demonstrated that glutamine was elevated during hyperammonemia, with myoinositol reduction, reflecting osmotic buffering.
CONCLUSIONS: Multimodal magnetic resonance neuroimaging showed novel, temporally specific imaging manifestations over the disease course in OTC deficiency. This prospective imaging study expands our understanding of the effect of hyperammonemia on the structure and biochemistry of the nervous system.
KEYWORDS: Neuroimaging, Neurometabolic Disorders, Genetics

465. Evaluation of Neurocognitive Function of Prefrontal Cortex in Urea Cycle Disorder
Gropman Andrea (Washington, DC, United States) Anderson Afrouz, Stratakis Constantine, Gandijbakhche Amir

OBJECTIVE: Hyperammonia due to ornithine transcarbamylase deficiency (OTCD) can cause a range of deficiencies in domains of executive function, working memory, and attention. To date, only a few fMRI studies have focused on neuroimaging data in population with OTCD. Yet, there is a need for monitoring the disease progression and investigating an underlying neurocognitive function in OTCD.
METHODS: In this study, we used non-invasive optical neuroimaging technique, functional Near Infrared Spectroscopy (fNIRS), to examine the hemodynamics of prefrontal cortex (PFC) based on neural activation in control and OTCD population while performing a Stroop task.
RESULTS: Results revealed a clear distinction in left PFC activation between controls and patients with OTCD, the controls showing higher level of activation compared to OTCD patients. OTCD subjects also showed diffuse bilateral increase in PFC activation compared to the controls with region-specific activation in left PFC.
CONCLUSIONS: This is a first study using fNIRS to examine a neurocognitive function in OTCD population and can provide a novel insight into the screening and monitoring UCD progression and examining neurocognitive changes.
KEYWORDS: Neuroimaging, Neurometabolic Disorders, Genetics

466. Brain MR angiography in pediatric neurological disorders: clinical manifestations and diagnosis in abnormal brain MR angiography at a single center

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OBJECTIVE: The magnetic resonance angiography(MRA) of brain is a non-invasive method of evaluating blood supply system of the brain. Even though there are some limitations in performing brain MRA in children, it has advantage for avoiding radiation and is sensitive enough to provide an adequate initial evaluation of cerebrovascular disease. The purpose of this study is to estimate the diagnostic value of brain MRA and investigate clinical symptoms and diagnosis in patients who showed abnormalities in brain MRA.
METHODS: From January 2008 to July 2019 at Asan Medical Center, total 657 children who underwent brain MRA were included in this study. Their electronic medical records including clinical symptoms, final diagnosis, and abnormal brain MRA findings were retrospectively reviewed.
RESULTS: A total 144 (21.9%, 69 male, mean age: 7.4 year) patients were found to have brain MRA abnormalities. The most common clinical symptoms for performing brain MRA were focal neurologic sign (23.6%), headache with or without neurological symptoms (20.8%) and seizure (13.2%). Seventy-one patients were diagnosed with Moyamoya diseases and the other 73 patients showed vascular abnormalities associated with cerebral infarction (23.2%; 14 vascular, 2 embolic, 1 infectious), neurogenetic diseases (19.1%; 5 genetic neurovascular disease, 4 neurocutaneous syndromes, 3 metabolic encephalopathy, 2 congenital structural anomaly), congenital vascular malformation (13.6%, 6 arteriovenous malformation, 2 aneurysm, 2 vein of Galen malformation).
CONCLUSIONS: Brain MRA is safe and useful assessment tool for pediatric neurological disorders including vascular and congenital abnormalities. However, further prospective investigation is needed to validate the diagnostic usefulness of brain MRA in pediatric neurologic disorder.
KEYWORDS: Neuroimaging, Stroke (including other Vascular Disorders)

467. Clinico-radiological correlation for establishing etiology of cerebral palsy in children aged 1-12 years

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OBJECTIVE: To determine the correlation between history-based and Magnetic Resonance Imaging(MRI) based etiology for establishing etiology in children with cerebral palsy(CP).
METHODS: 300 consecutive children aged 1-12 years with CP were enrolled from January 2018-June 2019. 221 MRI of the brain could be obtained. Each neuro-imaging was reviewed by a pediatric neurologist and neuroradiologist. History-based etiology and neuroimaging based etiology were separately documented and agreement between the two using Cohen's kappa was determined.
RESULTS: In 122 children the etiology based on history were corresponding to neuroimaging based etiology. In 99 children etiologies didn't match.In 120 children both etiology and neuroimaging based etiology matched with the clinical CP subtype. In 14 children both etiology

and neuroimaging based etiology didn't match with the clinical CP subtype. In 198 children, neuroimaging matched with the clinical subtype. There was a significant association between clinical history-based etiology and diagnosis of the type of CP (*P* value=0.000). Association between neuroimaging based etiology and the clinical diagnosis of the type of CP was statistically significant (*P* value=0.000). *Kappa coefficient* was 0.296 (CI-0.256-0.336) showing only a mild agreement between the two.
CONCLUSIONS: This low agreement suggests that neuro-imaging is a must in all children with CP to establish etiology. As in many cases, the diagnosis varies after imaging and thus helps in management and most importantly can give a clue towards a CP mimic which can have therapeutic and prognostic implications. Even a meticulously taken history can mislead.
KEYWORDS: Neuroimaging

468. Reversibility of a brain atrophy in anorexia nervosa – our experience
Kukuruzovic Monika (Zagreb, Croatia) Malenica Masa, Separovic Iva, Trbojevic Tena

OBJECTIVE: Eating disorder - anorexia nervosa has a significant negative effect on the peripheral and central nervous system. Various studies have been attempting to find the exact influence on morphology of the brain, but they are varied. The method of choice for a series of clinical entities such as neuro-motoric deviations, neuroendocrine disorders, cerebral seizures, tumors, vascular malformations, and structural changes, i.e. atrophy of the brain in eating disorders patients, is magnetic resonance imaging (MRI). Earlier research has suggested a reduction in total gray and white brain volume and recovered brain volume after somatic recovery.
METHODS: The retrospective review of data collected from available case histories of patients treated for the first time at the Eating Disorders Center.
RESULTS: We had followed 19 patients with a brain atrophy on MRI. Mean body mass and body mass index at diagnosis of eating disorders and brain atrophy findings was 43.6 kg (BMI 14.54 kg/m2) while the mean body weight and body mass index at atrophy recovery was 64.8 kg (BMI 20,58 kg/m2). The average duration required to recover atrophic brain changes was 2.2 years.
CONCLUSIONS: The development of brain atrophy is most commonly described in individuals with anorexia associated with a low body mass index. Somatic recovery leads to brain volume recovery, which shows our experience and it coincides with previous research.
KEYWORDS: Neuroimaging

469. A Rare and Unusual Case of an Intramedullary Infantile Hemangioma in a Neonate
Curcio Angela (New York, NY, United States) Maddocks Alexis, Feldstein Neil, Zanazzi George, May Alison

OBJECTIVE: Fifteen cases of intramedullary hemangiomas have been reported, only 2 of which were children who presented with hydrocephalus. We describe an uncommon presentation of an intramedullary hemangioma in a neonate without associated hydrocephalus or cutaneous findings.
METHODS: We conducted a detailed review of the clinical data and performed a literature search on intramedullary hemangiomas.

RESULTS: A 12 day-old full-term girl presented to her pediatrician with decreased movement in her left leg. A left leg x-ray was normal, and she was referred to a neurologist. At 27 days-old, she had a 1-minute episode of whole-body stiffening, unresponsiveness and eye rolling. On hospital neurologic evaluation, her left lower extremity was hypotonic, weak (2/5 proximal and 1/5 distal strength), areflexic at the patella with sustained ankle clonus and an upgoing toe. Head CT, brain MRI and EEG were normal. MRI spine demonstrated a heterogeneously enhancing, intramedullary spinal cord mass (1.3cm x 1.1cm x 5.8cm) from T4 to L1. Due to concern for a highly malignant tumor, the family opted for gross total resection. Pathologic examination was most consistent with a benign infantile hemangioma. The patient did not regain normal motor function in her left leg post-operatively.
CONCLUSIONS: Intramedullary infantile hemangioma is a rare but important differential in a neonate with a heterogeneously enhancing, expansile spinal lesion. In the absence of cutaneous findings, these lesions may be misinterpreted as alternative diagnoses, such as atypical teratoid rhabdoid tumors. Our patient presented prior to the development of hydrocephalus, and gross total resection may have prevented this intracranial consequence.
KEYWORDS: Neuroimaging, Rare Diseases, Teaching of Child Neurology

470. Infantile Subdural Hematoma and Venous Thrombosis Without Other Evidence of Trauma

Scheller Joseph (Baltimore, MD, United States)

OBJECTIVE: Abusive head trauma is a diagnosis considered when infants and toddlers are admitted to the hospital and are found to have subdural hemorrhages. Previous reports have suggested that infants and toddlers who have cerebral venous thrombosis due to medical causes don't develop subdural hemorrhages. We reviewed our experience with subdural hemorrhages and cerebral venous thrombosis to see if this was indeed the case.
METHODS: The author has an active pediatric neurology and forensic neurology and neuroimaging practice. I reviewed all infants referred to our clinic for a second opinion regarding the cause of an acute subdural hematoma. I included infants who had been seen by a child abuse specialist due to a suspicion of abusive head trauma. All infants had a full physical exam, both a head CT and MRI, a neck MRI, an eye exam, and a skeletal survey. I then excluded infants who had evidence of external injury, acute or chronic limb or rib fractures, scalp swelling, neck injury,
RESULTS: Ten infants were found to have both cerebral venous thrombosis and acute subdural hematoma without any other evidence of external injury. Seven were found to have bilateral retinal hemorrhages, one had unilateral retinal hemorrhages, and two had no retinal hemorrhages.
CONCLUSIONS: Infants can develop acute subdural hemorrhages in relation to cerebral venous thrombosis without any evidence of external trauma.
KEYWORDS: Neuroimaging, Trauma, Stroke (including other Vascular Disorders)

471. The Clinical Utility of Brain Magnetic Resonance Imaging in Children Hospitalized in a General Pediatric Department

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OBJECTIVE: To assess the benefit of brain magnetic resonance imaging (MRI) on the care of inpatient children. The clinical applicability and yield of brain MRI in the setting of an inpatient pediatric department has not been investigated.
METHODS: A retrospective chart review of children who were not post-trauma or known neurosurgical patients who underwent brain MRI during their hospitalization in a general pediatric department over a 5-year period. Indications for and outcomes of the brain MRIs were analyzed, in addition to other clinical parameters.
RESULTS: Of the 331 children who underwent brain MRI between 2014 and 2018, 148 (45%) had abnormal findings. High-risk headaches (P = .005) and focal seizures (P = .051) were significantly correlated with findings on brain MRI. Diagnostic and therapeutic yields were most significant in acute demyelinating events (P = .002), acute cerebrovascular disorders (P= .045), high-risk headaches when supported by neurologic and ophthalmologic findings (P < .001), focal seizures with evidence of multifocal epileptic activity on an electroencephalogram (P = .003), diplopia/strabismus and decrease in visual acuity when accompanied by cranial nerve palsy (P = .021), and optic nerve impairment (P = .023).
CONCLUSIONS: The contributions of a brain MRI in hospitalized children are pivotal in specific clinical situations. Brain MRIs should be considered in inpatient pediatric settings after a judicious decision-making process in order to optimize its diagnostic and therapeutic yield without compromising care.
KEYWORDS: Neuroimaging, Headache/Migraine, Epilepsy

472. Is MRI always necessary in patients with papilledema without atypical features?
Larsh Travis (Cleveland, OH, United States) Hsich Gary

OBJECTIVE: To investigate if computed tomography (CT) of the brain is sufficient for evaluation of pediatric papilledema with normal neurologic features.
METHODS: We reviewed medical records of children aged 18 years or younger between 2012-2019 with diagnostic codes for papilledema/optic disc edema, IIH, brain tumor, or CVT. Our study had 2 parts: 1) for patients presenting with papilledema and an otherwise normal neurological evaluation, we reviewed their CT and magnetic resonance imaging (MRI) to compare diagnostic yield, and 2) for all patients (with or without papilledema) diagnosed with brain tumor or CVT, we reviewed their clinical presentation and diagnostic yield of imaging.
RESULTS: Part 1: During 2012-2019, 142 pediatric patients with papilledema presented with otherwise normal neurologic features. 23 patients had both CT and MRI -- all 4 brain tumors were seen on CT, and none had CVT. An additional 8 patients had CT only – papilledema resolved in all 8 with no clinical worsening characteristic of brain tumor or CVT. Part 2: In patients with brain tumors, tumors were identified on CT in 55/56 patients. The single patient with a normal CT presented with focal seizures and a focal neurologic exam. In CVT patients, 10/13 had an abnormal CT; all 3 patients with normal CT presented with other abnormal neurologic features (seizures, mental status changes, abnormal exam) that had already prompted further evaluation.
CONCLUSIONS: In children with papilledema and otherwise normal neurological evaluation, CT imaging may be sufficient.
KEYWORDS: Neuroimaging, Headache/Migraine, Brain Tumors/Oncology

473. "Unlocking" clinical brain MRIs for quantitative analysis: Cross-validation of voxel-level DTI norms and application to individuals with cerebral palsy (CP)

Chin Eric (Baltimore, MD, United States) Hoon Alexander, Jantzie Lauren, Ye Xiaobu, Sair Haris, Meoded Avner, Robinson Shenandoah

OBJECTIVE: Quantitative MRI promises to improve sensitivity to brain abnormalities. We estimate the number of typical healthy participants needed to obtain a reliable diffusion tensor imaging (DTI) template for use as a voxelwise statistical norm for clinical cases of CP.
METHODS: Twenty-one healthy volunteers aged 23-40 (mean 32, 9 male) underwent brain MRI using clinical DTI protocols (b=800x40 directions, resolution 1.2x1.2x3mm) in an IRB-approved study. DTI underwent artifact correction (TORTOISE DIFFPREP) and robust nonlinear tensor estimation (RESTORE). Tensor templates were created using diffeomorphic registration (DR-TAMAS) of random subsets of n=3, 5, 10, 15, and 20 participants. Voxelwise mean fractional anisotropy (FA) was computed for each template then registered to the n=20 template. An eroded white matter mask was applied. Each template was used for nonlinear registration and computation of voxelwise t-scores for 1) a randomly-selected typical participant not included in creation of that template, and 2) a clinical scan from a 31 year old participant with CP (GMFCS V, periventricular leukomalacia).
RESULTS: For a random out-of-sample control participant, most voxels showed FA error < 0.1 at all sample sizes (74% at n=3 to 85% at n=20). Median voxelwise FA standard error decreased from 0.027 at n=3 to 0.013 at n=20 (for comparison, median voxelwise FA difference for the participant with CP was 0.11; Figure 1). t-score maps demonstrated decreased posterior white matter FA even using an n=3 template. More diffuse involvement becomes apparent with larger control groups (Figure 2).
CONCLUSIONS: Norms based on small control groups can identify quantitative abnormalities on clinical DTI.
KEYWORDS: Neuroimaging, Movement Disorders (including Cerebral Palsy), Neuroscience

NEUROMETABOLIC DISORDERS

474. Vitamin responsive neurological disorders in childhood and adolescence: Experience from teaching hospitals in India

Yoganathan Sangeetha (Vellore, India) Sharma Suvasini, Bidkar Sayli, Thomas Maya, Chandran Mahalakshmi, Oommen Samuel, Koshy Beena, Danda Sumita

OBJECTIVE: Insufficient dietary intake or poor absorption of vitamins and inherited defects in the synthesis, binding and utilization of cofactor forms result in various neurological disorders. The objectives of this study are to describe the phenotype and outcome of vitamin responsive neurological disorders in children and adolescents.
METHODS: The clinical, laboratory and neuroimaging data of children and adolescents with various vitamin responsive neurological disorders from January 2013 to December 2019 were extracted from the database of two teaching hospitals in India. Children with various mitochondrial disorders were excluded.
RESULTS: Among 95 patients included for analysis, 24 had biotinidase deficiency, one had cerebral folate deficiency and one had hereditary folate malabsorption. Homocystinuria due to

cystathionine beta-synthase deficiency was diagnosed in 4 children. Hyperhomocysteinemia due to methylenetetrahydrofolate reductase deficiency was diagnosed in 7 patients. Four children were diagnosed to have biotin-thiamine responsive basal ganglia disease. Pyridoxine dependent epilepsy was identified in 4 children and 1 child had pyridoxal phosphate deficiency. Diagnosis of L-amino acid decarboxylase was established in 4 patients. Nutritional B12 deficiency-related neurological syndrome was diagnosed in 35 patients. Diagnosis of hereditary megaloblastic anemia was established in one child and 8 patients were diagnosed to have methylmalonic aciduria. Thiamine responsive maple syrup urine disease was established in one child. The long-term neurological outcome depends upon the etiology.
CONCLUSIONS: The clinical manifestations of vitamin responsive neurological disorders are often variable. It is important to understand the clinical phenotypes to facilitate rapid diagnosis and early initiation of treatment and to prevent long-term neurological sequelae.
KEYWORDS: Neurometabolic Disorders, Rare Diseases, Genetics

475. Single Gene, Two Diseases, and Multiple Clinical Presentations: Biotin–Thiamine-Responsive Basal Ganglia Disease
Aydın Kürşad (İstanbul, Turkey) Kılıç Betül, Topçu Yasemin, Dursun Şiar, Erol İlknur, Dolu Merve, Taşdemir Haydar

OBJECTIVE: To present seven new genetically confirmed cases of biotin–thiamin-responsive basal ganglia disease (BTBGD) with different clinical and brain magnetic resonance imaging (MRI) characteristics.
METHODS: Genetic mutations, clinical presentations,brain MRI findings,treatment response,and prognosis of seven patients with BTBGD,diagnosed with SLC19A3 gene mutations were described.
RESULTS: Among seven patients (2 females;5 males,aged between 1 month-20 years) diagnosed with BTBGD, two had early infantile form, four had classic childhood form, and one was asymptomatic.Four different homozygous mutations were found in the SLC19A3 gene. Two patients with early infantile form presented with encephalopathy, dystonia, and refractory seizure in the neonatal period and have different mutations; one of them died without diagnosis at 42 days.Their MRI findings were similar and pathognomonic for the early infantile form.Three siblings had similar homozygous mutations: one presented seizure and encephalopathy at the age of 4 months,one presented seizure at 14 years,and another was asymptomatic at 20 years.Their MRI findings were similar and suggestive of the classic form. Other two siblings had similar homozygous mutations: one presented with developmental delay, seizure, and dystonia at 18 months,and the other presented with subacute encephalopathy and ataxia at 20 months.Their MRI findings were also similar and suggestive of the classic form.
CONCLUSIONS: BTBGD may present with different clinical characteristics or remain asymptomatic for a long time period even in a family or patients with similar mutation.The neonatal/infantile form may become fatal quickly with delayed diagnosis or if untreated.Brain MRI patterns may be an important biomarker for the early diagnosis of BTBGD that would save children’s lives.
KEYWORDS: Neurometabolic Disorders, Neuroimaging, Rare Diseases

476. Molecular Mechanisms of Sulfite Mediated Neurotoxicity
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OBJECTIVE: To define the molecular mechanism underlying sulfite mediated neurotoxicity, aiming to identify new therapeutic targets for the inherited disorders of sulfite oxidase and molybdenum cofactor deficiency.
METHODS: Pure embryonic mouse cortical neurons were prepared and cultured using standard protocols. Cultures were treated with sulfite or S-sulfocysteine, at concentrations reported in sulfite oxidase deficient patients, between days 7-10 *in vitro*. Cell death was quantified by costaining neurons with Hoechst and propidium iodide dyes. Intracellular ATP was measured with the CellTiter-Glo assay (Promega). Mitochondrial respiration was measured in a Seahorse XFe96 using a mitochondrial stress test kit (Agilent).
RESULTS: Exogenous sulfite applied to cortical neuron cultures caused neurite blebbing within 30 minutes of application and apoptotic cell death that began at 4 hours (pyknotic nuclei) and peaked at 12 hours (maximal lactate dehydrogenase release) post-treatment. Within the first 30 minutes, sulfite rapidly decreased intracellular ATP levels. This effect was dependent on the spontaneous reaction of sulfite with cystine in the culture media to form S-sulfocysteine, a known agonist of NMDA receptors. S-sulfocysteine depleted intracellular ATP levels in a dose-dependent manner similar to sulfite, and impaired baseline and maximal mitochondrial respiration. Blocking inotropic NMDA receptors or chelating extracellular calcium prevented the depletion of intracellular ATP, preserved mitochondrial function, and prevented sulfite and S-sulfocysteine mediated neurotoxicity.
CONCLUSIONS: The catastrophic CNS degeneration observed in typical sulfite oxidase and molybdenum cofactor deficient patients is likely caused by NMDA receptor overactivation triggering the excitotoxic cascade. NMDA receptor antagonists may offer benefit to patients.
KEYWORDS: Neurometabolic Disorders, Rare Diseases, Neuroscience

477. Effects of High Fat Caloric Restriction and Ketogenic Diet on PI3K/AKT/mTOR Signaling Axis
Turkdogan Dilsad (Istanbul, Turkey) Sonmez Ilayda, Yukseloglu Eren, Karabulut Seyda, Arisan Elif

OBJECTIVE: Increasing evidence shows that caloric restriction (CR) and ketogenic diet (KD) would protect from neuroinflammatory and neurodegenerative diseases. Activation of the low-energy sensor 5'-AMP activated protein kinase (AMPK) by CR is effective in performing some of these protective functions). We aimed to determine whether high fat and calorie restricted diet-based changes to liver tissue can activate p-AMPK.
METHODS: The study group consisted of 50 Winstar female rats (aged 6 weeks) which were stratified into 5 subgroups and received the following diets *ad libidum* for 7 weeks: 1- KD-p (70% fat of daily calorie needs) with palm kernel oil) 2- KD-o (with olive oil), 3- CR-KD-p (70% of total daily calorie), 4-CR-KD-o, 5-Standart diet with normal daily calorie intake. Serum β-hidroksibutirate levels were measured to verify the effectiveness of KD. At the end of 7 weeks, liver biopsy was done to 3 rats in each subgroup. Isolation of the total protein amount from frozen rat liver tissue was followed by immunoblotting assay to evaluate PI3K/AKT/mTOR signaling axis with its downstream target AMPK. Phospho forms of AKT, mTOR and AMPK were determined to evaluate differences among different KD models.

RESULTS: KD-o and CR-KD-o increased AMPK levels and triggered AMPK activation. This effect was more prominent in CR group. Palm oil had less impact on AMPK activation. SD was ineffective.
CONCLUSIONS: Calorie restricted high-fat diet enriched with unsaturated fatty acids stimulates the clearance mechanism of liver tissue through activation of AMPK at Thr 172, which may lead to autophagic induction.
KEYWORDS: Neurometabolic Disorders, Translational/Experimental Therapeutics

478. Pyruvate dehydrogenase deficiency- presenting as episodic paralysis in a three year old girl.
Singh Sonali (New Delhi, India) Sinha Rahul, Badal Sachendra, Jaunhari Prashant, Gulati Sheffali

OBJECTIVE: Pyruvate dehydrogenase deficiency has wide spectrum of clinical presentation. A three year old girl presented with episodic floppiness and elevated CSF lactate. Her exome sequencing showed heterozygous mutation in *PDHA1* gene (X-linked).
METHODS: Three year old girl born to non-consanguineous parents with uneventful birth history presented with episodic floppiness for last six months. She had premorbid motor developmental delay. For past six months she had episodes of sudden floppiness without alteration of sensorium, each lasting for 20-30 minutes. She had 3-4 such episodes daily. Frequency of these episodes increased during periods of illness. Laboratory investigations showed elevated CSF lactate - 3.5 mmol/L (Normal range: 1.2-2.1 mmol/L), normal CSF glucose-58mg/ dl and normal serum potassium - 3.7mmol/L. Working diagnosis of mitochondrial cytopathy was made. Her blood sample for next generation sequencing was sent. She was started on high dose thiamine along with coenzyme Q, carnitine, riboflavin, biotin, vitamin E.
RESULTS: Within two weeks of initiation of therapy frequency as well as duration of these episodes of floppiness decreased. Her exome sequencing detected a likely pathogenic heterozygous missense variation *c.901 C>G (p.Arg301gly, R301G)* in exon 9 *of PDHA1* gene. High dose thiamine was continued. At the end of three months she had no worsening.
CONCLUSIONS: PDH deficiency has varied presentation ranging from fatal neonanatal lactic acidosis to milder episodic ataxia. In this case symptoms of the girl mimicked periodic paralysis. Episodic weakness with normal potassium and elevated lactate should be investigated for this entity and a trial of high dose of thiamine should be given.
KEYWORDS: Neurometabolic Disorders, Genetics

479. Pitfalls and promises in the diagnostic odyssey of juvenile neuronal ceroid lipofuscinosis (CLN3 Batten disease)
Abreu Nicolas (Columbus, OH, United States) de los Reyes Emily

OBJECTIVE: To characterize how children with CLN3 Batten disease reach a genetically confirmed diagnosis and identify factors affecting diagnostic efficiency.
METHODS: Medical records were reviewed for all individuals with CLN3 Batten disease at Nationwide Children's Hospital's Batten Center of Excellence seen for initial evaluation from February 2019-January 2020.

RESULTS: Ten symptomatic children (3 girls) had available clinical genetic testing reports with biallelic pathogenic or likely pathogenic variants in *CLN3* and were included in the analysis. The median age at initial symptom onset was 64 months (range 42-85 months), with all children presenting with vision loss. The median time from symptom onset to ophthalmology consultation was 7.5 months (range 0-25 months), and a confirmed genetic diagnosis occurred 16 months from symptom onset (range 3-37 months). Diagnosing providers were mostly non-geneticists (Ophthalmology = 4, Neurology = 3, vs. Genetics = 3) who preferred using gene panels (n=8). Ancillary ophthalmologic assessments aiding in diagnosis included electroretinograms (n=7), optical coherence tomography (n=5), and visual evoked potentials (n=2). Examples of diagnostic delays from genetic test selection included serial single gene testing, inadequate coverage for deletions, and restrictive panel selection.
CONCLUSIONS: Keys to early diagnosis of CLN3 Batten disease include comprehensive ophthalmologic evaluation paired with appropriate genetic test selection. Next-generation sequencing gene panels have been helpful for efficient identification of symptomatic children, and we favor selection of a sufficiently broad panel based upon clinical findings. Deletion/duplication analysis should be always be considered, especially when evaluating for disorders in which copy number variants are known to occur.
KEYWORDS: Neurometabolic Disorders, Genetics, Rare Diseases

480. PHENOTYPIC SPECTRUM OF COBALAMIN METABOLISM DISORDERS- A CASE SERIES

Patel Vishal (Mumbai, India) Arora Anshita, Rathod Nishant, Udwadia-Hegde Anaita

OBJECTIVE: Genetic disorders of vitamin B12 (cobalamin) metabolism constitute an important fraction of inherited metabolic disorders. The phenotypic variability and age of onset are influenced by severity and location of the defect within the metabolic pathway. Here we describe eight patients of cobalamin metabolism disorders who presented at our centre with a spectrum of clinical presentations.
METHODS: We retrospectively studied 8 patients with cobalamin metabolism disorders and evaluated the clinical presentation, metabolic investigations and treatment of these patients and their correlation with genotype. Treatment was modified after the genetic diagnosis.
RESULTS: 4/8 patients had MTHFR gene mutation who presented in childhood/adolescence with varied clinical features of progressive spastic paraparesis, cognitive decline and encephalopathy. There was persistently high serum homocystine with subnormal serum B12. They were successfully treated with injectable methycobalamine along with methylfolate following the diagnosis.
Remaining 4/8 had presented in infancy with features of neuroregression, development delay, intractable seizures and behaviour problems. Metabolic investigations showed deranged acylcarnitine levels in 2/4 patients and high homocystine levels in 2/4 patients. They were subsequently diagnosed to have combined homocystinemia and methylmalonic acidemia (3/4) and isolated methylmalonic acidemia (1/4) based on genetic testing, which revealed mutations in MMADHC, MMACHC, HCFC1 and MMAB genes. Treatment was modified after the genetic diagnosis. Improvement was noted in all patients after modification in treatment.
CONCLUSIONS: Patients with cobalamin metabolism disorders can present with varied phenotypes. Thus, high index of suspicion is required to diagnose these patients at an early stage. Early initiation of treatment improves outcomes.

KEYWORDS: Neurometabolic Disorders

481. EVALUATION OF CLINICAL RATING SCALES IN ADRENOLEUKODYSTROPHY: MAJOR FUNCTIONAL DISABILITIES (MFD) VERSUS NEUROLOGIC FUNCTION SCORE (NFS)

Raymond Gerald (Baltimore, MD, United States) Kim Alexander, Cayton Vaught Kamaria, Bishop Jewels, Xiao Changrui

OBJECTIVE: ALD is a genetic disorder that affects the brain with 1/3 developing childhood disease. A challenge in trials are meaningful outcome measures. The Neurologic Function Scale, a measure of involvement is a 25-point scale. Experienced users have high inter-rater reliability, but requires training. To simplify the outcome measures but still provide meaningful information, the Major Functional Disabilities Scale (MFDS) was developed. MFDS looks at 6 measures impacting quality: Communication loss; blindness; tube feeding; incontinence; wheelchair dependence; loss of voluntary movements. The MFDS offers a simplified metric, but to date no comparison of reliability has been determined.
METHODS: Raters were asked to review 6 simulated scenarios scoring whether an MFD was present, then which MFD were present, then the same scenarios using the NFS. Four physician raters were naïve to NFS and MFDS scoring. Their results were compared to an experienced rater (GR).
RESULTS: All raters agreed on the presence of an MFD in all scenarios providing 100% agreement. There was 97% agreement between the naïve and the experienced reviewer on which MFDs were present. There was more variation in the scoring of NFS. Raters were able to accurately score unaffected individuals as 0, but there was wider variation in the scores of affected subjects.
CONCLUSIONS: In the evaluation of CCALD clinical progression, the presence or absence of major functional disabilities is easily determined with a high inter-rater reliability in scorers who have no prior experience with the disorder making this a simple and effective measure of outcome in trials

KEYWORDS: Neurometabolic Disorders, Translational/Experimental Therapeutics

482. Wernicke's encephalopathy in children with acute leukemia and after hematopoietic stem cell transplantation.

Natrusova Natalia (Moscow, Russian Federation) Burtsev Evgeny, Suleimonova Amina, Seliverstova Evgeniya, Bronin Gleb, Kirgizov Kirill, Shchederkina Inna

OBJECTIVE: Describe cases of Wernicke's encephalopathy (WE) caused by thiamine deficiency as rare complication of acute leukemia treatment (both with high dose chemotherapy and after hematopoietic stem cell transplantation – HSCT).
METHODS: clinical, laboratory, magnetic resonance imaging (MRI).
RESULTS: Boy P, 14 years old, and girl R, 17 years old, were treated for relapsed acute lymphoblastic leukemia, HSCT was performed. Boy M, 10 years old, was treated for acute myeloid leukemia by high dose chemotherapy before HSCT. Both of boys had resistant vomiting and loss of 10% and 15% of body weight. M. had severe gastrointestinal toxicity (grade 3-4 by CTCAE), appendectomy was performed. Parenteral nutrition was used for M and R. Impaired consciousness (12/13 score of Glasgow Coma Scale), progression of ataxia, muscular strength

loss and vegetative dysfunction symptoms were observed in both of boys. R was treated for grade 4 graft-versus-host disease. Neurological deficit was persistent at R (toxic encephalopathy, extrapyramidal disturbance, oculomotor dysfunction) without significant increase of symptoms during therapy. Thalamus (img.1) and mammillary bodies (img.2) damage was found in brain MRI. All children were treated by high dose of thiamine (3 days) intravenously and long continuation therapy afterwards. The regression of clinical and MRI symptoms was observed in boys. R died due to adenoviral infection.
CONCLUSIONS: Treatment of malignances, associated with malnutrition and digestive tract disorders could lead to WE. In pediatric practice it is usually underdiagnosed. More than third of cases were diagnosed postmortem according literature. Timely diagnosis and sufficient thiamine substitution can improve survival
KEYWORDS: Neurometabolic Disorders, Brain Tumors/Oncology, Neuroimaging

483. An International Prospective Natural History Study of NGLY1 Deficiency
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OBJECTIVE: To refine the clinical spectrum of NLGY1 deficiency and identify candidate endpoints for therapeutic trials.
METHODS: We performed prospective phenotyping of 26 individuals with NGLY1 deficiency. Remote assessments were performed at 4-month intervals; 12 participants underwent in-person clinical evaluations at a single center. Descriptive statistics are provided for the first year of an ongoing natural history study.
RESULTS: Mean age was 10.0 years (range 1.9-21.0) and 12/26 (46%) were female. All subjects had global developmental delay. Twelve underwent neuropsychiatric evaluation revealing moderate-to-profound cognitive impairment in 83%. The majority demonstrated hypo- or alacrima, decreased blink, and lagophthalmos with corneal involvement. All had axial hypotonia. Appendicular hypertonia, distal greater than proximal muscle wasting of the lower extremities, and hypo- or areflexia were frequently observed. 11/12 (92%) had a mixed or axonal length-dependent sensorimotor polyneuropathy. An abnormal sweat response was detected in 9/12 (75%). Video assessment revealed a hyperkinetic movement disorder that evolved to more predominant hypokinesia with age. 17/26 (65%) reported a history of seizures. Generalized epileptiform activity was captured on EEG in 7/12 (58%). Abnormal GlcNAc metabolites were observed in all urine specimens obtained, representing a putative biomarker. Historic data showed a transient severe elevation in liver enzymes in early childhood that improves with mild fluctuations.
CONCLUSIONS: We highlight a prominent sensorimotor polyneuropathy and evolution of a complex movement disorder in NGLY1 deficiency through detailed and frequent phenotyping of an international cohort. Candidate clinical endpoints will be assessed over time for correlation with disease severity.
KEYWORDS: Neurometabolic Disorders, Movement Disorders (including Cerebral Palsy), Rare Diseases

484. Clinical, radiological and ophthalmological follow-up, after 4 years of hydroxocobalamin dose intensification, in early onset cblC and cblA deficiency patients.

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OBJECTIVE: In spite of appropriate OHCbl treatment, early onset cblC deficiency patients may have insufficient control on biochemical markers and develop cognitive delay and maculopathy, and cblA deficiency patients, chronic renal insufficiency and optical atrophy. In contrast, hydroxocobalamin dose-intensification (OHCBL-DI) can produce excellent control on biochemical markers and better neurological and ophthalmological outcome. With prolonged OHCbl-DI, we hypothesized to preserve cognitive and ophthalmological outcome and evaluated the tolerance of OHCbl-DI.
METHODS: 3 cblC patients (pts 1-3) and one cblA patient (pt 4) received OHCbl-DI for control of biochemical markers. All patients had regular clinical and ophthalmological exam and control MRI after 3 years of age (pts 1-3) and age 12 years (pt 4)
RESULTS:

Patients.	pOHCbl	pHcy	uMMA	Eye fondus	OCT	Nystagmus.	MRI	Cognitive
1 (4 yo).	3,4	14,2.	31,0.	pfovea.	pfovea.	-	NL.	+
2 (4 yo).	3,4.	14,3.	47,0.	pfovea.	pfovea.	-	NL.	+
3 (4 yo).	4,3.	19,0.	9,0.	Nl.	Nl.	mild.	LOM.	+/++
4 (13 yo).	0,95.	-	122,0.	Nl.	Nl.	-	Nl.	Nl

Cognitive: + mild, ++ moderate delay; LOM: loss of myelin; Nl: normal; OHCbl: parenteral OHCbl dose: mg/kg; pHcy: plasma homocysteine (NL: 3.0 -13.0 µmol/l); uMMA: urinary methyl-malonic acid (Nl < 17,0 µmol/mmol crea); pfovea: perifoveal atrophy; OCT: optical coherence tomography: altered perifoveal photoreceptor layer; yo: years old (pts 1-3: c.271dupA, pt 4: c.439+4_439+7del and c.593_596del)
CONCLUSIONS: We confirmed that OHCBL-DI produced improvement in neurological and cognitive outcome in parallel with increased or stable brain myelination and appeared to be safe without producing side effect.
KEYWORDS: Neurometabolic Disorders, Genetics, Rare Diseases

485. Twenty-two-year clinical course of a patient with thiamine-responsive PDHC deficiency

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OBJECTIVE: To show a long-term prognosis of thiamine-responsive pyruvate dehydrogenase complex (PDHC) deficiency with thiamine therapy.
METHODS: We followed psycho-motor development, easy fatiguability, serum levels of lactate, pyruvate and thiamine in a male patient with thiamine-responsive PDHC deficiency for 22 years.
RESULTS: The patient presented with acute muscle weakness associated with febrile illness at the age of 1 year. Serum lactate and pyruvate levels were 6.7 mM and 0.6 mM, respectively. PDHC activity in the cultured lymphoblastoid cell lines were measured at 4 years of age.

Dichloroacetate-activated PDHC activity with 1 x 10^{-4} mM thiamine pyrophosphate (TPP) was 28% of normal while that with 0.4 mM TPP was 45% of normal. Molecular analysis revealed p.R88C (c.262C>T) in *PDHA1* exon 3. With 100 mg (7 mg/kg) of benzotiamine, he became able to walk > 1 km at age 4 years. At 5 years of age, the dose was increased to 300 mg (16 mg/kg), which further improved the motor activity. The dose was increased whenever the patient complained of fatigue or cramp. Since 14 years of age, he has been on 600 mg of fursultiamine without any fatigue on exertion and serum levels of total thiamine were 600-700 ng/ml (control, 24-66). Serum lactate levels remained high (3.0 – 3.9 mM). His IQ at age 10 years was 74 and he is currently 23 years old and employed full-time.
CONCLUSIONS: Keeping the serum thiamine level > 600 ng/ml could maintain the motor activity stable for > 8 years in a patient with R88C mutation in *PDHA1*.
KEYWORDS: Neurometabolic Disorders, Neuromuscular Disorders

486. Clinical and Radiographic Course of Arrested Cerebral Adrenoleukodystrophy
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OBJECTIVE: To gain insight into the natural history of arrested cerebral adrenoleukodystrophy (CALD), we quantified the change in Neurologic Function Score (NFS) and Loes Score (LS) over time in patients whose cerebral lesions spontaneously stopped progressing.
METHODS: We retrospectively reviewed a series of 22 patients followed longitudinally over a median time of 2.4 years (0.7 – 17.0). Primary outcomes were change in radiographic disease (LS/year) and clinical symptoms (NFS/year) between patients who never developed a contrast-enhancing lesion (GdE- subgroup), and those who did (GdE+ subgroup). Secondary analyses comparing patterns of neuroanatomical involvement and lesion number, and prevalence estimates, were performed.
RESULTS: Cerebral lesions were detected at a median age of 23.3 years old (8.0 – 67.6), with an initial LS of 4 (0.5 – 9). NFS was 0.5 (0 – 6). Change in NFS or LS per year did not differ between subgroups. No patients who remained GdE- converted to a progressive CALD phenotype. Lesion contrast enhancement was associated with disease progression ($r_s = 0.559$, $p < 0.001$). Four patients (18.2%) underwent step-wise progression, followed by spontaneous resolution of contrast enhancement, and re-arrest of disease. Three patients (13.6%) converted to progressive CALD. Nineteen patients (86.4%) have arrested CALD at most recent follow-up. The prevalence of arrested CALD is 12.4%.
CONCLUSIONS: Arrested CALD lesions can begin in childhood, and patients are often asymptomatic early in disease. The majority of patients remain stable. However, clinical and MRI surveillance is recommended as a minority of patients undergo step-wise progression, or conversion to progressive CALD.
KEYWORDS: Neurometabolic Disorders, Neuroimaging, Rare Diseases

487. A homozygous variant in the NFS1 gene identified by rapid WGS: A case of progressive weakness and hypotonia
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OBJECTIVE: Iron-sulfur (Fe-S) cluster proteins are involved in critical functions for gene expression regulation and incorporated as cofactors for respiratory chain complexes. Mutations in Fe-S protein synthesis and Fe-S cluster assembly lead to a spectrum of diseases that can result in metabolic crises.
METHODS: We report a rare, likely pathogenic variant of unknown significance in the NFS1 gene in a young infant.
RESULTS: A 7 month old previously healthy infant presented with two weeks of cold-like symptoms and one week of progressive weakness and poor feeding. His exam was notable for diffuse hypotonia and weak cry with a gradual loss of reflexes in an ascending pattern. Lumbar puncture and MRI brain were unremarkable. An MRI spine showed enhancement of the proximal musculature, and an EMG demonstrated reduced conduction amplitudes. The patient acutely declined with lactic acidemia, liver failure, cardiomyopathy, myositis and respiratory failure. Rapid whole genome sequencing revealed a homozygous missense mutation in the NFS1 gene c.215G>A (p.Arg72Gln). A muscle biopsy confirmed abnormal mitochondria and lipid accumulation. The infant eventually recovered with supportive care and nutritional supplementation.
CONCLUSIONS: Mitochondrial disorders are rare but can have fatal outcomes. We report a fourth patient with this missense homozygous mutation in NFS1, which is a highly conserved cysteine desulfurase important for Fe-S cluster biosynthesis. The same mutation was previously reported in three siblings from the same family who presented with lactic acidemia, hypotonia and electron transport chain dysfunction. Our patient recovered well despite a metabolic crisis leading to multiorgan failure.
KEYWORDS: Neurometabolic Disorders, Genetics, Rare Diseases

488. Prevalence of Sleep and Mood Disorders in Pediatric Mitochondrial Disease
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OBJECTIVE: Mitochondrial diseases are a genetically and phenotypically heterogeneous group of disorders with predilection for the nervous system. Analysis of associated sleep and mood disorders is limited in the literature particularly in the pediatric population. We used a text-based search of the electronic medical record (EMR) to identify the documented prevalence of sleep and mood disorders in a defined cohort of patients with mitochondrial disease at a tertiary care children's hospital.
METHODS: The IRB approved search was conducted within an established database of patients with mitochondrial disease (n=95). First, the EMR of each patient was searched for ICD codes referring to neuropsychiatric disorders. A second search used a two-clinician derived list of terms to search other fields of the EMR. Resulting diagnoses were analyzed for association with specific genetic information within the mitochondrial patient database.
RESULTS: 19% (18/95) of patients were diagnosed with a mood or sleep disorder, and 44% of these patients carried multiple diagnoses. The median age was 14 years. 3% were diagnosed with depression, 6% with anxiety, 4% with adjustment disorder, 3% with autism, and 8% with sleep disorder. Of the patients with neuropsychiatric diagnoses, 44% had mutations in nuclear DNA, 17% in mitochondrial DNA, and 22% were diagnosed by muscle enzyme assays.
CONCLUSIONS: One out of five pediatric mitochondrial disease patients had a mood or sleep disorder. There was no evidence of association with specific genetic diagnoses. A comprehensive

evaluation for mitochondrial disease should include assessment of mood and sleep, with appropriate referrals as indicated.
KEYWORDS: Neurometabolic Disorders

489. Natural history of CLN6 Batten's disease, Late infantile presentation
O'Neal Matthew (Columbus, OH, United States) de Halac Ines, Falke Ashley, de los Reyes Emily

OBJECTIVE: Mutations in the CLN6 gene cause neuronal ceroid lipofuscinosis (CLN6) , which is a severe neurodegenerative disorder leading to dementia, epilepsy, motor impairment, and visual degradation. CLN6 is a transmembrane protein located in the membrane of the endoplasmic reticulum.
METHODS: To determine the age of onset of motor and language decline in individuals with late infantile onset (<5) CLN6 disease utilizing the Hamburg LINCL scale. Data was obtained utilizing data sets from Dem-Child, Nationwide Children's hospital and Argentinian registries.
RESULTS: There were 24 patients available for analysis whose disease onset was less than 5 years of age. The mean baseline age (in months) of 38.21 ± 10.15 and 9 (39%) males. Longitudinal data for combined datasets showed a statistically significant decline in all motor-language summary scores over time (Figure 1). Time of age in months to drop 1 or 0 for motor score, at a median of 65 months. Time of age in months to drop to 1 or 0 in language showed a median of 60 months. Estimated slope of decline was -1.26± 0.33 points per year, each year, after start of decline.
CONCLUSIONS: This is the largest natural history cohort to document progression of disease. The importance of the natural history approach of a rare pathology like CLN6 is that is objectivizes the phenotypical differencesamong L I- CLN2 and CLN6 diseases, and at the same time it sets up the base line of symptoms evolution for comparisons in future therapeutic studies.
KEYWORDS: Neurometabolic Disorders, Rare Diseases

490. Effects of High Fat Caloric Restriction and Ketogenic Diet on Acute Inflammation and Oxidative System
Turkdogan Dilşad (Istanbul, Turkey) Karabulut Seyda, Sener Goksel

OBJECTIVE: Increasing evidence shows that ketogenic diet (KD) and calorie restriction decrease inflammation and oxidative stress. However acute inflammatory responses related with ketosis may be different based on tissue or acute metabolic state. We aimed to evaluate effects of high fat and calorie restricted diet-based changes on the inflammatory response after acute endotoxemia.
METHODS: The study group consisted of 52 Winstar female rats (aged 6 weeks) which were stratified into 4 subgroups and received the following diets *ad libidum* for 7 weeks: 1- KD (70% fat of daily calorie needs) 2- Calorie restricted (CR)-KD (70% of total daily calorie) 3- a carbohydrate-based eukaloric standart diet (E-SD), 4- CR-SD. Serum β-hidroksibutirate (BOHB) levels were measured to verify the effectiveness of KD or CR. At the end of 7 weeks, animals received intraperitoneal lipopolysaccharide (150 µg/kg) during postprandial phase. Serum inflammatory cytokines and superoxide dismutase (SOD) levels were measured.
RESULTS: Serum BOHB levels significantly increased in CR and KD groups compared to in eucaloric SD group. Hypoglycemia did not occur in any animals. Serum IL-1 and TNF-a levels increased in all groups and no significant difference was found among subgroups. Serum IL-6

levels significantly decreased in CR-SD group compared to the other groups (p=0,004). Serum SOD levels significantly increased in all groups on diets producing ketones mainly in CR-KD group compared to animals on E-SD (p=0,007).
CONCLUSIONS: Instead of high fat diets, only caloric restriction induced the response to acute inflammation at postprandial phase. All ketone-elevating dietary treatments are antioxidant.
KEYWORDS: Neurometabolic Disorders, Neuroscience

491. Cerebral folate deficiency in two siblings with compound heterozygous variants of the SLC19A1 reduced folate carrier
Lammert Dawn (Baltimore, MD, United States) Rothman Steven, Pellegrino Joan, Petropoulou Kalliopi, Zhang Guojun, Sakonju Ai

OBJECTIVE: There are several potentially treatable causes of cerebral folate deficiency (CFD), including defects in the proton-coupled folate transporter (PCFT; *SLC46A1*), folate receptor alpha (FRα; *FOLR1*), and 5,10 methyltetrahydrofolate synthetase. We describe two siblings harboring variants in the reduced folate carrier (RFC; *SLC19A1*), resulting in a new cause of CFD.
METHODS: We illustrate the clinical phenotypes and variable expression, including EEG and MR imaging, of two siblings, one with myoclonic epilepsy and brainstem degeneration, the other with oculomotor apraxia and ataxia. Whole exome sequencing of the siblings and their parents was undertaken. CSF studies included 5-methyltetrahydrofolate (5MTHF) and anti-FRα antibodies. We reviewed available functional data and performed structural prediction protein modeling of the variants.
RESULTS: MRI demonstrated symmetric lesions at 4 months in one sibling who presented with presumed ADEM-like illness with subacute encephalopathy and seizures, prompting genetic and metabolic workup. The sister was known to have oculomotor apraxia and ataxia. Whole exome sequencing revealed compound heterozygous mutations p.S46N and p.F141del in *SLC19A1* encoding RFC inherited in trans, one from each unaffected parent. Initial CSF 5MTHF was undetectable, while serum levels were within normal limits in both cases. Combined IV and oral folinic acid supplementation in one patient lead to a modest increase in CSF 5MTHF level.
CONCLUSIONS: Autosomal recessive RFC mutations represent a new, potentially treatable form of cerebral folate deficiency. This case highlights the importance of checking CSF 5-MTHF for both confirmation and management of these disorders and their spectrum of presentation with epilepsy and ataxia.
KEYWORDS: Neurometabolic Disorders, Genetics, Rare Diseases

492. Biotinidase deficiency a treatable IEM with infantile onset epilepsy and cutaneous involvement: Clinical profile and neurodevelopmental outcomes in five children at a tertiary care hospital in North India.
Badal Sachendra (Pune, India) Anand Vaisakh, Luhar Zulfiqar, Sirolia Vivek, Kaur Prabhjot, Singh Sonali, Kumar Atin, Jauhari Prashant, Chakrabarty Biswaroop, Gulati Sheffali

OBJECTIVE: Infantile onset epilepsy is common and often mismanaged, there is a need to sensitise about potentially treatable metabolic disorders.

METHODS: The clinico-laboratory-radiological profile, and final outcomes of five children diagnosed with Biotinidase deficiency between Jun 2017 and June 2019 are discussed.
RESULTS: All children presented with seizures onset between 2 -3.5 months, mean frequency of 8 per day with predominantly multifocal clonic type. Alopecia was present in two, eczema in two and one did not have cutaneous manifestations. SNHL was present in two and eye unaffected in all. Unfortunately history of sibling death with similar illness was present in all except one. EEG showed normal background in all except one and none had hypsarrythmia. CSF/Arterial lactate was raised and Biotinidase activity as measured by spectrometry was profoundly deficient in all children. MRI showed delayed-myelination in three children and diffusion restriction was noted in 4 children in PLIC, brain stem and cerebellum. Two children underwent MRS and both revealed lactate inversion. Response to Biotin at 20 mg per day was dramatic with seizure cessation within 24 hrs in all. At a mean follow up of 1.9 years none have cutaneous manifestations or neurological symptoms and are attaining normal development for age except two with speech delay. Exome sequencing confirmed homozygous pathogenic mutation in BTG gene in one case.
CONCLUSIONS: A potentially treatable IEM like biotinidase deficiency should be suspected in infantile onset epilepsy more so with cutaneous manifestations and abnormal neuroimaging with delayed myelination and diffusion restriction of early myelinating structures.
KEYWORDS: Neurometabolic Disorders, Epilepsy, Neuroimaging

493. Polymerase γ (POLG) related disorder causing childhood mitochondrial depletion/deletion syndromes presenting with variable neurological phenotypes: Chronic progressive external Ophthalomoplegia (CPEO), Alpers Hutenlocher and Paroxysmal movement disorder, Three genetically confirmed homozygous POLG mutation cases from a tertiary care center in North India.
Badal Sachendra (Pune, India) Anand Vaishakh, Panda Prateek, Luhar Zulfiqar, Sirolia Vivek, Jauhari Prashant, Chakrabarty Biswaroop, Gulati Sheffali

OBJECTIVE: POLG related Mitochondrial disorders result from mutations in nuclear genes encoding for protein involved in mitochondrial DNA replication and have varied neurological manifestations.
METHODS: The clinico-laboratory-radiological profile and neurological outcome of three children presenting between Jan 2017 and Dec 2018 are discussed .
RESULTS: *Case One:* Ten year girl symptomatic since preschool with progressive ptosis and proximal muscle weakness without diurnal fluctuations, facial and bulbar weakness. Child had axial weakness, external ophthalmoplegia, severe ptosis and head tilt. EPS revealed sensory axonal neuropathy without decremental response on RNST. CSF lactate was elevated muscle biopsy showed numerous COX negative fibres.On mitochondrial cocktail girl showed no further worsening clinically over two years follow up. *Case Two:* An 18 months male toddler presented with left Epilepsia partialis continua worsened by a febrile illness. EEG showed Rhythmic High amplitude Delta with superimposed Polyspikes (RHADS). At 9 month developed cholestatic jaundice with elevated transaminases and lost attained milestones, underwent liver biopsy which showed features of metabolic liver disease. Child diagnosed with Alpers Hutenlocher syndrome and succumbed to respiratory tract infection at 2 years age. *Case Three:* An 8.5 year boy presented with intermittent hyperkinetic movement disorder (Choreo dystonic) lasting hours to days since last one year without diurnal fluctuations. Duration and frequency of these

intermittent episodes was highly variable with symptom free period lasting a year on follow up of 4 years.
CONCLUSIONS: Nuclear genes encoding mitochondrial proteins are more prevalent in Mitochondrial disorders and do not follow mitochondrial inheritance and POLG related disorders predominate in this subgroup.
KEYWORDS: Neurometabolic Disorders, Epilepsy, Movement Disorders (including Cerebral Palsy)

494. Co-Assortment of MPS II (Hunter Disease) and Fragile XE syndrome
Mohan Arjun (Chennai, India) Kenney-Jung Daniel, Gupta Ashish, Lund Troy

OBJECTIVE: We present a 26 month old boy with an unusual gene deletion, resulting in a mixed phenotype with characteristics of both mucopolysaccharidosis type II (MPSII; Hunter disease) and Fragile XE syndrome.
METHODS: The patient was evaluated at the University of Minnesota as part of an assessment for hematopoietic stem cell transplant for MPSII. As a part of the workup for developmental delays with dysmorphisms, he received an array CGH, demonstrating a deletion involving both the IDS and AFF2 genes.
RESULTS: The patient was born at term following an uncomplicated pregnancy and delivery. Development was delayed, with the patient sitting at about 11 months and walking at 23 months. At the time of assessment for transplant (26 months), he still had no words. Poor eye contact and self-stimulatory behaviors (thumb-biting and hand-flapping) were prominent. Hearing tests were mildly abnormal. Dysmorphisms characteristic of storage disease were noted. Family history was negative for developmental or neurological disorders. Fragile X testing showed a normal number of CGG repeats (28) in the FMR1 gene. Urine testing showed elevated total glycosaminoglycans. A chromosomal microarray showed an Xq28 deletion, with deletion of the IDS gene (encoding iduronate-2-sulfatase, associated with MPSII) and partial deletion of the AFF2 gene (associated with the Fragile XE syndrome).
CONCLUSIONS: This case illustrates the potential for molecular and phenotypic variants among patients with metabolic disease, particularly in the context of gene deletions. Even in the context of known disease, testing for additional disorders can often be warranted in the context of atypical or severe phenotypes.
KEYWORDS: Neurometabolic Disorders, Genetics, Cognitive/Behavioral Disorders (including Autism)

495. Expanding Role of MR Spectroscopy: Timely Diagnosis and Treatment Initiation in a Case of Partial Ornithine Transcarbamylase Deficiency (OTCD)
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OBJECTIVE: Urea cycle-related brain disease may take on variable neuroimaging manifestations, ranging from normal to abnormal with or without a signature appearance. In the past, we have described the usefulness of multimodal imaging in identifying biomarkers of neuronal injury in UCD patients.
METHODS: We describe a three year old boy who previously presented with episodic altered mental status and abdominal pain in the past three months in the setting of mild infectious

illness, presenting to our institution with a similar episode. Parents elaborated that he was having episodes of tantrums and then would fall asleep for several hours. Additional family history information surfaced - mother had a lifelong history of being vegetarian because protein made her feel unwell.
RESULTS: A rapid screening revealed a high ammonia level and after reviewing his MR Spectroscopy, a diagnosis of OTC was made within 6 hours of presentation. MR spectroscopy showed the classic triad of OTC deficiency with high glutamate and low choline and myoinositol. Sodium phenylbutyrate and sodium benzoate therapy was initiated and patient was discharged after 3 days with no neurologic disability. Biochemical testing eventually revealed low citrulline, high glutamine and high orotic acid, corroborating with initial suspicion of OTCD based on MRS. Molecular diagnostics confirmed the diagnosis.
CONCLUSIONS: This case demonstrates the importance of obtaining MR spectroscopy study which can aid in expediting diagnosis and treatment since confirmatory testing (plasma amino acids and gene sequencing) do not result immediately.
KEYWORDS: Neurometabolic Disorders, Neuroimaging, Genetics

496. A boy with IARS2-related mitochondrial disease presenting with dilated cardiomyopathy
Mizuani Satoshi (Izumi, Japan) Nakajima Ken, Hirano Shodo, Obosi Taikan, Kimizu Tomokazu, Ikeda Tae, Mogami Yukiko, Yanagihara Keiko, Uehara Tomoko, Kosaki Kenjiro, Okamoto Nobuhiko, Suzuki Yasuhiro

OBJECTIVE: *IARS2* encodes nuclear-coded mitochondrial isoleucine-tRNA synthetase. To date, only ten patients with *IARS2* mutations have been reported. We report a case of Leigh syndrome with *IARS2* mutations.
METHODS: CASE REPORT） A 13-year-old Japanese boy was born at 39 weeks of gestation after uneventful pregnancy. At the age of 10 months, he developed acute dilated cardiomyopathy, which required respiratory support for 5 months. Myocardial biopsy revealed left ventricular noncompaction of unknown etiology. At 5 years of age, he was referred to our hospital because of psychomotor developmental delay. He exhibited short stature (height <-3.0 SD). At 6 years of age, he developed focal epilepsy, which subsequently evolved to West syndrome. Progressive bilateral cataracts developed during follow-up. Brain MRI revealed hyper-intensity in the bilateral basal ganglia on T2-weighted images. Although blood and CSF lactate levels were normal, MRS detected increased lactate peak in the basal ganglia. Mitochondrial DNA tests were negative. Muscle biopsy revealed variation in fiber size without ragged-red fibers. The diagnosis of Leigh syndrome was made based on neuroimaging. At 13 years, whole-exome sequencing identified nonsense and missense mutations of compound heterozygosity in *IARS2*, p.(Arg816*), p.(Arg817His). At the final evaluation, he was bed-ridden and had marked intellectual disabilities.
RESULTS: N/A (CASE REPORT)
CONCLUSIONS: Previous studies reported that *IARS2* mutations are associated with broad clinical phenotypes from non-syndromic cataracts to Leigh syndrome. Our patient exhibited dilated cardiomyopathy, in addition to cataracts and the clinical manifestation of Leigh syndrome.
KEYWORDS: Neurometabolic Disorders, Genetics

497. Recognition of acquired versus congenital etiologies in developmental regression.
Amin Hitha (Houston, TX, United States) Kristen Fisher, Shukla Nikita, Risen Sarah, Muscal Eyal, Lotze Timothy, Emrick Lisa

OBJECTIVE: Neurodevelopmental regression is a loss of previously acquired milestones. Workup may be extensive and should prioritize treatable disorders. We describe the presentation of acquired versus congenital causes of developmental regression.
METHODS: Retrospective case report of three previously healthy children, presenting with acute psychomotor regression. Initial diagnosis was either a treatable or non-treatable disorder, with subsequently alteration of diagnosis.
RESULTS: Patient 1 - 9 year old boy with lethargy, altered mental status; imaging consistent with autoimmune encephalitis. Despite treatment, he developed cystic changes in the basal ganglia. Detailed history revealed underlying delayed development, unrecognized by parents. Genetic testing three months after presentation revealed pathogenic variant in *ATP6* gene: diagnosed with Leigh disease. Patient 2 - 3 year old boy with ataxia and cranial neuropathies; imaging consistent with Neuromyelitis Optica (NMO), but was seronegative. Despite treatment, had recurrent symptoms with illness and worsening lesions. Reanalysis of genetic tests at 7 years of age showed pathogenic variant in the *PDHA1* gene: diagnosed with Pyruvate Dehydrogenase deficiency.
Patient 3 - 3 year old boy with dysphagia and chorea; imaging consistent with Leigh disease, referred for supportive care. Expanded workup 4 months after presentation showed Anti-N-methyl-D-aspartate receptor (NMDAR) antibodies: diagnosed with NMDAR encephalitis.
CONCLUSIONS: A. Detailed developmental history may discern red flags that aid diagnosis. B. With genetic analyses, there has been an expansion of phenotypes for neurogenetic disorders – these may be described as 'atypical'. C. While some phenotypes may mimic a treatable condition until confirmatory tests are obtained, recurrent symptoms may indicate a neurogenetic condition.
KEYWORDS: Neurometabolic Disorders, Demyelinating Disorders, Infections/Neuroimmunology

498. A Rare Case of 3-Hydroxyisobutyryl CoA Hydrolase deficiency (HIBCH Deficiency) - A Leigh Like Syndrome
Ali Sikander (Leeds, United Kingdom) Pervaiz Farah, Taylor Michael, Barski Robert, Hussain Shanawaz

OBJECTIVE: To describe the clinical, molecular, biochemical and neuro-radiological features of a child presenting with a leigh-like syndrome due to HIBCH Deficiency.
METHODS: Retrospective review of case notes, biochemical and neuro-radiological data.
RESULTS: A female infant born at term to non-consanguineous South Asian parents presented with developmental delay, failure to thrive and hypotonia in the first few months of life. An initial MRI at 11 months showed ill defined foci of hyperintenisty within the corpus striatum bilaterally. She subsequently presented acutely at 12 months with severe lactic acidosis, seizures and respiratory dysfunction in the contest of a non-specific viral illness. She required mechanical ventilation and bicarbonate infusions to correct the profound acidosis. A subsequent MRI Brain showed symmetrical acute striatal necrosis with diffusion restriction and a lactate inversion peak. Extensive workup for a presumed mitochondrial cause including respiratory chain enzymes and

also a pyruvate dehydrogenase assay were normal. An elevated "C4 Hydroxy carnitine (C4-OH)", a valine metabolite, was found in 3 separate acylcarnitine analysis. Subsequent analysis in fibroblasts of HIBCH enzyme was well below the normal range, confirming the diagnosis of HIBCH deficiency.
CONCLUSIONS: HIBCH is a very rare recessively inherited disorder of valine metabolism described to date in only around 8 patients in the literature. This rare mitochondrial mimic should be considered in patients presenting with a Leigh like presentation, in whom C4-OH is raised. Acylcarnitine analysis is a common readily available test which may help guide towards testing for HIBCH enzyme activity to confirm the diagnosis followed by genetic confirmation.
KEYWORDS: Neurometabolic Disorders, Movement Disorders (including Cerebral Palsy), Neuroimaging

499. Time course of serum neuron-specific enolase (NSE) levels from infancy to early adulthood in a female patient with beta-propeller protein-associated neurodegeneration (BPAN).
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OBJECTIVE: It is difficult to clinically identify children with BPAN, a subgroup of neurodegeneration with brain iron accumulation. Recent studies reported that serum levels of NSE are high in young children with BPAN. We reviewed the long-term time course of serum NSE levels in a patient with BPAN.
METHODS: [Case report] A 21-year-old female patient presented with febrile seizure and global developmental delay at 9 months. Initial blood tests revealed high serum NSE levels (77.4 ng/ml). Although repeated MRI was negative, BPAN was suspected based on the prolonged increase in serum NSE levels. MRI at 18 years of age revealed symmetrical lesions in the globus pallidus and substantia nigra. Direct Sanger sequencing identified a de novo *WDR45* mutation (c.2268A>T). At the final evaluation, her condition remained stable.
[Time course of serum NSE levels] The decrease in the serum NSE level exhibited a three-step pattern. The peak serum NSE concentration (70-90 ng/ml) was observed during the first two years of age and then decreased rapidly to <60 ng/ml in one year. High serum NSE levels (30-60 ng/ml) persisted between 3 and 11 years of age, but then decreased to <30 ng/ml and plateaued (around 20 ng/ml) after 13 years of age.
RESULTS: N/A (case report)
CONCLUSIONS: Our study confirmed that serum NSE levels can be a diagnostic biomarker of BPAN in children. After childhood, however, serum NSE values decrease and may have less value in identifying patients with BPAN.
KEYWORDS: Neurometabolic Disorders, Rare Diseases

500. Treatment responsive NDUFV1 mutation mitochondrial cytopathy
Sinha Rahul (Delhi, India) NM Shruthi, Luhar Zulfikar, Kaur Prabhjot, Kumar Atin, Gulati Sheffali

OBJECTIVE: 7 year old male child with NDUFVI mutation positive mitochondrial cytopathy who responded dramatically to mitochondrial cocktail.

METHODS: 7 year old male child born to non consanguineous marriage who presented with progressive left upper limb dystonia with gait instability and behavioural abnormality with spasticity on left side with brisk DTR and extensor plantars and dystonia left upper limb. The arterial lactate was 1.4mmol/l with normal TMS/GCMS. Eye, hearing and ECHO was normal. MRI Brain/MRS showed bilateral white matter signal changes in subcortical and periventricular region with cystic changes in right putamen and bilateral thalami and lower medulla to upper cervical cord (till C2 level) with no post contrast enhancement with no lactate peak. The CSF lactate was 1.7mmol/l and CSF OCB was negative. The exome study revealed NDUFV1 mutation on exon 8 which was homozygous autosomal recessive pathogenic variant suggestive of mitochondrial complex 1 deficiency and both the parents were heterozygous carrier for the same mutation. The child was started on mitochondrial cocktail (thiamine, biotin, Vit E, CoQ, riboflavin, folinic acid, pyridoxine). The child showed significant improvement in dystonia and gait instability after 12 weeks. The child is under follow up for last 3yrs and doing well in school.
RESULTS: In our case the child responded to mitochondrial cocktail and is doing well with minimal residual deficit.
CONCLUSIONS: Nuclear encoded complex I deficiency generally has a devastating clinical disease course, characterized by a severe neurological phenotype with very short life span. However the index case responded well to treatment.
KEYWORDS: Neurometabolic Disorders, Genetics

501. Pain in the forearms leading to a metabolic diagnosis
Serdaroglu Esra (Ankara, Turkey) Yildiz Yilmaz, Gökçe Erkan, Kurt Semiha

OBJECTIVE: Metabolic diseases especially in mild forms may present with unusual symptoms and mild laboratory test results.
METHODS: A ten-year-old boy was referred from orthopedics with a two-year complaint of pain in forearms. The pain was bilateral, diffuse in the forearm and hand region and waking him up at night. History revealed a neonatal pneumonia, snoring even after adenoidectomy, prophylaxis for acute rheumatic fever. Developmental milestones and school performance were satisfactory. There was consanguinity and an epileptic sister in the family. Physical examination showed relative macrocephaly, restricted movement of shoulder, elbow and finger joints, and claw hand appearance. There was no organomegaly.
RESULTS: Cranial magnetic resonance imaging revealed diffuse widened perivascular spaces. Concerning the long bones, the diaphyses were widened, trabeculation was coarse. He had bilateral (more prominent on left) severe carpal tunnel syndrome in electroneuromyography. There was a mild increase of urinary glucosaminoglycan (GAG) levels. Iduronate-2-sulphatase enzyme level was low (0,7 nmol/mg/hr [N>7.5]). He was diagnosed with mild/attenuated form of mucopolysaccoridosis type II (Hunter syndrome) and received enzyme replacement therapy (ERT) (elaprase).
CONCLUSIONS: Mucopolysaccharidosis type II (MPS II) results from the deficiency of lysosomal enzyme iduronate-2-sulphatase. Degradation of dermatan sulphate and heparan sulphate is disrupted and GAG accumulates in the cells. Accumulation results in airway obstruction, organomegaly, heart valve dysplasia, cardiomyopathy, restricted joints, skeletal deformities. ERT aims to decrease damage of GAG accumulation. ERT has good impact on life

expectancy and respiratory difficulties. Our patient presenting with carpal tunnel syndrome, was diagnosed with a treatable metabolic disease and benefited from ERT.
KEYWORDS: Neurometabolic Disorders, Rare Diseases

502. Late-onset Leigh syndrome with mild neurological manifestations associated with the m.9176T>C mutation.
Miyamoto Yosuke (Tottori, Japan) Narita Aya, Nishimura Yoko, Maegaki Yoshihiro

OBJECTIVE: The m.9176T>C mutation is a pathogenic variant of the mitochondrial complex V subunit gene *MT-ATP6* and is responsible for Leigh syndrome (LS). Although several reports on late-onset LS involving this variant are available, phenotypic variety makes severity and prognosis estimations difficult.
METHODS: We report a patient with late-onset LS having extremely mild neurological manifestations.
RESULTS: A 7-year-old boy was admitted to our hospital for the acute-onset unconsciousness. He was diagnosed with decompensated cardiac shock associated with acute myocarditis. One month later, unilateral exotropia and slight waddling gait were noticed. Elevated lactate and pyruvate levels were detected in the blood and cerebrospinal fluid. Brain magnetic resonance imaging (MRI) revealed bilateral T2 high-intensity areas in the dorsal brainstem, and a lactate peak was detected on proton MR spectroscopy. He was diagnosed with LS clinically, and subsequent administration of high-dose vitamins, coenzyme Q, and levocarnitine resulted in improved neurological and MRI findings. Thereafter, the m.9176T>C mutation was identified. The m.9176T>C mutation is reported as the third most common *MT-ATP6* variant, and most cases can be diagnosed in early infancy. Regarding late-onset LS associated with this variant presenting after age 6, only 7 cases are available, and 2 of these cases, including ours, showed no basal ganglia lesions with mild reversible neurological manifestations. Meanwhile, the well-described other four cases with basal ganglia lesions tended to show moderate-to-severe and permanent neurological deficits.
CONCLUSIONS: In late-onset LS associated with the m.9176T>C mutation, the absence of basal ganglia lesions at presentation may be related to the neurological severity and prognosis.
KEYWORDS: Neurometabolic Disorders, Neuroimaging, Genetics

503. Peroxisomal Disease: A Case of Zellweger Spectrum Disorder
Whalen Danielle (San Diego, CA, United States) Haas Richard

OBJECTIVE: Once thought to be distinct disorders, Zellweger syndrome, neonatal adrenoleukodystrophy, and infantile Refsum disease are now understood to be variants along the same continuum of peroxisome biogenesis disorders with differing degrees of symptom severity and multiorgan involvement. This case highlights the importance of timely diagnosis with regards to management, prognosis, and counseling.
METHODS: A comprehensive chart review as well as literature review was performed.
RESULTS: A two year old from Mexico with normal development until 15 months was admitted for PO intolerance secondary to UTI and subsequently found to have 8 months of progressive developmental regression, hypotonia, feeding difficulties, vision concerns, and liver dysfunction. Comprehensive workup including serum, urine, CSF, radiologic, and electroencephalographic studies were obtained and notable for MRI brain with extensive

bilateral symmetric, ill-defined, posterior dominant white matter changes as well as significant elevations in several very long chain fatty acids suggestive of underlying peroxisomal biogenesis disorder. Rapid whole genome sequencing confirmed in trans maternal c.1802G>A (p.Arg601Gln) and paternal c.2579G>A (p.Arg860Gln) likely pathogenic missense mutations in the PEX6 gene consistent with diagnosis of Zellweger spectrum disorder.
CONCLUSIONS: PEX6 encodes for an ATPase which plays a direct role in peroxisomal protein import, PTS1 receptor activity, and subsequent peroxisomal function. Rapid genome sequencing enabled diagnosis within weeks of presentation, and although no targeted therapies currently available, timely diagnosis of this progressive congenital disorder has allowed the family to make goal-directed care decisions including placement of G-tube to maximize time spent at home, deferment of liver transplant, and appropriate family planning.
KEYWORDS: Neurometabolic Disorders, Genetics, Rare Diseases

504. NDUFS6 mutations cause lethal neonatal mitochondrial complex I deficiency and distinct clinical-MRI pattern
Hakami Wejdan (Riyadh, Saudi Arabia) Tlili Kalthoum, Alhashem Amal, Tabarki Brahim

OBJECTIVE: To review and discuss the clinical, biochemical, neuroradiological and genetic findings from five new cases with the *NDUFS6* gene mutation with literature review.
METHODS: A case report of five new cases with *NDUFS6* gene with literature review.
RESULTS: We report five siblings from a consanguineous Saudi family with neonatal encephalopathy, respiratory failure, and severe lactic acidosis leading to early death. Brain magnetic resonance imaging (MRI) and magnetic resonance spectroscopy (MRS) showed abnormal signal intensity in the subcortical area and deep white matter of both cerebral hemispheres; the brain stem, basal ganglia, and spinal cord were also involved and associated with multiple areas of restricted diffusion and lactate elevation. Whole exome sequencing showed a homozygous novel pathogenic mutation in the *NDUFS6* gene (c.80G>A; p. Cys27Tyr).
CONCLUSIONS: This study further delineates the clinical, biochemical, and neuroradiological phenotypes associated with *NDUFS6*variants.
KEYWORDS: Neurometabolic Disorders, Neuroimaging, Genetics

505. CAD deficiency: clinical features, molecular genetics and therapeutic intervention
Zhou Ling (Beijing, China) Deng Jie, Zhou Ji, Li Hua, Wu Ye, Fang Fang

OBJECTIVE: To describe the clinical characteristics, neuroimaging findings and therapeutic intervention of CAD deficiency.
METHODS: A retrospective study was performed on five unrelated Chinese patients with CAD deficiency. The features of natural history, brain MRI, peripheral blood smear, EEG, molecular genetics, and therapeutic options were summarized.
RESULTS: (1) Clinical features: patients are presented as refractory epilepsy, infantile-onset psychomotor developmental delay with regression and anaemia with anisopoikilocytosis. The clinical profile of one patient aged 17-month-old was showed in Figure 1. (2) Epilepsy and EEG: focal onset epilepsy is most common, the interictal EEG was mainly characterized by generalized slow waves and multifocal epileptic discharges. (3) Brain MRI showed progressive cerebral and cerebellar atrophy. (4) Anaemia with anisopoikilocytosis: aneamia was usually mild

to severe, peripheral blood smears showed abnormal erythrocytes with varying size and abnormal morphology. (5) Uridine responsiveness: uridine supplementation (100mg/kg per day) was started at the median age of 1 year old, and seizure stopped in few days after uridine administration. The patients achieved the median seizure free period of 7 months, accompanied by resolution of anaemia, developmental progress, and prevention of the development of severe and non-reversible manifestations. (6) Genotypic features: ten unreported variants in *CAD* were identified, including six missense variations, one splicing site variation, two frame-shift variations, and one nonsense variation (Figure 2).
CONCLUSIONS: CAD deficiency is manifested as the triad of refractory epilepsy, developmental delay with regression and anaemia with anisopoikilocytosis, whereas responsive to uridine. This reinforces CAD deficiency as a treatable neurometabolic disorder.
KEYWORDS: Neurometabolic Disorders, Genetics, Rare Diseases

506. AAV-RNAi Mediated Gys1 Knockdown in the Brain Decreases Abnormal Glycogen Formation in the Mouse Models of Lafora Disease and APBD (Adult Polyglucosan Body Disease)

Gumusgoz Emrah (Dallas, TX, United States) Verhalen Brandy, Dear Matthew, Woodard Samuel, Evans Doretha, Minassian Berge

OBJECTIVE: Adult polyglucosan body disease (APBD) and Lafora Disease are rare, autosomal recessive glycogen storage disorders that present mainly with neurological symptoms. APBD is caused by mutations in the glycogen branching enzyme (*GBE1*) gene and characterized by progressive upper and lower motor neuron dysfunction, and premature death. Whereas LD is fatal progressive myoclonus epilepsy caused by loss of function mutations in *EPM2A* or *NHLRC1*. Currently, there is no treatment available for APBD or LD. These clinically distinct diseases share a common histopathology. Both APBD and LD are characterized by abnormal glycogen accumulation in various tissues. These poorly branched, insoluble aberrant cytoplasmic glycogen inclusions are the principal driver of the brain abnormalities seen in mouse models. Thus, the prevention of abnormal glycogen accumulation is a key to therapy. We hypothesized that inhibiting *Gys1* and decreasing glycogen synthesis in the brain might prevent abnormal glycogen formation and rescue the neurological phenotype. We used an AAV=RNAi approach to test this hypothesis.
METHODS: After screening multiple candidates in vitro, we packaged an artificial miRNA in a recombinant adeno-associated virus (rAAV2/9). We then injected neonatal mice with the rAAV-RNAi vectors via bilateral intracranial ventricular (ICV) injections. We aged mice to three months and harvested brain tissue biochemical and histopathological analysis.
RESULTS: Our preliminary results show that RNA interference (RNAi)-mediated silencing of *Gys1* mRNA provides a therapeutic benefit in LD and APBD mouse models by decreasing abnormal glycogen formation in the brain.
CONCLUSIONS: This study highlights the potential of AAV-RNAi gene therapy for the treatment of glycogen storage disorders.
KEYWORDS: Neurometabolic Disorders, Rare Diseases, Genetics

507. Expansion of the clinical spectrum associated with NDUFS8-related disorders to include progressive leukodystrophy

Andzelm Milena (Boston, MA, United States) Balasubramaniam Shanti, Yang Edward, Anselm Irina, Rodan Lance, Thorburn David, Christodoulou John, Srivastava Siddharth

OBJECTIVE: To expand the neuroimaging and clinical spectrum of *NDUFS8*-related disorder
METHODS: Clinically ascertained case series with functional and molecular genetic studies
RESULTS: We present 3 cases homozygous for the same pathogenic *NDUFS8* variant (c.460G>A, p.(Gly154Ser)), located in the [4Fe-4S] domain of the protein. They presented with late infantile regression and progressive leukoencephalopathy. MRIs were performed in 2 of 3 patients and demonstrated diffuse cerebral and cerebellar white matter involvement including corticospinal tracts, but notably had sparing of deep gray matter structures. Patient 1 and 2 both presented with regression and spasticity after a febrile illness at 10 and 6 months respectively. Patient 1 subsequently presented with weight loss 14 months after initial presentation despite meeting caloric goals, and had an acute decompensation in association with an upper respiratory viral infection and auto-antibody positive diabetic ketoacidosis without any previous history to suggest diabetes. Respiratory chain enzymology in patient 2 showed a marked reduction in muscle complex I activity, with activity I in liver being less severely affected.
CONCLUSIONS: *NDUFS8*-related disorders encompass a wide phenotypic spectrum, and with longitudinal neuroimaging these cases expand the clinical spectrum of *NDUFS8*-associated neurological disease to include progressive leukodystrophy with increasing brainstem and cerebellar involvement. In addition, we describe the emergence of autoimmune diabetes in a patient with mitochondrial disease, highlighting a possible pathogenic role of mitochondrial dysfunction in autoimmune disease.
KEYWORDS: Neurometabolic Disorders, Genetics, Neuroimaging

508. A Challenging Diagnosis: Mucopolysaccharidosis Type 3B with NAGLU Mutations
Yayıcı Köken Özlem (Ankara, Turkey) Değerliyurt Aydan, Bayram Ilıkan Gülşah, Teker Neslihan, Aktaş Dilek

OBJECTIVE: The aim is to present three pediatric cases with novel *NAGLU* gene mutations, who were diagnosed with mucopolysaccharidosis (MPS) type IIIB (Sanfilippo B syndrome) and to evaluate similarities and differences concerning clinical and laboratory features with cases in the literature.
METHODS: Three patients were referred to our clinic because of their peculiar facial features, delay in language development, seizures, behavioral problems at the age of 18, 11 and 17 respectively.
RESULTS: One patient was a male while the other two were sisters, all born to consanguineous parents but did not have a family history for similar diseases. On the follow up, all patients manifested progressive developmental regression concerning predominantly language. Examination revealed coarse face, organomegaly, joint stiffness and extreme height. Cardiac and ophthalmologic evaluations were unremarkable. Radiological investigations revealed hyperostosis of the skull and enlarged calvarium in all cases and vertebral anomalies in only one case. Cranial MRI showed cerebral atrophy and hyperintensity in periventricular white matter in T2-weighted and FLAIR images and secondary ventricular dilatation. Vertebral anomalies were present in the first case only.
CONCLUSIONS: Typical findings for MPS type III such as short stature, sensorineural deafness, dysostosis multiplex, abdominal hernia, cardiac and ophthalmologic involvement were

not present. Coarse face and progressive developmental regression accompanied by hepatosplenomegaly caused by heparane sulphate accumulation secondary to loss of alpha-N-acetylglucosaminidase activity, behavioral problems, sleep disturbances, epileptic seizures as well as radiologic features such as cortical atrophy, periventricular white matter changes and thickening of the diploe are some features that can help in the diagnostic process.
KEYWORDS: Neurometabolic Disorders, Genetics, Rare Diseases

509. Novel Presentation of D-2-Hydroxyglutaric Aciduria Mimicking Non-Accidental Trauma

Hewitt Angela (Rochester, MN, United States) Perales-Clemente Ester, Rinaldo Piero, Lanpher Brendan, Tillema Jan-Mendelt

OBJECTIVE: To describe a novel case of D-2-hydroxyglutaric aciduria (D2OHGA) in a 7 m.o. male whose presenting features mimicked non-accidental trauma (NAT) with loss of consciousness (but no definitive seizures), incidental bilateral subdural hematomas on head CT (Fig.1A), macrocephaly (OFC 47.5 cm, 99.8%, Fig.1F), and otherwise normal physical examination. Ophthalmology evaluation identified bilateral retinal hemorrhages (Fig.1B-C). Social and family histories revealed NAT risk factors.
METHODS: Evaluations for a metabolic disorder and NAT were initiated. A literature review of D2OHGA was conducted to evaluate if this condition could present with retinal hemorrhages.
RESULTS: MRI confirmed different chronological ages of subdural hematomas (Fig.1D-E). EEG was negative for potentially epileptogenic activity, but did demonstrate decreased right hemisphere amplitude. Skeletal survey, coagulopathy work-up, quantitative amino acids, and acylcarnitines were all negative/normal. Urine organic acids returned with elevated 2-hydroxy glutaric acid at 1098 mmol/mol creatinine (ref <20). Molecular genetic testing revealed a pathogenic splice site variant (c.685-2A>G) and a variant of uncertain significance (c.1256G>T) with evidence of pathogenicity in the D2HGDH gene. One published case report of D2OHGA described subdural, retinal, and skin hemorrhages with only marginally affected coagulation labs.
CONCLUSIONS: D2OHGA is a rare disorder that typically presents with developmental delay, hypotonia, and seizures. However, as in this case, it can also present with subdural hematomas and retinal hemorrhages mimicking NAT and no other symptoms. This illustrates the importance of screening for metabolic or genetic disorders when evaluating NAT.
KEYWORDS: Neurometabolic Disorders, Rare Diseases, Trauma

510. Arginase-1 Deficiency (ARG1-D) Masquerading as Hereditary Spastic Paraplegia: Implications for Diagnostic Testing

McNutt Markey (Dallas, TX, United States) Bechter Mark, Rao Ravi

OBJECTIVE: Arginase 1 Deficiency (ARG1-D) is a genetic disorder of arginine metabolism with progressive spastic diplegia which typically manifests in early childhood. Other manifestations include developmental delay, intellectual disability, seizures and hyperammonemia which may not be prominent leading to delays in diagnosis. Here, we report a patient with ARG1-D diagnosed initially with Hereditary Spastic Paraplegia (HSP). Although both disorders are characterized by progressive, lower extremity spastic paraparesis, ARG1-D is not generally considered in the differential diagnosis of HSP and the *Arg1*gene is not included in HSP gene sequencing panels

METHODS: N/A
RESULTS: A 24-year-old female presented with a 4-year history of slowly progressive leg weakness and recurrent falls. Clinical evaluation ruled out acquired causes and she was diagnosed with HSP despite a family history of ARG1-D in her sister. ARG1-D was discounted as a diagnosis based on late presentation and lack of clinical hyperammonemia. At age 27, ARG1-D was diagnosed based on biochemical data, family history, and homozygous loss-of-function mutations in the *Arg1* gene. Attempts to lower plasma arginine levels with severe protein restriction failed to substantially ameliorate the hyperargininemia. She is currently enrolled in a clinical trial of an investigative therapy, pegzilarginase, a human enzyme-based approach to lower plasma arginine levels.
CONCLUSIONS: This case is consistent with earlier literature reports that describe the potential for misdiagnosis of ARG1-D patients with spastic diplegia as HSP. Given similarities in neurological presentation and the recognized benefits of lowering plasma arginine levels in patients with ARG1-D, patients with HSP should undergo either genetic or biochemical testing.
KEYWORDS: Neuromuscular Disorders, Movement Disorders (including Cerebral Palsy), Rare Diseases

511. CLN1 Natural History Data: Retrospective and Prospective Analyses
Masten Margaux (Rochester, NY, United States) Collins Alyssa, Bonifacio Kristen, Vierhile Amy, Adams Heather, Mink Jonathan, Augustine Erika

OBJECTIVE: To characterize the natural history of the CLN1 form of Neuronal Ceroid Lipofuscinosis (NCL) using a combined retrospective and prospective approach.
METHODS: We used a retrospective systematic review of medical records (n=8; 7 female) and prospective in-person evaluations using the Unified Batten Disease Rating Scale (UBDRS) (n=12; 6 female). Retrospective analysis provided information about age at disease-onset and first symptom type. Prospective analysis provided age-at-onset of core clinical features and rate of disease progression. Individuals were categorized based on age-at-onset into infantile (0-1.5 years), late infantile (>1.5-5 years), or juvenile (>5 years) groups.
RESULTS: The average age (years) at first symptom was 4.3 in the retrospective cohort (range: 1.1-9.3) and 4.6 in the prospective cohort (range: 0.5-11.0), with nearly even distribution across categories: infantile onset (N=6), late-infantile onset (N=6), and juvenile onset (N=8). Initial symptom was vision loss (n=5; mean age 4 yrs), motor (n=4; 1.6 yrs). behavior (n=4; 5.4 years), cognition (n=3; mean age=4.4 yrs), or seizure (n=1; age 4 yrs). Motor impairment was the most frequent initial symptom in the infantile-onset group; behavior was the most frequent initial symptom in the late infantile and juvenile groups. No presenting symptom predicted category.
CONCLUSIONS: These data demonstrate substantial variation in age-at-onset and type of initial symptoms in children with CLN1 disease. They also demonstrate that the prospective and retrospective approaches are complementary. For comprehensive natural history studies of rare neurologic diseases such as CLN1, a combination of the two approaches is likely to be necessary
KEYWORDS: Neurometabolic Disorders, Genetics, Rare Diseases

512. Cobalamin E deficiency, a rare metabolic cause of pediatric neurodegeneration with peripheral neuropathy
Nori Sahiti (Bangalore, India) Karachunski Peter, Sarafoglou Kyriakie, Kenney-Jung Daniel

OBJECTIVE: To describe the clinical phenotype and management of medically refractory epilepsy and severe progressive peripheral neuropathy in a 10 year old Caucasian boy with cobalamin E deficiency, a rare metabolic neurodegenerative disorder (Prevalence: < 1/1000000).
METHODS: Medical chart review of patient followed at the University of Minnesota Masonic Children's Hospital.
RESULTS: The patient was born at term following an uncomplicated pregnancy and delivery. Newborn screening showed elevated homocysteine and reduced methionine levels. Subsequent testing of the *MTRR* (5-Methyltetrahydrofolate-Homocysteine Methyltransferase Reductase) gene showed pathogenic compound heterozygous mutations. Fibroblast cultures were consistent with cobalamin E deficiency.Therapy included supplementation with betaine, pyridoxine, riboflavin, folic acid and hydroxycobalamin (subcutaneous injections), and aspirin to prevent thrombus. The patient's developmental course was characterized by delayed milestones and prominent sensory ataxia. Seizures commenced at 6 months of age. By 10 years of age, the patient was ambulatory but with a severe axonal neuropathy resulting in sensory ataxia and bilateral foot drop, along with medically refractory multifocal epilepsy. Nerve conduction studies were remarkable for absent sensory responses. Brain MRI at 9 years of age showed only mild generalized atrophy.Therapeutic considerations include management of epilepsy and painful peripheral neuropathy while avoiding medications that could increase homocysteine or exacerbate behavioral problems. Currently, despite his disabilities, the patient remains highly conversational and participates avidly in specialized schooling.
CONCLUSIONS: This case illustrates the clinical course and management considerations inherent in the care of a child with cobalamin E deficiency.
KEYWORDS: Neurometabolic Disorders, Rare Diseases, Genetics

513. Insidious Mutations: A case of a POLG Heterozygote
McVicar Anna (Louisville, KY, United States) Turek Grant, Brown Martin, Puri Vinay

OBJECTIVE: POLG genes code for DNA polymerases that replicate mitochondrial DNA; mutations in these genes cause a spectrum of diseases. We report a case of neuropathy and encephalopathy with a compound heterozygous POLG mutation.
METHODS: A complete history and physical prompted a sequence of diagnostic testing including EEG, MRI, EMG and genetic testing. The final diagnosis prompted a review of the literature.
RESULTS: A 19yo female with a 5 year h/o progressive gait disturbance, weakness, recurrent infections and behavior changes was evaluated by neurology for focal onset seizures which had been refractory to multiple AEDs. She described an aura of photopsia prior to left-sided clonic jerking. Her seizures occurred in a catamenial pattern. Additional history included 2 years of worsening headache and anxiety. Exam revealed irritability, areflexia, distal symmetric sensory loss with sensory ataxia, pes cavus and tight heel cords. Diagnostic workup revealed bifrontal epileptiform discharges on EEG, severe axonal sensorimotor polyneuropathy on EMG, and right occipital encephalomalacia with colpocephaly on MRI. Genetic testing was initially nondiagnostic but exome testing of the patient and both parents revealed a compound heterozygous mutation in the POL-G gene.
CONCLUSIONS: This case highlights the insidious and pervasive nature of mitochondrial disorders which can begin with clumsiness, a mood disorder, weakness and/or headaches with none of these sentinel symptoms raising concerns for a serious underlying problem. Even after

the development of seizures, the involvement of multiple systems required clinical suspicion that a single unifying explanation could be found.
KEYWORDS: Neurometabolic Disorders, Genetics, Neuromuscular Disorders

514. UNDERSTANDING THE EXPERIENCE OF THE MITOCHONDRIAL DISEASE COMMUNITY DURING THE COVID19 PANDEMIC
Gordon-Lipkin Eliza (Bethesda, MD, United States) Kruk Shannon, Yeske Philip, Martin Lori, Hirano Michio, Cohen Bruce, McGuire Peter

OBJECTIVE: Individuals with mitochondrial disease (MD) are vulnerable to decline with infection. We aimed to understand the impact of the COVID19 pandemic on MD by identifying risk factors, frequency of insufficient healthcare resources and primary concerns of the MD community.
METHODS: An online questionnaire was distributed through MD advocacy groups in April 2020. Patients with MD or their caregivers completed the survey. The survey will be repeated monthly during the COVID19 pandemic.
RESULTS: Preliminary data include 180 respondents from 33 United States, 3 European countries. The most common types of MD were MD Not Otherwise Specified, Mitochondrial Myopathy, Leigh Syndrome and MELAS. The majority (59%) had a known pathologic variant. Comorbidities recognized by the CDC as risk factors for severe COVID19 were present in 78%. As of April 2020, regarding COVID testing, none reported positive, 3 requested/unable to receive, 3 were tested/awaiting results. Fever, cough, shortness of breath or pneumonia since January 2020 was present in 33%. Thirty-six percent of respondents had a household member whose job required public contact and 57% visited a healthcare center/provider during COVID19. Barriers to maintaining health included an inability to receive medications(10%), medical supplies(17%), home nursing(10%) and home therapies(31%). Greatest concern themes were: becoming infected, dying, being unable to receive treatment, being unable to support family.
CONCLUSIONS: Many patients with MD have risk factors for exposure or for severe COVID19-associated illness. During the pandemic, many patients have limited healthcare resources. Recognition of these issues and concerns by healthcare providers is important to support the mitochondrial disease community.
KEYWORDS: Neurometabolic Disorders, Rare Diseases, Infections/Neuroimmunology

515. Quality of Life Among Pediatric Patients with FKRP-related Muscular Dystrophy
Rasor Madalyn (Iowa City, IA, United States) Stephan Carrie, Miller Chandra, Zimmerman Bridget, Mathews Katherine

OBJECTIVE: To evaluate quality of life (QOL) data reported by a cohort of children with *FKRP* mutations and their parents relative to disease stage.
METHODS: Children enrolled in a dystroglycanopathy natural history study were invited to complete PedsQL™, PROMIS® Pediatric Pain Interference, Pediatric Fatigue short forms, and functional motor testing at annual visits. Mean PedsQL™ score for each domain and total score was obtained by fitting a generalized linear model using the generalized estimating equations method. We used linear regression to correlate PedsQL™ scores to participant performance on

motor function measures. Correlation coefficients were calculated using linear mixed effects model.
RESULTS: There was no relationship between PedsQL™ scores and age in any domain, but all domains showed significant correlation with motor function. This relationship was strongest for physical function domain (r=0.67) and weakest for emotional function domain (r = 0.28). There is a significant correlation between all child-reported PedsQL™ domain scores and both PROMIS® Pediatric Pain and Fatigue Interference scores. The correlation was highest for physical function domain and lowest for emotional function domain for pain and fatigue. Both children and their parents report a decline in QOL with increasing pain and fatigue.
CONCLUSIONS: Decline in motor function is associated with lower PedsQL™ score. The effect of this decline in motor function on QOL varies by domain with least impact on emotional functioning. QOL scores for children with LGMD2I are similar to those reported for other childhood neuromuscular diseases.
KEYWORDS: Neuromuscular Disorders

516. SUNFISH Part 2: Efficacy and safety of risdiplam (RG7916) in patients with Type 2 or non-ambulant Type 3 spinal muscular atrophy (SMA)
Day John (Palo Alto, CA, United States) Barisic Nina, Boespflug-Tanguy Odile, Deconinck Nicolas, Kostera-Pruszczyk Anna, Masson Riccardo, Mazzone Elena, Nascimento Andres, Saito Kayoko, Vlodavets Dmitry, Vuillerot Carole, Fuerst-Recktenwald Sabine, Fuhrer Sibylle, Gerber Marianne, Gorni Ksenija, Kletzl Heidemarie, Martin Carmen, Yeung Wai, Mercuri Eugenio, on behalf of the SUNFISH Working Group

OBJECTIVE: To determine the safety and efficacy of risdiplam (RG7916), a centrally and peripherally distributed oral *SMN2* pre-mRNA splicing modifier, in patients with Type 2 or non-ambulant Type 3 spinal muscular atrophy (SMA) treated for 12 months during confirmatory Part 2 of the SUNFISH (NCT02908685) study.
METHODS: SUNFISH is a multicenter, two-part, randomized, placebo-controlled, double-blind study (randomized 2:1, risdiplam:placebo) in patients, aged 2–25 years, with Types 2 or 3 SMA. SUNFISH is comprised of two parts: Part 1 (N=51) is a dose-selection study assessing the safety, tolerability and pharmacokinetics/pharmacodynamics of different risdiplam dose levels in patients with Types 2 and 3 SMA (ambulant and non-ambulant); confirmatory Part 2 (N=180) assesses the safety and efficacy of the risdiplam dose level that was selected from Part 1 compared with placebo in patients with Type 2 and non-ambulant Type 3 SMA. The primary objective of Part 2 is to evaluate the efficacy of risdiplam compared with placebo in terms of motor function as assessed by the change from baseline in the 32-item Motor Function Measure total score at Month 12.
RESULTS: In SUNFISH Part 1, no drug-related safety findings led to withdrawals from the study following 1 year of treatment with risdiplam (data-cut: 28th June 2019). Here, we will report data from confirmatory Part 2 of the SUNFISH study including baseline demographics, safety and efficacy data in participants who have received treatment with risdiplam or placebo for 12 months.
CONCLUSIONS: Part 2 of SUNFISH is currently ongoing.
KEYWORDS: Neuromuscular Disorders, Rare Diseases

517. JEWELFISH: Safety and pharmacodynamic data in non-naïve patients with spinal muscular atrophy (SMA) receiving treatment with risdiplam (RG7916)

Chiriboga Claudia (New York, NY, United States) Bruno Claudio, Duong Tina, Fischer Dirk, Kirschner Janbernd, Mercuri Eugenio, Fuerst-Recktenwald Sabine, Gerber Marianne, Gorni Ksenija, Kletzl Heidemarie, McIver Tammy, Warren Francis, Muntoni Francesco, on behalf of the JEWELFISH Study Group

OBJECTIVE: To assess the safety, tolerability and pharmacokinetic/pharmacodynamic (PK/PD) relationship of risdiplam (RG7916), a centrally and peripherally distributed oral *SMN2* pre-mRNA splicing modifier, in non-naïve patients with spinal muscular atrophy (SMA) who have been treated with risdiplam in the ongoing JEWELFISH study (NCT03032172).
METHODS: JEWELFISH is a multicenter, open-label study evaluating the safety, tolerability and PK/PD relationship of daily oral risdiplam in non-naïve patients with SMA, aged 6 months to 60 years. JEWELFISH participants previously received RG7800 (RO6885247), nusinersen (SPINRAZA®), olesoxime or onasemnogene abeparvovec-xioi (ZOLGENSMA®).
RESULTS: We have previously presented safety data from 45 patients with SMA (data-cut: 28th June 2019) who received risdiplam for up to 28.9 months (nine patients previously received RG7800, 24 patients received nusinersen and 12 patients received olesoxime). No drug-related safety findings leading to withdrawal were reported. In an earlier analysis of SMN protein in whole blood, while patient numbers were limited (n=18), the magnitude of SMN protein increase (>2-fold) was comparable to that in SUNFISH Part 1 (NCT02908685) in patients with Type 2 and 3 SMA who had not previously received *SMN2*-targeting therapy. We will present updated data on safety and PK/PD from patients within the JEWELFISH study, including new patients, and reasons for discontinuing previous treatment regimens.
CONCLUSIONS: The JEWELFISH study is ongoing in sites across Europe and the US.
KEYWORDS: Neuromuscular Disorders, Rare Diseases

518. RAINBOWFISH: A study of risdiplam (RG7916) in infants with presymptomatic spinal muscular atrophy (SMA)

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OBJECTIVE: To assess the efficacy, safety, PK and PD of risdiplam (RG7916), a centrally and peripherally distributed oral *SMN2* pre-mRNA splicing modifier, in presymptomatic infants with genetically diagnosed spinal muscular atrophy (SMA) who have been treated with risdiplam in the ongoing RAINBOWFISH study.
METHODS: RAINBOWFISH (NCT03779334) is an open-label, single-arm, multicenter study in infants with genetically diagnosed presymptomatic SMA. RAINBOWFISH is actively enrolling infants aged from birth to 6 weeks of age (at first dose), regardless of *SMN2* copy number. Primary analyses will be conducted when the last enrolled infant with two *SMN2*copies reaches 12 months of treatment. The primary objective is to evaluate the efficacy of risdiplam in infants with two *SMN2* copies and CMAP ≥1.5mV at baseline as determined by the proportion of infants sitting without support after 12 months of treatment for five seconds (assessed by the BSID-III). Secondary endpoints include the development of clinical symptoms, survival and

permanent ventilation, achievement of motor milestones, motor function, growth measures, nutritional status, degree of innervation by CMAP, PK and respiratory effects by plethysmography.
RESULTS: RAINBOWFISH will provide valuable information about presymptomatic administration of risdiplam alongside the ongoing FIREFISH (Type 1 SMA, NCT02913482), SUNFISH (Type 2/3 SMA, NCT02908685) and JEWELFISH (patients with SMA who have previously received olesoxime, onasemnogene abeparvovec-xioi or therapies targeting *SMN2* splicing, NCT03032172) studies. Here, we will report the baseline demographics of enrolled infants and preliminary PK/PD data of risdiplam in a presymptomatic population of SMA.
CONCLUSIONS: The RAINBOWFISH study is currently recruiting at selected sites worldwide.
KEYWORDS: Neuromuscular Disorders, Rare Diseases

519. Combination therapy with nusinersen and AVXS-101: a real-world clinical experience
Veerapandiyan Aravindhan (Little Rock, UT, United States) Arya Kapil, Harada Yohei

OBJECTIVE: Two FDA approved gene modifying therapies are currently available for Spinal muscular atrophy (SMA). Objective is to describe our center's experience in treating SMA patients with dual therapy of nusinersen and AVXS-101.
METHODS: Retrospective review
RESULTS: We describe 3 cases of SMA 1 (2 copies of *SMN2*) who received both nusinersen and AVXS-101. Case 1 was diagnosed at 6 months of age and started nusinersen a month later. Case 2 was started on nusinersen immediately after diagnosis at 1.5 months. Both showed improvements with nusinersen. They received AVXS-101 at 21 (9.5 Kg) and 18 months (10.5 kg) of age respectively and continued to show improvements. Nusinersen was continued on both patients. Mild elevation of liver enzymes was noted after AVXS-101 treated with prophylactic oral steroids. Significant elevation of liver enzymes noted in both patients after thy received subsequent nusinersen maintenance doses. This resulted in hospitalization, liver biopsy, intravenous corticosteroids, and prolonged oral steroid treatment for case 2 and prolonged oral steroid for case 1. Case 3 was diagnosed at 5 months and received AVXS-101 at 6 months of age. Nusinersen was started at 9 months as there was no improvement after AVXS-101. Patient remains alive and stable at 15 months of age.
CONCLUSIONS: These cases illustrate the clinical experience of combination gene therapy. Prolonged period of liver enzymes elevation and steroid treatment can be seen. Better outcomes are seen with early AVXS-101 treatment. Worsening liver function may be related to combination therapy. Further data will be presented at the meeting.
KEYWORDS: Neuromuscular Disorders, Genetics

520. Mini-COMET study: Safety, immunogenicity, and preliminary efficacy for repeat avalglucosidase alfa dosing in infantile-onset Pompe disease (IOPD) participants who were previously treated with alglucosidase alfa
Kronn David (Valhalla, NY, United States) Brassier Anaïs, Broomfield Alexander, Davison James, Hahn Sihoun, Kishnani Priya, Kumada Satoko, Labarthe François, Ohki Hirotaka, Pichard Samia, An Haack Kristina, Johnson Judith, Lan Yu, Chien Yin-Hsiu, Mini-COMET Investigators

OBJECTIVE: Report safety, immunogenicity, and preliminary efficacy for avalglucosidase alfa administered to alglucosidase alfa-experienced IOPD participants during the Mini-COMET 25-wk primary analysis period (PAP).
METHODS: Mini-COMET (NCT03019406), an ongoing phase 2, multi-stage, open-label, ascending-dose, 3-cohort study, primarily evaluates avalglucosidase alfa safety in IOPD participants aged <18y. Participants demonstrated clinical decline (Cohorts 1 [n=6] and 2 [n=5]) or sub-optimal response (Cohort 3 [n=11]) during prior alglucosidase alfa treatment (stable dose ≥6mo). In the PAP, Cohorts 1&2 received avalglucosidase alfa 20 or 40mg/kg IV qow, respectively, and Cohort 3 avalglucosidase alfa 40mg/kg qow (n=5) or alglucosidase alfa (same dose as prior 6mo [20mg/kg qow up to 40mg/kg qw]; n=6).
RESULTS: Table 1 shows baseline characteristics/medical histories. All participants completed the PAP without missed infusions/dose decreases. Safety data (Table 2) were consistent with alglucosidase alfa and avalglucosidase alfa safety profiles, and Pompe disease. No serious/severe treatment-related TEAEs, TEAE-related permanent discontinuations, or deaths occurred. GMFM-88 showed improving trends across all cohorts. Pompe-PEDI functional skills improved/stabilized in participants of all cohorts. Left ventricular mass Z-score (LVMZ) was normal in all but 1 participant with abnormal baseline LVMZ, who improved to normal range at Wk25. Six participants developed anti-avalglucosidase alfa antibodies (median peak titer=6400), including 1 with boosted antibodies and 5 with new seroconversion during the PAP. All but 1 participant decreased anti-drug antibody over time (peak titer=6400 at last available timepoint).
CONCLUSIONS: Avalglucosidase alfa was well-tolerated and showed trends of clinical improvement in IOPD participants who were alglucosidase alfa-experienced and had previously demonstrated incomplete clinical response. Funding: Sanofi Genzyme.
KEYWORDS: Neuromuscular Disorders, Rare Diseases

521. Spinal intrathecal Ommaya reservoir for administration of nusinersen in spinal muscular atrophy
Marks Warren (Fort Worth, TX, United States) Acord Stephanie, Baldwin Marcie, McCarty Amgie, Bailey Laurie, Honeycutt John

OBJECTIVE: In December 2016, nusinersen (Spinraza) was approved for the treatment of spinal muscular atrophy (SMA) due to defects of the SMN1 protein. Many patients with SMA have undergone spinal instrumentation, making repeated spinal administration difficult. Often this necessitates repeated anesthesia and radiation exposure. Implanted reservoirs offer a safe alternative.
METHODS: Placement of spinal Ommaya reservoir was offered as part of a care option for patients that have undergone (or are undergoing) spinal instrumentation. This is a review of all nusinersen-treated SMA patients at our center.
RESULTS: Between February 2017 and December 2019 thirty-eight SMA patients were treated with nusinersen. Eight patients underwent placement of Ommaya reservoir. Mean age at placement was 17 years (range 5-23 years). One patient (age 5 years) was done in conjunction with spinal instrumentation; all others had prior stabilization/fusion. There was a single infection necessitating removal of the Ommaya but not spinal hardware. Two patients had CSF leak that required hospitalization for supportive care; one had surgical revision of the dural closure. Medication administration is done in the office. Using standard LP administration, all

patients are done in either the IR suite or an operative procedure room with varying degrees of anesthesia support. Two patients were hospitalized (one twice) for post procedure headache.
CONCLUSIONS: Ommaya reservoir placement for chronic administration of intrathecal medications seems to be a viable alternative in selected patients. This is important as the number of new medications that may require repeated intrathecal injection is increasing.
KEYWORDS: Neuromuscular Disorders, Rare Diseases

522. Clinical and genetic spectrum of Ullrich congenital muscular dystrophy
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OBJECTIVE: To analyze the phenotypic and genotypic characteristics of children with Ullrich congenital muscular dystrophy (CMD).
METHODS: We prospectively analyzed the clinical course and mutation spectrum among children with genetically proven Ullrich CMD, in our muscular dystrophy cohort from Jan 2018 onwards. Genetic testing was performed through next-generation sequencing of targeted genes panel of myopathies and mutations were confirmed by Sanger sequencing.
RESULTS: Eight patients (six boys) with pathogenic mutation in collagen VI coding genes were identified. Phenotypic features included: delayed attainment of motor milestones (8, 100%), generalized muscle weakness and wasting (8, 100%), distal joint hyperlaxity (8, 100%), prominent calcaneum (3, 37.5%), scoliosis (3, 37.5%), and calf hypertrophy (1, 12.5%). The disease progression was associated with development of joint contractures and the median age for these were: distal joints contractures (n=8, 3y), neck contracture (n=5, 4.5y), and tendoachilles contractures (n=4, 4y). Five patients (62.5%) who had onset in infancy failed to attain ambulation. Three patients (37.5%) attained ambulation with support between 24 and 30months and ambulation was lost after a median period of 9months. Genetically, COL6A1 mutation was identified in 5 (62.5%), in COL6A2 in 2 (25%) and in COL6A3 in 1(12.5%) patient. Five patients had heterozygous mutations with autosomal dominant inheritance. Two novel mutations were identified: chr21:47404385; T>T/C(heterozygous, dominant) and chr21:47404304_ 47404305delGT(homozygous, recessive).
CONCLUSIONS: This study highlights the clinico-genetic heterogeneity and the clinical course of children with Ullrich CMD. No definite genotype-phenotype associations were identified. Nonetheless, the onset in infancy and autosomal dominant inheritance may predict a more severe phenotype.
KEYWORDS: Neuromuscular Disorders, Genetics

523. FIREFISH Part 2: Efficacy and safety of risdiplam (RG7916) at in infants with Type 1 spinal muscular atrophy (SMA)
Darras Basil (Boston, MA, United States) Baranello Giovanni, Masson Riccardo, Mazurkiewicz-Bełdzinska Maria, Rose Kristy, Vlodavets Dmitry, Xiong Hui, Zanoteli Edmar, El-Khairi Muna, Fuerst-Recktenwald Sabine, Gerber Marianne, Gorni Ksenija, Kletzl Heidemarie, Scalco Renata, Servais Laurent, on behalf of the FIREFISH Working Group

OBJECTIVE: To determine the efficacy and safety of risdiplam (RG7916), a centrally and peripherally distributed oral *SMN2* pre-mRNA splicing modifier, in infants with Type 1 spinal muscular atrophy (SMA) treated for 12 months during the confirmatory Part 2 of the FIREFISH (NCT02913482) study.

METHODS: FIREFISH is an ongoing, multicenter, open-label study of risdiplam in infants aged 1–7 months at enrollment with Type 1 SMA and two copies of the *SMN2* gene. Part 1 (n=21) assesses the safety, tolerability and PK/PD of different risdiplam dose levels. In FIREFISH Part 1, there have been no drug-related safety findings leading to withdrawal from the study following ≤30 (median 19) months of treatment (data-cut: 2nd July 2019). The primary objective of confirmatory Part 2 (n=41) is to investigate the efficacy of risdiplam at the dose selected in Part 1. The primary efficacy endpoint is the proportion of infants sitting without support for 5 seconds after 12 months of treatment, as assessed by Item 22 of the Gross Motor Scale of the BSID-III. Additional secondary endpoints will also be measured, including the achievement of motor milestones, and safety.
RESULTS: The primary endpoint of FIREFISH Part 2 at 12 months was met (data-cut: 14th November 2019). Here, we will report efficacy and safety data in participants who have received treatment with risdiplam for ≥12 months at the dose selected in Part 1.
CONCLUSIONS: Part 2 of FIREFISH will provide important data on the efficacy and safety of risdiplam in a broad population of infants with Type 1 SMA.
KEYWORDS: Neuromuscular Disorders, Rare Diseases

524. A Mitochondrial tRNA Mutation Causes Axonal Charcot-Marie-Tooth Disease in a Large Family from the Venezuelan Andes

Fay Alex (San Francisco, CA, United States) Garcia Yngo, Margeta Marta, Maharjan Sunita, Yin Sitao, Bassaganyas Laia, McMahon Tom, Hou Ya-Ming, Fu Ying-Hui, Ptacek Louis

OBJECTIVE: To identify the genetic cause for a progressive peripheral nerve disease in a large Venezuelan family.
METHODS: Next-generation sequencing of nuclear and mitochondrial DNA (mtDNA) was performed for three affected family members. Muscle biopsies from four family members were used for analysis of muscle histology and ultrastructure, mtDNA sequencing, and RNA quantification. Lateral femoral cutaneous nerve biopsies were collected from two affected family members for ultrastructural studies.
RESULTS: Clinical examination and electrodiagnostic testing showed a motor and sensory polyneuropathy with predominantly axonal features. Pedigree analysis revealed inheritance only through the maternal line, a pattern consistent with a mitochondrial DNA disorder. MtDNA sequencing identified a mutation in the mt-tRNA^{Val}gene, m.1661A>G, which is predicted to disrupt a Watson-Crick base pair in the tRNA T-stem-loop. This mutation was present at nearly 100% heteroplasmy in both blood and skeletal muscle. Muscle biopsies showed chronic denervation/reinnervation changes, with subtle abnormalities suggestive of mitochondrial pathology, while biochemical analysis of electron transport chain (ETC) enzyme activities showed reduction in multiple components of the ETC. Northern blots from skeletal muscle total RNA showed reduction of mt-tRNA^{Val}, but not mt-tRNA^{Leu}(UUR), in subjects compared to unrelated age- and sex-matched controls. Nerve biopsies from two affected family members demonstrated ultrastructural mitochondrial abnormalities (hyperplasia, hypertrophy and crystalline arrays) consistent with a mitochondrial neuropathy.
CONCLUSIONS: Our findings identify a previously unreported cause of Charcot-Marie-Tooth (CMT) disease, a mutation in the mitochondrial tRNA-Valine, in a large Venezuelan family. This work expands the list of CMT-associated genes from protein-coding genes to a mitochondrial tRNA gene.

KEYWORDS: Neuromuscular Disorder, Rare Diseases, Neurometabolic Disorders

525. Demographics and safety data from patients with nmDMD receiving ataluren in the Strategic Targeting of Registries and International Database of Excellence (STRIDE) Registry

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OBJECTIVE: Duchenne muscular dystrophy (DMD) is a severe neuromuscular disorder caused by a lack of functional dystrophin.Ataluren promotes readthrough of an in-frame premature stop codon to produce full-length dystrophin. STRIDE (NCT02369731) is an ongoing registry providing real-world data on ataluren use in patients with nmDMD. The study objectives are to describe the demographics of the STRIDE population and the interim safety results as of 31 January 2019.
METHODS: Data from enrolled patients are collected at consent; for patients who initiated ataluren as part of a commercial or early access program before enrollment, data for the period prior to enrollment are obtained retrospectively. Patients will be followed for ≥5 years or until study withdrawal.
RESULTS: At data cut-off, 220 boys were enrolled in STRIDE in 11 countries and received ≥1 ataluren dose. Total mean±SD exposure to ataluren was 822±368 days, equivalent to 495 patient-years. Safety outcomes were consistent with the known safety profile of ataluren. Fourteen boys discontinued the study. Of 220 boys enrolled, 210 had genetically confirmed nmDMD, most of whom were Caucasian (66.7%), with mean age of 10.6±3.6 years at the consent date. Mean age at first symptoms was 2.8±1.8 years (n=193), and age at nmDMD confirmation was 5.2±2.9 years (n=200). Median time between first symptoms and nmDMD confirmation was 1.6 years (n=186). Most patients used concomitant corticosteroids (191/220 [86.8%]).
CONCLUSIONS: STRIDE constitutes the first drug registry for patients with nmDMD. Analyses of data from STRIDE patients will provide insights into the real-world long-term effectiveness and safety of ataluren.
KEYWORDS: Neuromuscular Disorders, Rare Diseases, Genetics

526. Thrombotic Microangiopathy (TMA): A potential adverse reaction post Zolgensma (onasemnogene abeparvovec-xioi) therapy for Spinal Muscular Atrophy (SMA)

Arya Kapil (Little Rock, AR, United States) Millner Rachel, Louis Cassandra, Moss Michele, Douglass David, Prabha Nayana, Saylam Ezgi, Agarwal Amit, Veerapandiyan Aravindhan

OBJECTIVE: To report a case of TMA in a 6 month-old patient with SMA type 1 after Zolgensma administration.
METHODS: Case report
RESULTS: A 6 month-old SMA type 1 patient received the recommended dose of Zolgensma. At the time of injection, she had been intubated and mechanically ventilated for respiratory failure for approximately 2 weeks and her vitals were within normal limits. Blood urea nitrogen (BUN) 7 mg/dl; Creatinine (Cr) 0.1 mg/dl; platelets (Plt) 503/ul; hemoglobin (Hb) 10.3 mg/dl. Five days post injection, the patient developed hypertension (140s-150s/80s-90s mmHg), hematuria, proteinuria, acute kidney injury (BUN 52, Cr 0.6), hemolytic anemia (schistocytes on

peripheral smear, elevated reticulocyte count of 7.5%, Hb 6.5 and elevated LDH 4208) and thrombocytopenia (Plt < 30,000) all consistent with TMA. Infectious workup was negative; ADAMTS13 activity was normal (92%); DAT was negative; homocysteine was normal; C3 and CH50 were normal but C4 was low at < 8. TMA functional testing showed evidence of complement activation, but no evidence of abnormally functioning inhibitory factors or antibodies to inhibitory factors. Therefore, the patient was not thought to have atypical hemolytic uremic syndrome. The patient was treated with antihypertensives, fluid management, platelet and RBC infusions as well as (starting on the thirteenth day post Zolgensma infusion) 5 cycles of plasmapheresis. TMA resolved and child became normotensive on a single antihypertensive.
CONCLUSIONS: Physicians and families should be aware of Zolgensma potentially causing TMA.
KEYWORDS: Neuromuscular Disorders, Rare Diseases

527. Single-center experience with treatment of nusinersen in children with spinal muscular atrophy

Kim Jonsoo (Chungju, Republic of Korea) Kim Wonseop

OBJECTIVE: Nusinersen has recently been approved for intrathecal treatment of spinal muscular atrophy (SMA). Clinical trials data concerning use of nusinersen is lacking. We describe our center's experience in using intrathecal nusinersen for children with SMA in the clinical setting.
METHODS: Intrathecal procedure were hospitalized according to a standard protocol. All procedures required moderate and deep sedation using intravenous midazolam or ketamine to minimize movements. Vital signs and the need for oxygen, analgesia during the procedure were monitored. Functional assessment including HFMSE motor milestones were performed at baseline and 45 and 120 days after start of treatment.
RESULTS: Five female patients with SMA type 2 with 3 copies SMN2 gene) successfully completed the loading regimen with Nusinersen, aged from 38.7 to 84.8 months. All patients had mild scoliosis but did not need ventilatory support. All procedures were performed safely without any complications and only two patients had a fever shortly after the procedure. After 3 months of treatment, all children improved by ≥4 points in HFMSE score (mean 2.2 points). Three of them (60.0%) showed functional improvements since 3rd dose administration. In particular, parents reported that the child's overall strength and endurance improved and his ability to cough improved compared to before the start of treatment.
CONCLUSIONS: Intrathecal nusinersen can be administered safely and showed an improvement of motor function in a short period of treatment. Long-term observation and follow-up of patients are crucial to understand the clinical impact of treatment with nusinersen.
KEYWORDS: Neuromuscular Disorders, Genetics

528. Generation of Ultrasound Muscle-Based Parameters for Evaluation of Hypotonia in Children aged 1month to 18 Years

Kaur Prabhjot (New Delhi, India) Kumar Atin, Chakrabarty Biswaroop, Jauhari Prashant, Pandey R, Gulati Sheffali

OBJECTIVE: To describe ultrasound muscle parameters (visual grading using Heckmatt scale, muscle thickness (MT), thickness ratio (TR) and echo-intensity (EI)) in children aged 1month to

18 years with hypotonia (peripheral & central); and develop criteria to differentiate between (i) normal & hypotonic subjects, (ii) different sub-types of peripheral hypotonia.
METHODS: This cross-sectional study was conducted at a tertiary care center in New Delhi (India) between June 2018 and July 2019. Ultrasound of forearm (FA), deltoid, quadriceps femoris (QF) and tibialis anterior (TA) was done.
RESULTS: Total of 185 subjects were enrolled (Peripheral hypotonia-125, Central hypotonia-30, normal-30). The best cut-offs for differentiation between different groups and sub-groups of hypotonia are as follows (with sensitivity & specificity, respectively): Hypotonic and normal subjects: MT (70%, 69%) & TR (70%,70%) of QF Peripheral from central hypotonia: EI of FA (70%,70%) Inherited neuropathy from rest etiologies of peripheral hypotonia: MT of FA (72%,75%) Muscular dystrophy from rest etiologies of peripheral hypotonia: TR of deltoid (70%, 71%) Neuronopathies from peripheral neuropathies: EI of deltoid, FA & QF (>70%,>70%) Congenital Muscular Dystrophies from Congenital myopathies: EI of deltoid, FA& QF (>60%) and MT of deltoid (~70%)
CMDs from peripheral neuropathies: muscle echogenicity of deltoid, FA & QF (~70%)
CONCLUSIONS: Skeletal-muscle ultrasound can be used to differentiate between different etiologies of peripheral hypotonia. In clinical scenarios, where differentiation between two or more etiologies is challenging, the above generated parameters can be used to narrow down differentials and plan further work-up.
KEYWORDS: Neuromuscular Disorders, Neuroimaging

529. Trofinetide: a Novel Approach to Rett Syndrome
Neul Jeffrey (Nashville, TN, United States) Percy Alan, Benke Timothy, Berry-Kravis Elizabeth, Glaze Daniel, Jones Nancy, Corriveau Joshua, Youakim James

OBJECTIVE: Rett syndrome (RTT) is a significantly debilitating neurodevelopmental disorder with no approved treatments. Trofinetide is a synthetic analog of glycine-proline-glutamate (GPE), the *N*-terminal tripeptide of the insulin-like growth factor 1 (IGF-1) that demonstrated significant dose-dependent improvements on RTT-specific measures as compared with placebo in a Phase 2 study (Guan et al., 2015; Glaze et al., 2019). The objective of this presentation is to describe a Phase 3 study design utilizing novel scales to investigate trofinetide's efficacy and safety versus placebo in patients with Rett syndrome.
METHODS: This 12-week, double-blind, randomized, placebo-controlled study will evaluate trofinetide's efficacy and safety in 184 females, 5 to 20 years old, with RTT (Clinicaltrials.gov NCT04181723). The coprimary endpoints are the Rett Syndrome Behavior Questionnaire (RSBQ) and Clinical Global Impressions-Improvement (CGI-I) scales. The CGI assessment leverages RTT-specific anchors developed for the CGI-I and CGI-S (Severity) to heighten the consistency and specificity of the evaluations; the clinical domains include communication, ambulation, hand use, social (eye contact), autonomic (respiration), seizures, and attentiveness. Additionally, secondary endpoints will include novel and existing scales to further evaluate the impact of trofinetide on patients' ability to communicate, patients' overall quality of life, and impact of RTT on caregivers. This study will be followed by a 40-week, open-label extension study.
RESULTS: Trial results are not yet available.

CONCLUSIONS: Significant unmet needs remain in the treatment of patients with Rett syndrome. The data from this Phase 3 study may support trofinetide's use as an impactful and tolerable treatment for RTT.
KEYWORDS: Neuromuscular Disorders

530. Escalating Dose and Randomized, Controlled Study of Nusinersen in Participants With Spinal Muscular Atrophy (SMA); Study Design and Updated Enrollment for the Phase 2/3 DEVOTE (232SM203) Study to Explore High Dose Nusinersen
Finkel Richard (Orlando, FL, United States) Day John, Ryan Monique, Mercuri Eugenio, De Vivo Darryl, Pascual Pascual Samuel, Montes Jaqueline, Gurgel-Giannetti Juliana, Mitchell-Sweeney Nancy, Foster Richard, Sun Peng, Ramirez-Schrempp Daniela, Kandinov Boris, Farwell Wildon

OBJECTIVE: To describe the design of the 3-part, Phase 2/3 DEVOTE study (NCT04089566) that will examine the safety/efficacy of nusinersen administered intrathecally at higher doses in participants with 5q SMA.
METHODS: Part A is an open-label safety evaluation of later-onset SMA participants (n=6;age 2–15 years, inclusive;SMA onset age >6 months) who will receive three 28mg loading doses at 14-day intervals followed by two 28mg maintenance doses every 4 months. After safety evaluation, Part B will enroll ~125 participants with infantile-onset (age ≤7 months at informed consent;2 *SMN2* copies;SMA onset age ≤6 months) or later-onset SMA (age 2 to <10 years;SMA onset age >6 months;sat but not walking independently;HFMSE score ≥10 to ≤54). Part B is a pivotal, double-blind, active-controlled trial with randomization (1:2 ratio) to the approved dose or two 50mg loading doses 15 days apart with 28mg maintenance doses every 4 months thereafter. After Part B safety evaluation, Part C will enroll ~20 participants of any age/SMA type on approved nusinersen dose ≥1 year who will receive one 50mg loading dose with 28mg maintenance doses every 4 months thereafter.
RESULTS: Primary objective is to evaluate the clinical efficacy of nusinersen administered at higher doses. Key endpoints include, for infantile-onset SMA: CHOP INTEND, HINE-2 motor milestones and event-free survival; for later-onset SMA: HFMSE, RULM, and WHO motor milestones. Secondary and exploratory endpoints include safety/tolerability, biomarker assessment, QoL, and PK. Updated enrollment data will be presented.
CONCLUSIONS: Enrollment began in February 2020 with a target enrollment of ~150 participants from ~50 centers globally.
KEYWORDS: Neuromuscular Disorders

531. Paraneoplastic Syndrome Presenting as a Neuromuscular Disorder
Freed Abbey (Los Angeles, CA, United States) Ramos-Platt Leigh, Rosser Tena

OBJECTIVE: A 15 year old previously healthy male presented to the hospital with back pain, muscle twitching, and difficulty urinating. Two months prior to admission, he developed burning lower back pain radiating to his waist and legs. Two weeks prior to admission, he developed intermittent muscle twitching involving his face, arms, hands, legs, and feet. He endorsed unintentional 10 pound weight loss and night sweats for 2 months. Neurologic examination demonstrated mild left lumbosacral tenderness to palpation, fasciculations in multiple muscle

groups with intact strength, no sensory deficits, and 3+ reflexes throughout with plantar flexor responses.
METHODS: The following neurodiagnostic studies were obtained: MRI full spine with and without contrast, MRA full spine, needle electromyography, and nerve conduction velocity. CSF and serum studies were sent to evaluate for infectious, nutritional, endocrine, inflammatory, and paraneoplastic processes.
RESULTS: MRI and MRA full spine were unremarkable. EMG/NCV demonstrated neurogenic changes in the left vastus and anterior tibialis concerning for a neurogenic process affecting L2-L5. CSF and infectious studies were unremarkable. Serum paraneoplastic panel was significant for elevated N-Type Calcium channel antibody at 0.18 (normal <0.03) and elevated Neuronal Voltage-Gated Potassium channel antibody at 0.11 (normal <0.02).
CONCLUSIONS: The positive paraneoplastic panel supports neurologic autoimmunity as the cause of his neuromuscular and autonomic symptoms. He received 5 days of pulse steroids with resolution of symptoms. This case demonstrates the importance of evaluating for paraneoplastic processes when other neurodiagnostic testing is negative as paraneoplastic syndromes have a wide range of clinical presentations.
KEYWORDS: Neuromuscular Disorders, Infections/Neuroimmunology

532. Clinical exome sequencing as first tier testing in the diagnosis of pediatric neuromuscular disease
Herman Isabella (Houston, TX, United States) Lopez Michael, Marafi Dana, Pehlivan Davut, Calame Daniel, Abid Farida, Lotze Timothy

OBJECTIVE: Diagnosis of pediatric neuromuscular disease (NMD) is clinically challenging due to genetic and phenotypic heterogeneity. Yet, correct and timely clinical and molecular diagnosis is imperative to inform prognosis, treatment options, and recurrence risk. Pediatric NMD patients undergo time-consuming, costly and invasive testing with variable diagnostic yield. Given the rapid advancement in next generation sequencing (NGS), we hypothesized that applying clinical exome sequencing (ES) as first tier testing in pediatric NMD will increase molecular diagnostic yield.
METHODS: A retrospective chart review of NMD patients seen at Texas Children's Hospital Muscular Dystrophy Association (MDA) clinic between 2010 and 2016 was performed. Demographics, clinical presentation, and test results were collected. Genetic testing results were cross-referenced to publicly available databases, including gnomAD, OMIM, and ClinVar.
RESULTS: A total of 106 patients from 106 families were included. ES significantly improved molecular diagnostic yield. 46% of patients were found to have pathogenic variants in known disease genes by ES compared to 21% with other molecular testing strategies. Importantly, 33% of patients remained without a molecular diagnosis, suggestive of novel disease genes and/or mechanisms not readily detected by current technology.
CONCLUSIONS: Correct and timely molecular diagnosis of pediatric NMD is imperative to inform prognosis, treatment options, and recurrence risk. With the advent of NGS, diagnostic yield of rare diseases is at an all-time high. In this study, we show that ES significantly improves diagnostic yield of pediatric onset NMD and suggest that clinical ES should be considered as first tier testing.
KEYWORDS: Neuromuscular Disorders, Genetics, Rare Diseases

533. Hereditary axonal neuropathy and neuromyotonia: A mini-series in three cases
Oncel Ibrahim (Ankara, Turkey) Temucin Cagri, Ceylan Ahmet, Topaloglu Haluk

OBJECTIVE: Hereditary axonal neuropathy with neuromyotonia is a distinct clinical entity associated to the HINT1 gene, encoding *histidine triad nucleotide-binding protein 1.*
METHODS: We present three cases with neuromytonia and peripheral neuropathy.
RESULTS: Patient 1 was a 15 years old male from a consanguineous family with gait disturbance and frequent falls. Pes planus, high stepping and distal atrophy in lower limbs were present. DTRs were diminished. ENMG studies showed sensory-motor axonal polyneuropath conjuction with neuromyotonia. A homozigout missense mutation (c.110G>C(p.R37P)) was found in *HINT1*gene sequencing. Patient 2 was a 17 years old girl from a consanguineous family presented with numbness, muscle stiffness and muscle weakness noticed in the last two years. DTRs were hypoactive. Serum CK level was 546 U/L. There was chronic motor axonal polyneuropathy in electrophysiology along with neuromyotonia. A mutation in the HINT1 gene was detected. Patient 3 was a 17 year old male from a consanguineous family, presented with weakness and pain of lower limbs. Physical examination showed muscle weakness in limbs and distal atrophy. He had steppage gait, stocking-glove pattern sensory loss and muscle stiffness. DTRs were absent. Serum CK level was 1500 U/L. ENMG showed sensory-motor axonal neuropathy and neuromyotonia. Genetic test for HINT1 gene is pending. HINT1 binds nucleotides, is involved in the nervous system, and may have role in signaling. All three patients benefit from carbamazepine treatment.
CONCLUSIONS: Neuromyotonia and elevated CK levels in blood are peculiar laboratory findings in hereditary neuropathies associated with HINT1 gene. Patients usually respond to sodium channel blocking drugs, preferably carbamazepine.
KEYWORDS: Neuromuscular Disorders, Rare Diseases

534. Botching Up Botulism: Overlapping Symptoms Leading to a Delayed Diagnosis, a Case Report of Three Patients
Liu Suzanne (Salt Lake City, UT, United States) Candee Meghan

OBJECTIVE: Non-infantile pediatric botulism is rare and can be difficult to distinguish from mimics such as Guillain-Barré syndrome (GBS), myasthenia gravis, Lambert-Eaton syndrome, toxic ingestion, and stroke. Early diagnosis can be challenging.
METHODS: We present a triad of individuals with botulism, including two adolescents and one adult.
RESULTS: The first patient was a 13-year-old male who presented with altered mental status, vomiting, ataxic gait, diplopia, and shortness of breath. He had asymmetric ptosis, ophthalmoplegia, lacked a gag reflex, was diffusely weak, and areflexic. Work up included cerebrospinal fluid testing, spine magnetic resonance imaging, electromyogram (EMG) and serum studies. Sufficient stool sample for botulism testing could not be obtained. Ultimately, a working diagnosis of GBS, specifically acute motor axonal neuropathy or AMAN variant, was favored. He was treated with intravenous immunoglobulins. Days later, our patient's friend and neighbor presented with acute onset of descending weakness and difficulty swallowing. Weeks later, our patient's mother was hospitalized with respiratory failure and her stool testing was positive for botulinum toxin. Testing of home canned green beans, which the patient, his friend, and mother had all consumed, was also positive for the toxin.

CONCLUSIONS: This case highlights the challenge of an early and accurate botulism diagnosis and the importance of an extensive potential exposure history. Foodborne botulism is a rarity in the United States and early signs and symptoms of the disease frequently overlap with GBS. Although all 3 members of our triad made a full recovery, earlier diagnosis allows for timely administration of antitoxin and a faster recovery.
KEYWORDS: Neuromuscular Disorders, Infections/Neuroimmunology

535. Survey of patients with spinal muscular atrophy on the island of Shikoku, Japan
Urate Risako (Toon, Japan) Okamoto Kentaro, Saito Isao, Aibara Kaori, Jogamoto Toshihiro, Motoki Takahiro, Fukuda Mitsumasa, Nishio Hisahide, Ishii Eiichi, Eguchi Mariko

OBJECTIVE: Spinal muscular atrophy (SMA) is an inherited neuromuscular disorder associated with spinal motor neuron loss characterized by generalized muscle weakness. Only a few reports exist on SMA epidemiology in Japan. We estimated the prevalence of each type of SMA on Shikoku, Japan's fourth-largest major island. We also discuss the effects of nusinersen therapy in SMA patients.
METHODS: We sent a questionnaire to all 131 hospitals in Shikoku that have pediatrics or neurology departments between March and September in 2019, asking whether each hospital has ever treated SMA patients. If they had, we sent a second questionnaire to obtain more detailed information on the clinical data and treatment of each patient.
RESULTS: A total of 117 hospitals (89.3%) responded to our first questionnaire, and 21 SMA patients were reported, 16 of whom had homozygous deletion of *SMN1*. Of the 21, nine had SMA type 1, five were type 2, five were type 3, one was type 4, and one was unidentified. The estimated prevalence for all instances of SMA and 5q-SMA was 0.56 and 0.43 per 100,000 people, respectively. Thirteen patients had received nusinersen therapy. Its outcomes varied from no obvious effects and being unable to sit to being able to sit independently.
CONCLUSIONS: Our data showed the prevalence of SMA types 2 and 3 was relatively low on Shikoku compared with previous reports from other countries. Remaining motor function may be one predicting factor.
KEYWORDS: Neuromuscular Disorders

536. Clinical spectrum of Congenital Muscular Dystrophy - A seven year experience from a tertiary care centre of North India
Singh Sonali (Delhi, India) Kamila Gautam, Sinha Rahul, Jauhari Prashant, Chakrabarty Biswaroop, Sharma MC, Kumar Atin, Gulati Sheffali

OBJECTIVE: To study the clinical spectrum of congenital muscular dystrophies at a tertiary care centre of North India.
METHODS: Twenty three patients of Congenital muscular dystrophy were retrospectively studied from Jan 2013 to Dec 2019.
RESULTS: Twenty three patients (12 males and 11 females) with biopsy diagnosis of CMD were analysed. Isolated motor delay was the most common presenting feature seen in 39% (n=9). Other presenting features included progressive proximal muscle weakness, floppy infant and global developmental delay in 32% (n=8), 16% (n=4) and 8% (n=2) respectively. Four patients (17%) had positive family history of similar illness. CPK levels were highly variable ranging from 76 to 6955 units/litre which were nonspecific. Neuroimaging revealed periventricular white

matter hyperintensities in 17% (n=4). Structural abnormalities of the brainstem, multiple cerebellar cysts and lissencephaly was seen in one patient. Muscle biopsy and immunohistochemistry revealed merosin negative CMD(n=7), merosin positive CMD (n=3), Fukuyama muscular dystrophy(n=3), Ullrich muscular dystrophy (n=3), Laminin 2 mutation positive muscular dystrophy (n=2) and unclassified muscular dystrophy (n=5). The genetic test could not be done due to affordability issues. We are currently doing a study on NGS in all muscle dystrophies.
CONCLUSIONS: Congenital muscular dystrophy has a variable clinical manifestations and muscle biopsy with specific staining helps in delineating the specific types. Accurate diagnosis is important for planning genetic testing and prognostication as no specific treatment is available.
KEYWORDS: Neuromuscular Disorders

537. Commercial RNA Sequencing to Confirm Genetic Diagnosis of 5q Spinal Muscular Atrophy
Zarei Sanam (Iowa City, IA, United States) Mathews Katherine

OBJECTIVE: Approximately 95-98% of individuals with a clinical diagnosis of spinal muscular atrophy (SMA) are homozygous for deletion in both copies of *SMN1*, typically deletion of exon 7. 2-5% of patients are compound heterozygotes with a deletion on one allele and an inactivating mutation on the other allele.
METHODS: We report a 14 year old girl with a clinical phenotype, muscle biopsy, and EMG/NCV results consistent with 5q SMA, a single deletion in *SMN1,* no second mutation on DNA sequencing and absent *SMN1* transcript.
RESULTS: Our patient was seen for hypotonia at age 2 years and never walked independently. She had progressive weakness and developed restrictive lung disease and scoliosis. CK was 124. EMG/NCV studies at 27 months showed denervation in all muscles tested. Quadriceps muscle biopsy revealed fiber type grouping and grouped atrophy consistent with SMA and a sural nerve biopsy was normal. SMA testing confirmed heterozygous deletion of *SMN1* and 3 copies of SMN2. Sequencing did not identify a point mutation in the second allele. A 29 gene panel found no non-5q SMA mutations. The clinical diagnosis remained 5q SMA type 2. Commercial RNA sequencing from blood at 14 years revealed no *SMN1*expression, consistent with 5q SMA.
CONCLUSIONS: Our case demonstrates utility of *SMN1* RNA sequencing as a means of confirming 5q SMA in a patient with clinical features of SMA, supporting neurophysiological and neuropathology findings, and normal DNA sequencing results. With diagnosis, patients can be eligible for nusinersen, onasemnogene abeparvovec or newer treatments specific to this form of SMA.
KEYWORDS: Neuromuscular Disorders, Genetics, Rare Diseases

538. Heterotopic ossification in a patient with Duchenne Muscular Dystrophy: case report
Barra Rafael (Rio de Janeiro, Brazil) Machado Gisele

OBJECTIVE: The main purpose of this case report is to describe a patient with Duchenne muscular dystrophy that developed heterotopic ossification as a complication.
METHODS: This is a case report based on patient's medical record. Medline/ PubMed research was made using Duchenne muscular dystrophy, heterotopic ossification and ectopic calcification as keywords.

RESULTS: W. was a 12 years of age boy with Duchenne muscular dystrophy that fell from his wheelchair, causing direct trauma in his right knee. He was diagnosed with a fracture in the distal third of the right femoral metaphysis. He underwent a surgical correction. Four months after this event he complaint of pain in the left knee region, especially in postural maneuvers transfers. Radiographs of knees and hips were performed, and demonstrated images of calcifications in the hip joint (Image 1). A CT scan of the pelvis was performed, suggesting the presence of heterotopic ossification located in the hips bilaterally (Image 2). Bone Morphogenetic Proteins are important cytokines that control multiple processes of differentiation. It have been demonstrated changes in signaling of these proteins both in heterotopic calcification and animal models of Duchenne muscular dystrophy. The presence of heterotopic calcification in a patient with Duchenne muscular dystrophy leads us to suggest that bone morphogenetic proteins may be involved in this complication.
CONCLUSIONS: To the best of our knowlegde, this is the first case report of a patient with Duchenne muscular dystrophy that developed heterotopic calcification. However, more detailed studies need to be conducted to better understand the molecular basis of this process.
KEYWORDS: Neuromuscular Disorders

539. Partial hemizygous deletion of exon 7 of dystrophin gene as disease causing for Duchenne muscular dystrophy
Myrzaliyeva Bakhytkul (Almaty, Kazakhstan) Lepessova Marzhan, Kalmakhanova Kazyna, Gabbassova Akmaral, Ashimova Aidana

OBJECTIVE: A description of Duchenne muscular dystrophy (DMD) caused by a partial deletion of exon 7 in the dystrophin gene.
METHODS: *Ciinical cases of* 2 patients with DMD. Performed methods were clinical, neurological and genetic studies.
RESULTS: 2 Brothers, aged 15 and 6 years. Nationality - Kazakhs. Parents are not relatives. A family history - positive.
Patient#1 is 15 yo. Independent walking from 28 month of life, delayed speech development. Disease debut at age 7 years: abnormal *gait, difficulty climbing stairs*, weakness. CK 5181. DMD diagnosis was made at 9 yo. Loss of ability to walk in 11 yo. *Objective*: non-ambulatory. Diffuse muscle hypotonia, areflexia, muscle hypotrophy. Multiple contractures. Symptoms of dilated cardiomyopathy. The patient died at the age of 16 from heart failure. *Patient#2 is* 6 yo. Independent walking from 17 month of life, normal speech development. Disease debut at age 4 years: abnormal *gait, difficulty climbing stairs*. CK 8679. DMD diagnosis was made at 5 yo. Objective: Macroglossia. Muscle hypotonia, hyporeflexia. Myopathic gait. Positive Gower's sign. Calf pseudohypertrophy. *Genetics:* PCR (19 exons): no deletions were detected. MLPA (79 exons): duplication and deletion were not detected. Gene sequencing (*patient #2*): no clinically significant pathological variants were found. By NGS reexamination, a hemizygous deletion starting at the genomic position chrX: 32827671 (NM_004006.2: c.589) and extending into intron 7 was identified.
CONCLUSIONS: Deletion involving exon 7 have been previously described as disease causing for Duchenne muscular dystrophy. The family needs a study of carriage of a pathological mutation in mother and sisters.
KEYWORDS: Neuromuscular Disorders, Genetics, Rare Diseases

540. Contemporary Treatment Practices in Patients with Spinal Muscular Atrophy: Initial Findings from the RESTORE Registry

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OBJECTIVE: Spinal muscular atrophy (SMA) is a progressive, debilitating disease characterized by motor neuron loss, muscle weakness, respiratory failure, and early death. While recent advancements have dramatically improved prognosis, real-world data on treatment outcomes remain limited – particularly for patients who switch treatments. RESTORE is a comprehensive registry of patients with SMA, specifically designed to overcome the recognized limitations of existing single-product registries.
METHODS: RESTORE is an ongoing, prospective, multicenter, multinational, observational study, assessing outcomes in SMA patients; informing patients, caregivers, regulatory agencies, and researchers on the effectiveness and safety of approved and emerging treatments; and collecting information on healthcare resource utilization and caregiver burden. The RESTORE database incorporates data from patients enrolled in partnering registries and the onasemnogene abeparvovec-xioi (formerly AVXS-101) managed-access program. Follow-up duration is 15 years from enrollment or until death.
RESULTS: As of 3 January 2020, the RESTORE database comprises information from 64 patients and 25 active sites in the United States. This cohort permits descriptive analyses of patients with a range of baseline characteristics at time of dosing, including individuals who have switched therapies, and who received treatment under managed/expanded-access programs at a variety of treatment centers. RESTORE is rapidly expanding globally, with 53 sites currently in start-up.
CONCLUSIONS: The RESTORE registry represents a pivotal resource for enhancing our understanding of SMA disease course under differing treatment regimens, and off therapy, in a diverse set of patients. This study was sponsored by AveXis, Inc., a Novartis Company.
KEYWORDS: Neuromuscular Disorders

541. Reversible Visual Involvement in Critical Illness Polyneuropathy

Rizk Tamer (Saint John, New Brunswick, Canada) Mudawi Khalid

OBJECTIVE: Neuro-muscular weakness in pediatric patients admitted to pediatric intensive care unit is common. This could partly be related to improved survival of sick children with sepsis and/or multi-organ dysfunction. Etiology, prognosis, and long-term outcome remain to be areas of controversy and vagueness. To our knowledge, this is the first case to describe reversible visual involvement in critical illness polyneuropathy and myopathy cases.
METHODS: We describe PICU course of a 3-year-old boy who developed severe fulminant sepsis with the need of urgent intubation, ventilation, inotropic support, neuromuscular blocking agents, steroids, and broad-spectrum antibiotics, including aminoglycosides. Weakness of all limbs was noticed on day 7. This was associated with visual disturbances.
RESULTS: He was diagnosed with critical illness polyneuropathy and myopathy. His outcome was favorable. This case report highlights the unique combination of CIP/CIM features

associated with visual impairment and also suggests that full recovery is possible for this clinical presentation.
CONCLUSIONS: Neuromuscular disease should be suspected in critically ill children with muscle weakness and failure to wean from ventilation. Visual involvement can occur with CIP/CIM and can fully reverse, as in our case. This may be due to reversible optic neuropathy. Although CIP/CIM can cause significant morbidity in critically ill children, incidence seems lower than adults and also clinical course seem to be milder. These conditions generally, however, overlap clinically and electrophysiologically in the pediatric and adult age groups. Prospective clinical studies will be required to better characterize the frequency and natural history of these clinical entities in pediatric practice.
KEYWORDS: Neuromuscular Disorders, Critical Care

542. Real world impact of newborn screening for spinal muscular atrophy: 2 year Australian pilot
Farrar Michelle (Sydney, Australia) Kariyawasam Didu, Herbert Karen, D'Silva Arlene, Sampaio Hugo, Alexander Ian, Shih S, Chambers Georgina, Wiley Veronica

OBJECTIVE: To determine the impact of spinal muscular atrophy (SMA) newborn screening (NBS) and treatment on patients, families and Australian health system.
METHODS: A population-based SMA NBS pilot programme of all newborns in the state of New South Wales commenced in August 2018. Screening performance and temporal course, treatment pathways, health outcomes, costs, and opinions of families were prospectively assessed.
RESULTS: As of 31 Dec 2019, 151,135 newborns were screened with 14 proven to have SMA. NBS enabled early identification of symptomatic SMA in 5/14 (36%) newborns by clinical and/or neurophysiological examination: apparent at initial specialist evaluation in and emerging during initiation of disease-modifying treatments in 3(age range 16-33 days, 4 with 2xSMN2, 1 with 3xSMN2). Approved therapy with nusinersen commenced at mean-age of 27 days (range 16-37) in 7 infants (3 females, 4 with 2xSMN2), with mean baseline CHOP-INTEND of 49 (range 33-59(max 64)). During follow-up (mean-age 195 days, range 43-431), all nusinersen treated patients were alive, demonstrated gains in motor function and milestones and 85% fed exclusively by mouth and did not require any ventilatory support. There was universal parental support for SMA NBS in those who opted for proactive management. Additional follow-up of health and quality-of-life outcomes, costs and implementation experiences will be presented.
CONCLUSIONS: Preliminary data suggests NBS has significant clinical practice utility for early diagnosis and treatment of SMA, improving health outcomes across the clinical spectrum captured. This pilot study is informing ongoing improvements and sustainability in NBS programs and clinical care.
KEYWORDS: Neuromuscular Disorders, Rare Diseases, Translational/Experimental Therapeutics

543. Immunomonitoring reveals alterations in B-cells associated with muscle disease activity among individuals with Juvenile Dermatomyositis
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Cardenas Jacob, Gu Jinghua, Smitherman Cynthia, Nguyen Phuong, Hong Seunghee, Pascual Virginia

OBJECTIVE: Juvenile Dermatomyositis (JDM), the most common pediatric inflammatory myopathy, bridges the realms of neurology and rheumatology. We used blood immunomonitoring to identify markers of JDM disease activity (DA).
METHODS: We evaluated 35 JDM patients, 4 childhood lupus (cSLE) patients and 14 heathy controls (HC) for this study. Clinical measures of DA including the Manual Muscle Testing (MMT-8) were recorded. Blood was collected for RNA sequencing and flow cytometry studies. A 14-color flow cytometry panel was used to examine B and T- cell subsets. Differential gene expression analysis was performed using DESeq2. Pathway and gene ontology analysis utilized the Database for Annotation, Visualization and Integrated Discovery.
RESULTS: JDM peripheral blood mononuclear cells profiling revealed an expansion of conventional memory B cells ($CD20^+$ $CD27^+IgD^-$) lacking follicular markers (CXCR5-) compared with HC ($p<0.01$). This expansion was associated with worse (lower) manual muscle testing score (MMT-8) (Spearman's rho =0.13; p=0.05). T-helper 2 cells ($CD4^+CD45RA^-$ $CXCR5^-CCR6^-CXCR3^-$) were also expanded in JDM PBMCs ($p<0.01$). While an interferon signature was present both in SLE and the majority of JDM patients, a distinct B cell signature was evident in 50% of the JDM patients, 75% of whom exhibited a predominately muscle phenotype.
CONCLUSIONS: JDM patients show unique alterations in their B cell compartment. An expansion of extrafollicular conventional memory B cells associates with muscle DA. At the transcriptional level, B cell-related genes were over-expressed in JDM compared to cSLE. These findings suggest that interactions of B and T-cells in the extrafollicular compartment may contribute to muscle disease in JDM.
KEYWORDS: Neuromuscular Disorders, Infections/Neuroimmunology, Translational/Experimental Therapeutics

544. Using Artificial Intelligence to Identify Risk Factors for Patient-Reported Functional Outcomes in Patients with Fascioscapulhumeral Muscular Dystrophy (FSHD)

Katz Natalie (Kansas City, MO, United States) Cernik Colin, Delbango Rango, Hogan John, Statland Jeffery

OBJECTIVE: To analyze patient-reported data from the National Registry for FSHD to identify risk factors which are predictive of functional outcomes.
METHODS: A de-identified, prospective cohort study was evaluated using multiple concurrent epidemiological and artificial intelligence (AI) methods to assess interactions between key characteristics including: age, gender, genetics (# of D4Z4 repeats, 1-10), age of symptom onset and diagnosis, use of assistive devices, wheelchair use, job loss due to FSHD, and progressive functional burden/disability. These data were also used to develop AI algorithms to identify risk factors that were predictive of patient functional decline.
RESULTS: Data from 578 participants with FSHD type 1 with an average of 9 annual follow-up reports were analyzed. Over half (n = 320, 55%) of participants reported symptom onset prior to age 18. Patients with 1-3 repeats were 7.6x more likely to be diagnosed prior to age 18 (95% CI 7.03, 8.19), 1.8x more likely to be female (CI 1.23, 2.33), and 10.3x more likely to use a

wheelchair prior to age 25 (CI 9.46, 11.14). Currently, AI techniques are being used to search for additional predictors of functional outcomes; data will be presented at the time of the meeting.
CONCLUSIONS: Many patients with FSHD type 1 have symptom onset in their pediatric years. Identification of risk factors using AI technology that are predictive of functional decline will allow for improved clinical care, and may help refine clinical trial design by identifying predictors of clinical outcomes of importance.
KEYWORDS: Neuromuscular Disorders, Rare Diseases

545. Diagnostic delay in Serbian pediatric patients with spinal muscular atrophy- are we reaching the goal?
Brankovic-Sreckovic Vesna (Belgrade, Serbia) Djordjevic Stefan, Kosac Ana, Nikolic Dimitrije, Brkusanin Milos, Todorovic Slobodanka, Milic Rasic Vedrana

OBJECTIVE: Early diagnosis of spinal muscular atrophy (SMA) is crucial in the current therapeutic era. We aimed to investigate the diagnostic delay for Serbian children with different types of SMA.
METHODS: This study included patients with a genetically confirmed diagnosis of SMA type 1, 2, and 3 followed-up at the two tertiary referral centers between 2000 and 2020. We analyzed the age of onset and genetic confirmation, and the diagnostic delay. The Kruskal–Wallis and Mann-Whitney tests were used to compare the diagnostic delay for different SMA types.
RESULTS: Of 106 eligible patients, 86 (81%) were included in the analyses. There were 16, 35, and 32 patients with SMA type 1-3, respectively. The median age of onset was 2.5 months (range 1-4 months), 7 months (range 3-18 months), and 24 months (range 12-120 months) for patients with types 1-3, respectively. The diagnostic delay was 23.8 months (range 0-144.6 months) for type 3, followed by 8.6 months (range 1.87-155.8 months) for type 2, and 2.2 months (range 0.47-9.83 months) for type 1, and was statistically different between the disease types.
CONCLUSIONS: Diagnostic delay is common in SMA, and it depends on the disease type. In our cohort, it was greatest for SMA type 3 which is in accordance with the literature. However, the diagnostic delay for patients with SMA type 1 and 2 is considerable. Therefore, it is crucial to reduce the diagnostic delay, especially for SMA type 1, so that the disease-modifying therapy can be initiated in a timely manner.
KEYWORDS: Neuromuscular Disorders, Rare Diseases, Genetics

546. What percentage of patients with Duchene Muscular Dystrophy are potentially treatable with gene therapies?
Passi Gouri (Indore, India) Paharia Manjari

OBJECTIVE: Gene therapies potentially available for children with Duchene Muscular Dystrophy (DMD) are the exon skipping technologies and stop codon read through small molecule like Ataluren. In a small cohort from Central India we evaluated what percentage of children could theoretically be treated with either of these therapies.
METHODS: All children attending our Pediatric Neurology Clinic in the last three years who had undergone genetic testing were included into our study. Results of PCR/ MLPA/ NGS were analysed. Percentage of children who could have benefitted from either exon skipping or Ataluren were collated.

RESULTS: A total of 48 boys mean age 7.7 yrs (range 4-15) fulfilled clinical diagnostic criteria for DMD. The yield of polymerase chain reaction (PCR) was 3/5 (60%) and Multiplex Ligation Probe Amplification (MLPA) was 36/43 (83.7%). Six of 7 who were negative on MLPA, underwent NextGen exome sequencing. Of these 4 were confirmed to have DMD and 2 as limb girdle muscular dystrophy (LGMD). The commonest single exon deletion was 45 and multiexon deletion was 45-49. Patients who were potentially treatable by exon skipping were 23/45 (51.1%) and 1 child had a nonsense mutation amenable to treatment with ataluren.
CONCLUSIONS: In a small cohort of 48 children with Duchene muscular dystrophy 53.3 % were potentially treatable by various gene and pharmacy-gene therapies.
KEYWORDS: Neuromuscular Disorders, Translational/Experimental Therapeutics, Genetics

547. The 7-year progression of proximodistal dysferlinopathy in another Acadian patient
Bourcier Dax (Moncton, New Brunswick, Canada) Bourque Sophie, Mamelona Jean, Brais Bernard, Urtizberea Andoni, Crapoulet Nicolas, Marrero Alier

OBJECTIVE: The two most common phenotypes of dysferlinopathies are Limb-girdle muscular dystrophy (LGMD) type 2B and distal Miyoshi's myopathy (MM). A proximodistal (PD) phenotype, combining features of both LGMD2B and MM, has been proposed to be a standalone phenotype accounting for 6-35% of dysferlinopathies. This is the first report describing dysferlinopathies in the Acadian population from the Canadian Maritimes, the majority of which had a PD phenotype.
METHODS: We compare the clinical phenotypes of ten unpublished cases of dysferlinopathy in Acadian patients, and elaborate on the case of a 19 year-old Acadian. He presented with substantially elevated serum creatine kinase levels at age 13, before the occurrence of rapidly declining distal posterior legs and limb-girdle myopathy during puberty. His disease progression is characterized by seven years of clinical, imaging and laboratory documentation. The absence of dysferlin (Figure 1), pathogenic homozygous DYSF mutations, and two homozygous TTN mutations were found. The parents were 3rd degree cousins and no extended family members were symptomatic.
RESULTS: Similar to previously reported cases of PD dysferlinopathy, our patient showed macrophage infiltration on histology, and a fast disease progression supported by MRI series and clinical observations. The majority of Acadian cases, from three different DYSF mutations, also presented with a PD phenotype. Modifier genes, environmental factors, or other unknown mutations have been proposed to explain phenotypic variability, and our patient had two homozygous mutations in A-band TTN.
CONCLUSIONS: Proximodistal dysferlinopathy should be considered as a rare but plausible diagnosis in Acadian patients presenting with progressive distal and proximal myopathy.
KEYWORDS: Neuromuscular Disorders, Rare Diseases, Genetics

548. Guillain-Barré syndrome (GBS): A Review of Epidemiology, Clinical Findings, and Outcomes at an Academic Children's Hospital
Batley Kaitlin (Dallas, TX, United States) Hynan Linda, Castro Diana

OBJECTIVE: Guillain-Barre syndrome (GBS), an immune-mediated polyneuropathy, is the most common cause of acute flaccid paralysis in children. Our study aimed to identify the

presenting features, management, and outcomes of pediatric patients with GBS at a diverse institution in the United States.
METHODS: This retrospective chart review includes 77 patients diagnosed with GBS.
RESULTS: This study highlights the wide diversity of the U.S., with 33 patients (42.8%) identifying as Hispanic, 28 (36.3%) Caucasian, 11 (14.3%) African American, 2 (2.6%) Indian, and 3 (3.9%) reporting "other."
EMG/NCS was performed in 54 patients, with 35 (64.8%) found to have acute inflammatory demyelinating polyneuropathy (AIDP), consistent with studies that have reported AIDP to be more common in the U.S. and Europe. However, a large number were found to have an axonal variant (12 patients, 22.2%), which may be due to the predominance of Hispanic patients in our study, as AMAN/AMSAN is more prevalent in Latin America.
Patients with an axonal variant were found to have more severe disease, consistent with the literature. This was made evident by the larger proportion of patients with AMAN/AMSAN that lost the ability to ambulate (p=0.04) and had longer hospital admissions (p=0.091). Patients with an axonal variant also had a higher Hughes scores on presentation (p=0.121), at nadir of illness (p=0.009), and on discharge from the hospital (p=0.002).
CONCLUSIONS: This chart review adds to our understanding of patients with GBS in the U.S., with emphasis on the varying presentations and outcomes among different races/ethnicities in this diverse region of the country.
KEYWORDS: Neuromuscular Disorders

549. ACTA1 mutation in a patient with facial and distal muscle weakness
Ryan Conor (Minneapolis, MN, United States) Litchy William, Engel Andrew, Selcen Duygu

OBJECTIVE: *ACTA1* encodes a skeletal and cardiac muscle protein, actin, critical for muscle contraction. We report a case of a patient with chronic weakness with a variant in *ACTA1*.
METHODS: Clinical evaluation, EMG, muscle biopsy, whole exome sequencing.
RESULTS: A 21-year-old woman with symptoms suspicious for congenital myasthenia, had difficulty holding her arms overhead, playing sports, running, performing fine motor tasks and fatigued easily since in her early teens. She had reduced muscle bulk, mild weakness of facial, and distal more than proximal limb muscles, and was hyporeflexic. The wrist and finger extensors were selectively weak. Her father and paternal grandfather had similar symptoms, and were diagnosed with a form of muscular dystrophy. The serum creatine kinase level was normal. The EMG showed myopathic features with no repetitive compound muscle action potentials with a single stimulus and no decrement with 2 Hz repetitive nerve stimulation. A single fiber EMG study was mildly abnormal. A deltoid muscle biopsy showed a nemaline myopathy, associated with type 1 fiber preponderance. Whole exome sequencing revealed a c.197T>G (pI66S) variant in *ACTA1*.
CONCLUSIONS: The patient highlights that the mutations in actin can mimic symptoms and signs of congenital myasthenia or an autosomal dominant distal muscular dystrophy.
KEYWORDS: Neuromuscular Disorders

550. Neurologic Work-up of Infantile Botulism: A 10-year experience
Batley Kaitlin (Dallas, TX, United States) Rhem Brittney, Almatrafi Mohammed, Most Zachary, Zahlanie Yorgo, Wetzel Dawn, Evans Amanda, Hanners Natasha, Castro Diana

OBJECTIVE: Infantile botulism is a rare disease caused by ingestion of *Clostridium botulinum* spores, which produce a toxin that blocks neuromuscular transmission. Initial symptoms are nonspecific, including weakness, hypotonia, poor feeding, cranial nerve deficits, and constipation. Presence of botulinum toxin in stool is the confirmatory test, but the diagnosis is a clinical one based on history and physical exam. EMG/NCS provides supplementary information, typically showing decreased amplitude of motor action potentials and an incremental response to fast repetitive nerve stimulation (RNS).
METHODS: This retrospective study analyzed data of 24 patients treated with botulism immunoglobulin from 2010 to 2019.
RESULTS: The most common finding on nerve conduction testing was reduced CMAP amplitude. Six out of 20 patients had supportive findings on RNS. However, 10 out of 24 patients were found to have sensory abnormalities on EMG/NCS as well. Abnormalities were noted on two out of 13 MRI scans of the spinal cord, one of which showed enhancement of the nerve roots of the cauda equina. This patient also had elevated protein in CSF and EMG/NCS findings concerning for an inflammatory neuropathy.
CONCLUSIONS: This study highlights the neurologic work-up pursued in patients diagnosed with Infantile Botulism over a 10-year period at a large academic institution. Many patients were found to have sensory abnormalities on NCS, which has not been reported previously in the literature. Interestingly, one patient also had imaging and CSF findings consistent with an inflammatory neuropathy, raising the question of a link between the two disorders.
KEYWORDS: Neuromuscular Disorders, Infections/Neuroimmunology

551. A COMPARISON OF PATIENT OUTCOMES IN TWO TYPE 2 SPINAL MUSCULAR ATROPHY (SMA) CHILDREN RECEIVING NUSINERSEN (SPINRAZA) OR ONASEMNOGENE ABEPARVOVEC (ZOLGENSMA)

Lopez-Alberola Robert (Miami, FL, United States) Alfaris Basma

OBJECTIVE: With limited long-term data with either of the two FDA approved treatments for SMA, a comparison of outcomes between these was done.
METHODS: Two age (two year old, 3 months apart), gender (females), and SMA type (Type 2, with 3 copy numbers of SMN2 gene) - matched patients received treatment. Patient 1 received Spinraza starting at 14 months of age, and Patient 2 Zolgensma at 23 months of age. Assessment was done by clinical observation and measuring CHOP-INTEND Scores over an 8 month period.
RESULTS: From a clinical perspective, Patient 1 is now able to scoot, pull to a stand with assistance, and bear weight for 30 seconds, and when held with support can take a few steps. Patient 2 crawls, stands and bears weight independently, and walks with minimal assistance, using a cane for up to 20 minutes. CHOP-INTEND scores improved from baseline in both patients over time, with no regression, and continued improvement noted in Patient 2, as compared to Patient 1 (Table 1.).
CONCLUSIONS: This data represents the first head to head study of the two approved SMA treatments. Although both patients improved from baseline with motor gains, Patient 1 plateaued over time with no further gains, whereas patient 2 continued to progress. The data suggests superior efficacy of gene therapy, targeting the diseases' underlying pathology of the SMN1 gene, over the other treatment, with alternate splicing of the SMN2 gene. These results also support the use of gene therapy in older SMA patients.
KEYWORDS: Neuromuscular Disorders, Genetics

552. The Cure SMA Annual Community Update Survey: Results from the 2020 survey on the SMAIS and ACEND

Belter Lisa (Elk Grove Village, IL, United States) Cruz Rosángel, Lewin Foster, Jarecki Jill

OBJECTIVE: The purpose of this study is to present results from the new SMA Independence Scale (SMAIS) and the transfer and mobility modules of the Assessment of Caregiver Experience with Neuromuscular Disease (ACEND) using the Cure SMA Annual Community Update Survey.
METHODS: Cure SMA launched their Annual Community Update Survey in early April 2020. The survey was emailed to over 4,000 Cure SMA database members affected with SMA and their caregivers. The survey consisted of several modules, including modules on demographics, health care, unmet needs, and quality of life. Individuals affected with SMA (18 years and older) were invited to complete the SMAIS instrument and all caregivers were invited to complete the transfer and mobility modules of the ACEND. The SMAIS evaluates patients' activities of daily living and independence. The ACEND is a disease-specific measure used to quantify the experience of caregivers of children with a neuromuscular disease.
RESULTS: Data will be analyzed for both affected individuals who completed the SMAIS and caregivers who completed the ACEND. Descriptive statistics will be used to summarize the SMAIS and ACEND results for the entire cohort and will also be stratified by SMA type, current motor function, and by health status (including ventilation use and scoliosis surgery).
CONCLUSIONS: The results of this study will quantitatively describe the experience and impact of living with SMA on both the affected individuals and their caregivers. These results can highlight the need to develop SMA support programs and gauge potential improvements in caregiver QOL following SMA treatments.
KEYWORDS: Neuromuscular Disorders

553. Congenital myopathy with fiber-type disproportion in a patient with a de novo heterozygous p.Pro2195Leu mutation in RYR1

Coyne Liam (Syracuse, NY, United States) El Dokla Ahmed, Pellegrino Joan, Sakonju Ai

OBJECTIVE: Mutations in ryanodine receptor 1 (*RYR1*) are the most common monogenic cause of congenital myopathy. One subtype, congenital fiber-type disproportion (CFTD), has been described as a recessive RYR1-related myopathy. It is unknown whether RYR1 can dominantly cause CFTD. Here, we present a patient with CFTD and RYR1 p.Pro2195Leu mutation heterozygosity.
METHODS: Review of history, laboratory, imaging, and genetic studies.
RESULTS: The 16-year-old underweight female presents with weakness and physical exam findings notable for proximal muscle weakness, decreased muscle bulk, and hyporeflexia. Her pediatric history is notable for congenital hypotonia, motor delay, failure to thrive, and corrected scoliosis. At 6 years old, initial investigation revealed minimal elevation in blood lactate, glycine and alanine; unremarkable mitochondrial studies; unrevealing mitochondrial genome sequencing; predominant and small type 1 fibers on muscle biopsy indicating fiber-type size disproportion; and heterozygosity for two autosomal recessive mutations on whole-exome sequencing: *TYMP* c.929-6_929-3delCCGC (predicted pathogenic, mitochondrial neurogastrointestinal encephalopathy syndrome), and *FLCN* c.2602A>G (associated with

myofibrillar myopathy). The *FLCN* mutation was paternally inherited and her father is asymptomatic. Whole-exome sequencing also revealed a heterozygous, *de novo* c.6584C>T (p.Pro2195Leu) mutation in *RYR1*. Recent neuromuscular gene panel testing confirmed this *RYR1* variant of uncertain significance, which was previously reported in a heterozygous patient with unexplained CFTD.
CONCLUSIONS: Two patients with heterozygous RYR1 p.Pro2195Leu mutation have CFTD without another identifiable cause of myopathy. This suggests p.Pro2195Leu is a novel dominant cause of CFTD, thus broadening the clinical spectrum of dominant RYR1-related myopathies to include CFTD, congenital hypotonia, failure to thrive, and scoliosis.
KEYWORDS: Neuromuscular Disorders, Genetics, Rare Diseases

554. Two de novel mutations of COL6A2 in Ullrich congenital muscular dystrophy: a Chinese family report
Hu Jun (Fuzhou, China) Chen Yanhui

OBJECTIVE: Ullrich congenital muscular dystrophy (UCMD) is one of the Collagen-VI-related myopathies caused by mutations of *COL6A1*, *COL6A2*, and *COL6A3* genes. UCMD is characterized by muscle weakness, distal joint hyperlaxity, proximal joint contracture, and progressive respiratory failure. There is no cure for UCMD. The report is to show early diagnosis, genetic counseling, and prenatal diagnosis are important for the family with a child of UCMD who wants to give birth again.
METHODS: A Chinese family (two brothers and a fetus) suffering from UCMD underwent neurological examinations and molecular genetic analyses by whole-exome sequencing. Muscle pathology of quadriceps femoris from the younger brother was performed too.
RESULTS: The brothers had the typical manifestations of the early-severe subtype with UCMD: never walk independently, torticollis, scoliosis, proximal joint contracture, distal joint hyperextension, right hip joint dislocation, and calcaneal protuberance (figure 1). They carried two *de novel* mutations of *CO6LA2* (c.1353 (exon16)_c.1354 (exon16) insC, p.Arg453ProfsTer42 / c.2105 (exon26) G>A, p.Trp702Ter). One was frameshift, the other was nonsense. Both the mutations affected protein pathogenicity. The fetus also carried the mutations confirming in the amniotic fluid (figure 2 A, B). The muscle pathology was consistent with myogenic damage and regarded as collagenopathy (figure 2 C, D). A similar misfortune is avoided again by the clear diagnosis, genetic counseling and prenatal diagnosis in the family.
CONCLUSIONS: This study demonstrates once again the importance of early diagnosis, genetic counseling, and prenatal diagnosis for UCMD. It enriches the UCMD gene pool and provides a better understanding of the disease in China.
KEYWORDS: Neuromuscular Disorders, Genetics, Rare Diseases

555. Successful remission in a female adolescent with anti-MuSK antibody-positive myasthenia gravis with immune suppressants
Yu Jeesuk (Cheonan, Republic of Korea) Hwang Jeongju

OBJECTIVE: To report a rare case of myasthenia gravis with MuSK antibody who developed in a female adolescent and showed successful remiission after treatment for 2 years
METHODS: Clinical features and anti MuSK antibody levels were reviewed. Anti MuSK antibody was checekd based on radioimmunoassay.

RESULTS: Myasthenia gravis (MG) is a neuromuscular disorder characterized by muscle weakness with diurnal fluctuation. 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. A 13-year-old girl was referred to the pediatric neurologic clinic 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 revealed positive response, and repetitive nerve stimulation test showed a decrement of compound muscle action potential. Serum creatine kinase was normal, and anti-AChR antibody was negative. However, anti-MuSK antibody was positive (65.1 nmol/L, reference value ≤ 0.02). Initially, pyridostigmine was prescribed, and steroid was added at day 8, and then azathioprine at day 21. She showed complete recovery at day 28 on medication. During follow-up, she did not show any exacerbation of the symptoms, therefore medication could de tapered off after 2 year of treatment. Recent titer of MuSK antibody was 1.32nmol/L.
CONCLUSIONS: We report a sccessful remission in a 13-year-old-girl wth anti-MuSK antibody-positive myasthenia gravis with immune suppressants.
KEYWORDS: Neuromuscular Disorders, Rare Diseases

556. Clinical Spectrum of Pediatric Myasthenia in Bangladesh: Analysis of 40 patients.
Debnath Bithi (Dhaka, Bangladesh) Hussain Mohammad, Mian Mohammad, Saha Narayan, Chowdhury Rajib

OBJECTIVE: To analyze the clinical characteristics, types, diagnostic and treatment trends of pediatric myasthenia gravis in Bangladesh
METHODS: This prospective study was carried out in the National Institute of Neurosciences and Hospital, Dhaka, Bangladesh from January 2017 to December 2019. Children <18 years with ≥1 of the following were included: (1) fluctuating ptosis or extraocular weakness, (2) skeletal muscle weakness or fatigue, and (3) any of: positive Acetylcholine receptor (AChR) antibodies, abnormal repetitive nerve stimulation test (RNST) or response to acetylcholinesterase inhibitor. Forty patients met the inclusion criteria and were classified according to Myasthenia Gravis Foundation of America (MGFA).
RESULTS: Among 40 patients, 52.5% had ocular (class 1), 42.5% had generalized myasthenia gravis (class II-35%, III-5%, IV-2.5%) and 5% congenital myasthenic syndrome. Ptosis (85%) was the commonest presentation. The mean age of presentation was 12.32± 5.26 years (range 2-<18 years) and most (60%) of the patients were >12 years of age. Female to male ratio was 1.35:1. AChR antibody was positive in 56%. RNST was abnormal in 58.33% cases (p value was significant for generalized MG). Thymoma was found in 5% cases. 45% patients needed prednisolone in addition to pyridostigmine. Azathioprine was given in 7.5% cases. Relapse occurred in 22.5% patients, among whom one patient needed ventilatory support.
CONCLUSIONS: Ocular MG was more common with ptosis being the commonest presentation. More than half of the patients had seropositivity and abnormal RNS test. Most showed improvement with pyridostigmine and steroid. Thymoma was rare and relapse was noted in more than one fifth of patients.
KEYWORDS: Neuromuscular Disorders

NEUROREHABILITATION

557. Plasticity in the developing brain: neurophysiological basis for motor reorganization in a clinical pediatric cohort

Batschelett Mitchell (Memphis, TN, United States) Schiller Katherine, Gibbs Savannah, Holder Christen, Holcombe Billy, Wheless James, Narayana Shalini

OBJECTIVE: Plasticity of the developing brain may be observed following motor cortex injury (MCI). Timing of injury, size, etiology, and location influence either the acquisition of motor representation to the contralesioinal hemisphere – interhemispheric reorganization (IEHR), or the maintenance of motor representation within the lesioned hemisphere – intrahemispheric reorganization (IAHR). IEHR most likely occurs following injury before 2 years of age, however injury etiology's role is understudied. We hypothesized that IEHR would be more prevalent following traumatic injuries, as opposed to developmental disorders, and that corticomotor representation would be shared following IEHR.
METHODS: We retrospectively examined 55 patients with reorganized motor maps found through the use of transcranial magnetic stimulation (TMS). Hand motor cortex center of gravity (COG) was calculated, and the distance between normal and reorganized COGs was measured.
RESULTS: COG distances in patients with IEHR were significantly shorter ($p<0.001$) than those with IAHR. A significant effect of injury etiology on motor reorganization ($p<0.001$), independent of timing and age of injury, was found, as IEHR was more likely to result following traumatic injuries (Table 1; Figure 1).
CONCLUSIONS: The results provide evidence of shared corticomotor representation in the case of IEHR, implying that IEHR proliferates existing ipsilateral pathways through axonal sprouting within an action-dependent model of corticomotor development. The nature of developmental disorders to resist IHER is also implied. Novel information obtained with TMS regarding developmental motor plasticity is demonstrated. These data aid in understanding basic reorganization principles, facilitating better and more useful therapeutic techniques to improve functional recovery following MCI.
KEYWORDS: Neurorehabilitation, Neuroimaging, Epilepsy

558. To evaluate efficacy of Sensory Integration Therapy(SIT) reinforced with standard therapy in improving gross motor function in spastic cerebral palsy children aged >3 to 12 years with GMFM level I-III with sensory processing abnormalities

Sirolia Vivek (New Delhi, India) Singhal Mita, Singh U, Jauhari Prashant, Chakrabarty Biswaroop, Sharma Shobha, Khan Sanjeeda, Pandey R.M., Gulati Sheffali

OBJECTIVE: To compare the efficacy of Sensory Integration therapy as an adjunct to Standard therapy with standard therapy alone in improving motor skills as per GMFM 88(Five component) score.
METHODS: This Randomized control open labeled trial was conducted at a tertiary care center in New Delhi (India) between July 2018 to August 2019.
RESULTS: Total of 60 subjects were enrolled (30 in each arm). Control arm received only standard therapy where as Intervention arm received both standard and individualized sensory integration therapy.Mean GMFM-88 scores were compared after 12 weeks. 1. Significant improvement in total GMFM scores was seen post intervention in both the groups, though the

change was higher in the intervention group compared to standard group with a mean difference of -5.0(-6.2, -3.9) in intervention group and -3.5(-4.3,-2.6) in control group 2. While comparing in between two groups,there was no significant improvement in the total GMFM scores in the intervention group as compared to standard group (p- value- 0.985 and EF(95%CI): -0.1 (-8.5,8.3) 3. The effect size was 1.4(-0.1, 2.9) and p- value 0.074 was non significant between the groups at the end of 12 weeks of intervention after adjusting GMFCS level and Baseline scores.
CONCLUSIONS: Sensory integration therapy along with standard therapy when compared with standard therapy alone does not cause significant improvement in gross motor skills. Further studies are needed to ensure and beyond --+
KEYWORDS: Neurorehabilitation, Movement Disorders (including Cerebral Palsy), Translational/Experimental Therapeutics

559. Design and Implementation of a US Pediatric Rehabilitation Resource Center
Lo Warren (Columbus, OH, United States) DeLuca Stephanie, Heathcock Jill, Darragh Amy, Ramey Craig, Ramey Sharon

OBJECTIVE: There is a shortage of high impact, adequately powered trials in pediatric medical rehabilitation (PMR) despite the need for efficacious and coordinated treatments. Unique factors about child development and childhood disabilities complicate the design, conduct, and analysis of PMR clinical trials. To increase the quality and impact of these trials, we must strengthen the research competencies of pediatric rehabilitation scientists and clinicians. This may include attracting new scientists and clinicians with relevant expertise to engage in PMR research.
METHODS: We obtained five year support for a US-based Pediatric Rehabilitation Resource Center to 1) provide courses, workshops, webinars, and demonstrations related to the design, conduct, analysis, and reporting of high-quality, high-impact PMR clinical trials - including complex, multicomponent, and multiphase treatments; 2) support interdisciplinary research collaborations in multi-site clinical trials; 3) develop measurement techniques and advance our understanding of neurobiological mechanisms and biobehavioral outcomes in PMR; 4) fund pilot studies to yield preliminary data for future PMR clinical trials; and 5) to disseminate expertise in PMR
RESULTS: NA
CONCLUSIONS: We have developed an innovative national infrastructure center based at Virginia Tech Univ with partners at Ohio State University and Nationwide Children's Hospital to expand and strengthen clinical rehabilitation research in children. The center will use the members' research expertise in developmental psychology, physical therapy, occupational therapy, neurology, biostatistics, and neuroscience to support innovation and discovery in PMR research with an emphasis upon cerebral palsy and other pediatric neuromotor disorders. Long-term we expect to increase the quality and impact of PMR clinical trials.
KEYWORDS: Neurorehabilitation, Movement Disorders (including Cerebral Palsy), Stroke (including other Vascular Disorders)

560. Developmental Status of Institutionalized Children: A Preliminary Study
Suh Jee Hyun (Seongnam-si, Republic of Korea)

OBJECTIVE: The institutional children are well known to suffer from structural neglect. We investigated the developmental status of the institutionalized children by Korean Denver II developmental screening test (K-DDST II) to identify the developmental problems.
METHODS: A retrospective study was conducted in eleven institutionalized children in one orphanage. Children were screened for the developmental status by K-DDST-II. Children were measured for height, weight, and head circumference to determine their physical development. In this study, we calculated the equivalent age of each items of K-DDST-II. The developmental index was calculated by dividing the equivalent age by the actual age.
RESULTS: In this study, the average age of the eleven children was 30.09 months. 9.09% of the children had delayed the social development, 45.45% delayed the development of fine motor, 27.27% delayed the language development, and 27.27% delayed the gross motor development. In this study, the developmental index of personal-social category was 106.65%, which was better than average. Instead, the developmental index of fine motor was 75.76% and the risk of development delay was the highest.
CONCLUSIONS: The personal-social category of the K-DDST-II are related to activity of daily living (ADL). Institutionalized children had more opportunities for ADL training compared with the home-reared children. However, the fine motor category was the most delayed category, which had fewer educational opportunity in institutionalized children. The institutional child should be given more opportunities for fine motor training. In addition, it is necessary to consider the combination of appropriate assessment tools to properly assess the institutionalized children.
KEYWORDS: Neurorehabilitation, Rare Diseases

561. Appropriate Intensity and Timing of Physical Therapy in Children with Cerebral Palsy

Suh Jee Hyun (Seongnam-si, Republic of Korea)

OBJECTIVE: To determine the proper intensity of physical therapy (PT) and the timing to reduction of the intensity of PT for improvement of physical function of children with cerebral palsy (CP).
METHODS: This study is a retrospective study. The 24 children with CP were conducted short term intensive PT. The CP children were divided into five groups (under 12mo, from 12mo to 24mo, from 24mo to 36mo, from 36mo to 48mo, over 48mo) for evaluation of the proper timing to reduction of the intensity of PT. The GMFM-88 scores at before, the beginning and the end of the intensive PT were evaluated. And the difference of the GMFM score between the two time points were evaluated.
RESULTS: There was significant difference in total GMFM score and GMFM score of A, B, C, D and E dimensions compared with the beginning and the end of the intensive PT. When comparing the five age groups, the difference of the total GMFM scores significantly different between the groups. And the difference of total GMFM was significantly different between under 48months and over 48months.
CONCLUSIONS: The intensive PT up to 48 months would be the good treatment option for improvement of gross motor function in CP children.
KEYWORDS: Neurorehabilitation, Movement Disorders (including Cerebral Palsy)

562. The Complex Relationship between Pediatric Sleep, Pain, and Neurodevelopment

Morris Erin (Minneapolis, MN, United States) Wang Sonya

OBJECTIVE: To examine current evidence of the bidirectional relationship between neonatal/pediatric sleep and pain and its impact on neurodevelopment. This review serves as a critical examination of the literature and the needs for future research on sleep and pain in both the outpatient and inpatient settings.
METHODS: The Pubmed online database was queried from January 1, 1960 to March 1, 2020. This search produced 664 articles applicable to pain and sleep in the pediatric population. In all, 600 abstracts were attainable and screened. Of these, 104 articles were utilized for this review.
RESULTS: In the outpatient setting, the effect of sleep on subsequent pain, both next day pain and development of chronic pain, appears to be greater than the effect pain on sleep. Disrupted sleep increases nociceptive sensitivity in the short term which increases risk of long term chronic pain. Inpatient sleep in neonatal and pediatric patients is significantly fragmented, particularly in the critical care setting and especially with pharmacologic interventions for sedation and pain. Overall, better sleep in both settings, especially preserved REM sleep, is important for recovery and improved neurodevelopment after discharge.
CONCLUSIONS: The relationship between sleep and pain is complex, especially during critical periods of pediatric neurodevelopment where alterations to a normal sleep structure can have a lifelong impact. Further research is needed into the complex alterations of sleep in chronic pain conditions as well as treatments to improve sleep in both the inpatient and outpatient pediatric settings.
KEYWORDS: Neurorehabilitation

NEUROSCIENCE

563. Cytokine-induced differentiation of hematopoietic cells into microglia-like cells in vitro

Igarashi Ayuko (Tokyo, Japan) Sakuma Hiroshi, Hayashi Masaharu, Noto Daisuke, Miyake Sachiko, Okumura Akihisa, Shimizu Toshiaki

OBJECTIVE: Microglia are the immune cells of the central nervous system. Several in vitro methods have been reported to induce the formation of microglia from hematopoietic cells, using granulocyte-macrophage colony stimulating factor and interleukin-34 (IL-34). However, the phenotype of these cells has not been fully characterized. The objective of the present study was to clarify the differential roles of colony-stimulating factors and transforming growth factor-b (TGF-b) in the differentiation of hematopoietic cells to microglia-like cells.
METHODS: Murine bone marrow lineage-negative (BMLN) cells were co-cultured with astrocytes for 1 week in the presence or absence of colony-stimulating factors. Surface markers for microglia were examined by flow cytometry.
RESULTS: BMLN cells co-cultured with astrocytes developed into microglia-like cells (CD11b+ CD45lo F4/80lo CX3CR1hi), whose expression pattern of surface markers was distinct from bone marrow-derived macrophages (CD11b+ CD45hi F4/80hi CX3CR1lo). Morphologically, microglia-like cells were found to possess actively extending and retracting long branched processes. Additionally, these cells were found to proliferate significantly during differentiation and this was dependent on colony-stimulating factor 1 receptor signaling.

Macrophage colony-stimulating factor or granulocyte-macrophage colony-stimulating factor induced the differentiation of BMLN cells into CD11bhi CD45hi cells that were different from microglia. In contrast, IL-34 induced differentiation into CD11b+ CD45lo microglia-like cells with relatively higher CX3CR1 expression. Although TGF-b failed to induce the formation of microglia-like cells with process-bearing morphology, BMLN cells cultured with both IL-34 and TGF-b developed into microglia-like cells that had finely branched processes and lower F4/80 expression.
CONCLUSIONS: IL-34 and TGF-b collectively promote the development of microglia-like cells from hematopoietic cells.
KEYWORDS: Neuroscience, Infections/Neuroimmunology, Cognitive/Behavioral Disorders (including Autism)

564. Measures of cortical inhibition by transcranial magnetic stimulation (TMS) coupled with deltoid electromyography.
Liu Jingjing (Boston, MA, United States) Tsuboyama Melissa, Kaye Harper, Jannati Ali, Pasichnik Alisa, DiBacco Melissa, Pearl Phillip, Rotenberg Alexander

OBJECTIVE: LICI is a noninvasive measure of cortical excitation: inhibition ratio (E:I) obtained by ppTMS typically obtained from distal muscles. However, LICI data from proximal muscles are lacking. We aim to compare LICI obtained from deltoid versus APB and evaluate the effects of a range of ISI and stimulus intensities on deltoid LICI.
METHODS: Five healthy individuals underwent ppTMS at supra-threshold intensities (120% or 150%rMT) with an ISI of 100 or 200 ms. MEPs were recorded using sEMG electrodes placed over bilateral APB and deltoid muscles. 20 trials were performed for each stimulus intensity and ISI combination. LICI was calculated using logarithmic ratios of MEPs produced by the first and second TMS pulses.
RESULTS: Although paired-pulse inhibition was expected, some pairs of pulses corresponded to MEP facilitation in both muscle groups. 200 ms ISI was associated with more reliable facilitation in the deltoids than 100 ms ISI (40% vs. 3.2% of sessions, $p<0.001$), but the rate of facilitation did not differ in APB as a function of ISI (12.9% vs. 6.3%, $p=0.426$). The likelihood of paired-pulse facilitation was greater at 150% rMT stimulation intensity.
CONCLUSIONS: Different ISI and stimulus intensities can affect cortical E:I, both in proximal and distal muscles. To the best of our knowledge, this is the first report demonstrating LICI measurements in proximal muscles, and showing that longer ISI may result in a facilitory response in deltoid but not APB, perhaps due to different interneuron excitatory and inhibitory function or more complex neural network affection between proximal and distal muscles.
KEYWORDS: Neuroscience

565. Elevated Central Apnea Hypopnea Index Demonstrates Poor Positive Predictive Value for Abnormal Brainstem Imaging Results in Pediatric Patients
Stowe Robert (Philadelphia, PA, United States) Andronikou Savvas, Tapia Ignacio

OBJECTIVE: The evaluation of an elevated central apnea hypopnea index (CAHI) or prolonged (≥20 seconds) central apnea in pediatric patients typically includes brain imaging with emphasis on possible brainstem pathology. However, there is little evidence guiding the threshold of polysomnographic variables that will accurately predict abnormal and actionable

imaging results. We sought to evaluate if additional polysomnogram variables may predict brainstem pathology.
METHODS: A 10-year retrospective review of patients 0-18 years old who received a brain MRI for central sleep apnea (CSA) diagnosed via polysomnography was performed. Demographics, history, polysomnogram variables, MRI results, and treatments were compared.
RESULTS: Seventy-three patients (67.1% male) were included. Median age was 5.0 (interquartile range [IQR] 2.3-7.9) years. Median CAHI was 5.6 (IQR 3.1-9.6) events/hour. Most patients had normal (43.8%) or incidental, benign (28.8%) MRI findings; 21.9% had non-contributory brain abnormalities. Six patients (8.2%) were found to have brainstem pathology. These patients had a median CAHI of 15.2 (IQR 9.9-33.1) and two-thirds demonstrated hypoventilation. All other patients had a median CAHI of 5.5 (IQR 3.0-8.3); 10.4% demonstrated hypoventilation. Although positive predictive values were low, the negative predictive values of CAHI > 9 and hypoventilation for brainstem pathology were 98.1% and 96.8%, respectively.
CONCLUSIONS: Most patients with CSA have non-diagnostic brain MRIs. Our small cohort of patients with brainstem pathology suggests they may have higher CAHI and a greater incidence of hypoventilation. Patients not meeting thresholds of CAHI > 9 and/or hypoventilation may not require brain imaging whereas those who meet such marks may benefit from referral for brain imaging.
KEYWORDS: Neuroscience, Neuroimaging

566. Dissociable systems for recognizing places and navigating through them: causal and developmental evidence.
Wahab Stephanie (Alpharetta, GA, United States) Kamps Frederik, Radwan Sama, Dilks Daniel

OBJECTIVE: Recent fMRI evidence suggests that human visual place processing is supported by two functionally distinct systems: one for “visually-guided navigation”, including the occipital place area (OPA), and one for “scene categorization” (e.g., recognizing a kitchen), including the parahippocampal place area (PPA). It is unknown, however, whether these systems arise along differential timelines in typical development and whether they are causally dissociable. We addressed these questions by testing navigation and categorization abilities in typically developing children and adults with Williams syndrome (WS), a genetic disorder involving cortical thinning of the OPA.
METHODS: Participants performed a “categorization task” and a “navigation task” while viewing images of places. During the categorization task, participants imagined standing in a room, and indicated whether they were in a bedroom, kitchen, or living room. During the navigation task, participants imagined walking through the room and indicated whether they could leave through a door on the left, center, or right wall by following a path on the floor that only connects to one of the three doors.
RESULTS: We found that i) navigation and categorization develop along differential timelines in typical development, with the navigation maturing more slowly across childhood than the categorization system; and ii) that WS adults are selectively impaired in navigation relative to mental-age matched controls (i.e., typical developing 7 year olds).
CONCLUSIONS: Taken together, our results provide the first developmental and causal evidence for dissociable visually-guided navigation and scene categorization systems, and further suggest that this distinction may have a genetic basis.

KEYWORDS: Neuroscience, Rare Diseases, Cognitive/Behavioral Disorders (includeing Autism)

567. ASSESSMENT OF PROGNOSTIC FACTORS AND NEURODEVELOPMENTAL OUTCOMES OF FILIPINO CHILDREN AFTER NEONATAL SEIZURES SEEN AT THE PCMC NEURODEVELOPMENTAL PEDIATRICS OPD

Jao Bernice Louise (Quezon City, Philippines) Lopez Annelyn Fatima, Avendaño Ermenilda

OBJECTIVE: To determine the prognostic indicators and neurodevelopmental outcomes of Filipino children age 3 – 7 years and 11 months who had neonatal seizure, seen at the Philippine Children's Medical Center Neurodevelopmental Pediatrics Clinic.
METHODS: A retrospective cohort analysis was conducted among 80 children age 3 – 7 years and 11 months with clinical seizures during neonatal period and seen at the Neurodevelopmental Pediatrics Clinic from May 2018 to March 2019. Chart reviews and parent interviews were conducted. Patients were evaluated using the Battelle Developmental Inventory Scale, 2nd edition. The data was analyzed using Stata Version 14. Frequencies and percentages were used for categorical data. Simple and multiple logistic regressions determined the prognostic factors for adverse neurodevelopmental outcomes.
RESULTS: Out of the 80 patients included in the study, 91% had an adverse overall outcome (cerebral palsy, epilepsy, sensory impairment, global developmental delay). Infection was the most common etiology followed by hypoxic ischemic encephalopathy. Place of delivery, neuroimaging, EEG findings, and type of seizure were potential predictors of overall outcome. However, using multiple logistic regression, only EEG findings was found as a significant predictor of overall outcome. Children with at least 5 risk factors are 4.75 times more likely to have an adverse overall outcome.
CONCLUSIONS: Valuable information regarding the neurodevelopmental outcomes of children with neonatal seizure can be ascertained from the various prognostic indicators. Children with more risk factors have an adverse overall outcome. Early detection of infants at risk for an adverse neurodevelopmental outcome offers the opportunity for intervention at a young age.
KEYWORDS: Neuroscience, Cognitive/Behavioral Disorders (including Autism), Epilepsy

568. Subependymal nodules in Tuberous Sclerosis: Changes in lesions remote to the Foramen of Monro

Cooper Yasmeen (Cambridge, United Kingdom) Cross Justin, Parker Alasdair

OBJECTIVE: Tuberous sclerosis complex (TSC) patients often have periventricular subependymal nodules (SEN) identified on MRI. The growth potential of SENs near the Foramen of Monro (FoM) is well described. Previous research described no growth potential in SENs remote to the FoM (remote SENs).
METHODS: We retrospectively reviewed brain MRIs of children from our regional paediatric TS clinic, covering 4.6 million children. We identified children with remote SENs >6mm, and a minimum of 4 years between MRIs.
RESULTS: 14 children had a 4-year follow-up; 3/14 had remote SENs. Two didn't grow over 8-10 years follow-up. One showed progression: the first scan showed a subtle signal change in the right caudate head but no clear lesion. 6 years later, a discrete 8.3x7.3mm lesion was visible. 2

years subsequently, the lesion was 8.3x5.9mm. Other SENs demonstrated a variation in size of 4mm across sequential scans, with no net growth.
CONCLUSIONS: The variation in size shows the effect of different MRI protocols/ slice thickness and orientation in some children. In others, involution or growth were demonstrated. 2019 Delphi consensus guidelines on TS management recommend rescanning asymptomatic TS patients without SEN >10mm every 1-3 years until the age of 25, and then to stop. Most remote SENs do not grow, but change can occur. There is insufficient evidence to assume that all remote SENs will never require intervention. We recommend further research with follow-up of a cohort of TSC patients with remote SENs over at least 15 years until they are over 25 years old.
KEYWORDS: Neuroscience, Neuroimaging, Rare Diseases

569. Brachial Plexus Birth Injury Natural History: A Single Center Study
Files Helen (Memphis, TN, United States) Caron Elena

OBJECTIVE: Evaluate the natural history of brachial plexus birth injury (BPBI) within the multidisciplinary Le Bonheur Children's Hospital BPBI clinic. Goals of this project were: 1. Assess the natural history of BPBI using the AMS (Active Movement Scale), 2. Assess what/if any demographic factors are associated with BPBI outcomes, 3. Assess what treatment(s) result in higher AMS scores, within a single center.
METHODS: 1: Obtain AMS scores from patient's charts and compare AMS scores at individually prescribed intervals (1 and 6 months of age). 2: Obtain demographic information from clinic notes and identify factors influencing outcome 3: Obtain treatment information including surgery, rehabilitation and botulinum toxin and compare information to others with similar localization and AMS scores before intervention
RESULTS: Results from about 55 infants and children will be analyzed by August 2020. Literature review would predict more than half the children would experience spontaneous recovery within the first-year of life. We also expect that those children who require neurosurgery at 3 - 6 months of age or orthopedic surgery after 1 year of age to show greater AMS scores than those receiving Physical Therapy alone.
CONCLUSIONS: From this study, we hope to concur with or refute data regarding brachial plexus injuries that have been reported in the literature and to uncover ways in which to improve Le Bonheur's BPBI clinic outcomes.
KEYWORDS: Neuroscience, Trauma, Neurorehabilitation

570. A Survey of EEG Services in Sub-Saharan Africa
Kander Veena (Cape Town, South Africa) Wilmshurst Jo

OBJECTIVE: To investigate EEG services in SSA and the need for paediatric EEG training.
METHODS: A survey of EEG services in SSA was circulated (June-December 2019), to clinicians who care for paediatric neurology patients (n=305 participants; 35 African countries). Ethical approval from UCT, Cape Town, South Africa (481/2018).
RESULTS: 73/305 (24%) surveys were adequately completed (figure 1). Respondent's information is seen in Figure 2. 66% (48/73) had access to a neurologist. In 71% (34/48) neurologists were managing children and adult, and 25% only children. Where there was no neurologist (25/73) children with epilepsy were seen by a range of medical personnel. EEG waiting times ranged from under a week to 6 months. Only 3% performed over 1000 EEG

studies a year whilst 85% performed under 500. 30% of EEG technicians were informally trained, 44% formally trained and 12% both. EEG studies were performed by a diverse group. EEGs were read by a variety of personnel (paediatric and adult neurologists; EEG technicians; psychiatrists. 7% were outsourced. 27% had > 1 year of paediatric EEG training and 44% under a year. 77% supported apprenticeship training.
CONCLUSIONS: There is a great need to strengthen EEG services for children in SSA. Also, to identify viable training curriculums which are innovative, both in the models of training used, and the health care practitioners recruited to train.
KEYWORDS: Neuroscience, Epilepsy, Teaching of Child Neurology

571. Formation and Synaptic Properties of the Feedback Circuit Connecting Thalamic Reticular Nucleus and Dorsal Geniculate Nucleus in Mice
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OBJECTIVE: The inhibitory feedback loop connecting thalamic reticular nucleus (TRN) and dorsal lateral geniculate nucleus (dLGN) play an important role in regulating thalamocortical activity, modulating sensory processing and mediating some pathological rhythms including those of absence epilepsy. Here we examine when and how these circuits arise.
METHODS: We employed transgenic mice to visualize when inputs arrive and optogenetics to assess when functional patterns of connectivity emerge. Using confocal microscopy, we examined multiple coronal sections across multiple early-postnatal ages to determine when projections arrived in their target nucleus. By combining optogenetics with in vitro whole cell patch clamp physiology we studied when these synapses became functional and their maturation across early postnatal life.
RESULTS: TRN terminals arrive in dLGN at early postnatal ages and span the entire nucleus by the end of the first postnatal week. In TRN, thalamocortical terminals appear during the second postnatal week and steadily increase until the third week. Postsynaptic activity in both circuits is initially weak, of low amplitude and unable to follow repeated stimuli at rates >5Hz. However, by the third postnatal week responses are of large amplitude and can follow high rates (>50Hz) of stimuli.
CONCLUSIONS: Together, these data suggest that the reciprocal connections between dLGN and TRN develop in a coordinated manner. The maturation of postsynaptic responses in these circuits coincides with the maturation of patterns in cortical activity highlighting the importance of this intrathalamic circuit for thalamocortical sensory processing as well as the generation of some cortical rhythms.
KEYWORDS: Neuroscience, Neonatal & Fetal Neurology, Epilepsy

572. Development and validation of ICSD-3 based screening questionnaire with overnight PSG for sleep disorders in children and adolescents: a community and hospital based study
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OBJECTIVE: The objective of the study was to develop a screening questionnaire based on ICSD-3 for sleep disorders in children and adolescents and validate it with overnight PSG.
METHODS: *Development of the questionnaire*: A questionnaire was developed in English and Hindi and content validated by consensus of 5 pediatric specialists (3 neurologists, 1

endocrinologist and 1 pulmonologist), 1 adult neurologist, 1 oto-rhino-laryngologist and 1 biostatistician. *Study population*: Respondents of the questionnaire were parents of children and adolescents, aged 2-18 years, recruited from a public school and a tertiary care teaching hospital in north India consisting of normal and diseased (cerebral palsy, asthma, Duchenne muscular dystrophy and spinal muscular atrophy) subjects. *Overnight PSG and clinical evaluation*: A subset of subjects with either present or absent sleep disorders on questionnaire underwent overnight PSG and detailed clinical evaluation (blinded to the outcome of the questionnaire) within 4 weeks of applying the questionnaire.
RESULTS: The questionnaire had 36 questions, of which 33 had binary (yes/no) responses, the other 3 having a single phrase response. Overall 750 (559 normal and 191 diseased) completely filled questionnaires were obtained (951 approached) and 100 cases (68 positive and 32 negative on questionnaire) underwent overnight PSG and clinical evaluation (103 approached).
The Cronbach α was 0.8. The sensitivity, specificity, positive and negative predictive value against combination of overnight PSG and clinical evaluation were 84.21%, 83.33%, 94.11% and 62.5% respectively.
CONCLUSIONS: The developed screening questionnaire has reliable psychometric properties. Further studies should be planned for individual subtypes of sleep disorders.
KEYWORDS: Neuroscience

573. Reference values for opening pressure of cerebrospinal fluid in the pediatric population

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OBJECTIVE: To determine the reference intervals for opening pressure (OP) of the lumbar cerebrospinal fluid (CSF) in children in a latin american population.
METHODS: Ambispective cross-sectional study. Lumbar punctures (LP) performed by the neuropediatrics unit in a high-level pediatric hospital between February 2017 and January 2020 were included. Patients with diagnoses associated with increased OP and users of modifying drugs were excluded. The data were analyzed with Normality tests and parametric statistics were performed.
RESULTS: 151 LP were included in patients from 2 months to 17 years, 76 were female (50,33%), with an average age of 3.1 years. The mean OP was 19.56 cm H2O (SD 7.76 cm, 95% CI 18.31-20.81), with a pressure range between 2 and 41.5 cm. Those younger than 10 years had lower OP, mean 18.55 cm (SD +/-6.80 cm, 95% CI 17.27-19.83), with statistically significant difference compared to older children (p 0.023). Those of weigh <30 kg had a statistically significant difference compared with those with higher weight (p 0.012). No statistically significant difference was found between OP values and sex (p 0.431).
CONCLUSIONS: The average CSF OP was 19.56 cm H2O (SD 7.76 cm). Mean +/- 1.96 SD is proposed as a reference range, therefore 4.35 to 34.77 cm H2O for children between 1 month and 17 years which will include 95% of values. Statistically significant differences were found in the OP of children < 10 years old and weighing < 30 kg, without modifications associated with sex.
KEYWORDS: Neuroscience

574. Eating Disorder Risk Among Adolescents Presenting to a Specialty Concussion Clinic
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OBJECTIVE: A higher prevalence of eating disorders (ED's) is observed among adolescents and athletes. In this pilot study, we aim to assess the prevalence of eating disorder risk in patients who present with concussion.
METHODS: Consecutive new patients evaluated in a multidisciplinary concussion clinic received questionnaires including the SCOFF ED Screening Tool, Patient Health Questionnaire (PHQ-9 or PHQ-A for adolescents), and Generalized Anxiety Disorder 7 (GAD-7). Patients 12-21 years old with a referral diagnosis of concussion were included. A positive screen for ED behaviors was defined as answering 'yes' to ≥1 question on the SCOFF and/or reported poor appetite, weight loss, or overeating on the PHQ-9/PHQ-A. Chi-square and t-tests were used to assess group differences in demographic and questionnaire data.
RESULTS: Fifteen patients (67% female, mean age 14.9±2.4 years) completed the questionnaires; time from injury ranged from 3 days to >1 year. Injury mechanisms included sport (n=12), fall (n=2), and struck (n=1). Seven (47%) patients had positive ED behavior screens. There was no statistically significant association between positive ED screen and age, mechanism of injury, time since injury, or total SCOFF or PHQ-9 scores. A significant association was seen between positive screen and total GAD-7 score (p=0.027).
CONCLUSIONS: Our findings indicate that a clinically significant proportion of adolescents presenting to a concussion clinic may be at risk of ED. Further research should be conducted to better assess the prevalence of subclinical and clinical ED's within this population and to characterize the impact of ED behaviors on concussion management and recovery.
KEYWORDS: Neuroscience

PALLIATIVE CARE

575. Prevalence and background characteristics of children with medical complexity in Tottori, Japan: a population-based longitudinal study
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OBJECTIVE: To investigate the prevalence, background characteristics, and secular trends of children with medical complexity (CMC) in Tottori, Japan.
METHODS: CMC was defined as patients aged <20 years requiring daily medical care and use of devices. The national health insurance claims data were used for patient enrollment. The study period was divided into three periods: period 1, 2007–2010; period 2, 2011–2014; and period 3, 2015–2018. Moreover, the severity of CMC was classified into four categories according to patients' self-mobility and communication abilities.
RESULTS: The prevalence of CMC was 1.88 per 1000 population in 2018, which increased by approximately 1.9 times during the study period. The number of CMC who presented with severe motor and intellectual disabilities was unchanged during the periods 1–3, whereas those with relatively preserved intellectual abilities (group 4 CMC) increased by 1.7 times. The

distribution of underlying disorders did not change significantly. The number of CMC who required respiratory management and oxygen therapy increased by 1.3 and 1.8 times, respectively, during periods 1-3.
CONCLUSIONS: The prevalence of CMC increased almost twice during the 12-year study period, and the number of patients in group 4 CMC remarkably increased. With the advancement of medical technology and disease management, underlying disorders of CMC may change over time. Additionally, this study showed that the need for medical care and devices differed based on underlying disorders and severity of CMC; therefore, individualized medical, welfare, and administrative services and education on various types of CMC must be provided.
KEYWORDS: Palliative Care

RARE DISEASES

576. A Clinical and Genetic Study of Neuronal Ceroid Lipofuscinosis from India – A Developing Country Experience

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OBJECTIVE: To describe the clinical, neuroimaging and genetic spectrum of Neuronal ceroid lipofuscinosis (NCL) from India
METHODS: Retrospective review and prospective follow-up of children with genetically confirmed NCL evaluated from the Pediatric Neurology Units of 2 centers from North and South India.
RESULTS: Twenty-four children from North India and 17 children from South India were evaluated. Of the 24 children in northern NCL cohort, mean age of onset was 3.5 years. Presenting concerns were myoclonic seizures (14/24) and regression (7/24). Consanguinity was observed in 4 families. The 17 children from Southern India presented between ages 2 and 5 years, with myoclonus, regression and movement disorders; consanguinity was present in 9 families. On neuroimaging, diffuse cerebral (52%) and cerebellar atrophy (57%), and periventricular white matter hyperintensities (28%) were noted. In the North Indian cohort, pathogenic variations
were *TPP1* (23.8%), *CLN8* (19%), *CLN6* (19%), *CLN5* (14%), *PPT1*(14%), and *MFSD8* (9.5%). Amongst the South Indian
cohort, *MFSD8* (29.4%), *CLN2* (23.5%), *CLN6* (17.6%), *KCTD7*(5.8%), *GRN (5.8%), CLN8* (5.8%), and *CLN1* (11.7%). All had worsening cognition with progressive myoclonic jerks and were bed bound to vegetative state.
CONCLUSIONS: This is the largest study of genetically confirmed NCL from India and represents comparison of genetic data from Northern and Southern parts of the country. While *CLN2, CLN8 and CLN6* are common from North India, CLN7, CLN2CLN6 are more common from South India.
KEYWORDS: Rare Diseases, Genetics, Neurometabolic Disorders

577. ARIMOCLOMOL TREATMENT IN NIEMANN-PICK DISEASE TYPE C AFFECT BIOMARKERS IN PATIENTS AND RESCUE MUTATED NPC1 PROTEIN

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OBJECTIVE: Niemann-Pick Type C (NPC) is a rare, relentlessly progressive, neurological lysosomal storage disease caused by mutated NPC1 (95%) or NPC2 protein. Arimoclomol, a small molecule amplifier of Heat Shock Proteins (in particular HSP70), has shown positive results in a Phase II/III trial in NPC. Patient genotypes from the trial were studied in relation to disease progression, and key biomarkers evaluated. Arimoclomol's effect on mutated NPC1 protein in cell lines was also studied.
METHODS: All patients in the trial had a genetically confirmed NPC diagnosis. Expression of HSP70 and accumulation of unesterified cholesterol were measured in peripheral blood mononuclear cells while cholestane-triol was quantified in serum samples from patients. Functional NPC1 protein was quantified in a panel of NPC fibroblast cell lines with genotypes similar to the clinical cohort.
RESULTS: A total of 61 different mutations in the *NPC1* gene, 15 of which has not been previously reported to the ClinVar or NPCdb2 databases, was found in the clinical study. Three patients had functional null mutations on both alleles of *NPC1*, leading to a particularly aggressive disease course. In patients, arimoclomol increased the expression of HSP70 and reduced accumulation of unesterified cholesterol in peripheral blood mononuclear cells, as well as reduced the cholestane-triol levels in serum. In NPC fibroblast cell lines covering the most prominent *NPC1* mutations arimoclomol treatment increased the amount of properly processed NPC1 protein.
CONCLUSIONS: Arimoclomol treatment has a positive impact on disease relevant biomarkers in patients and increases functional NPC1 protein across disease relevant genotypes.
KEYWORDS: Rare Diseases, Genetics, Translational/Experiemtnal Therapeutics

578. Burden of Illness in Aromatic L-Amino acid Decarboxylase (AADC) Deficiency
DiBacco Melissa (Boston, MA, United States) Hinahara Jordan, Goss Tom, Pearl Phillip

OBJECTIVE: AADC deficiency is an ultra-rare disorder of monoamine synthesis for which viral-mediated gene therapy is being studied. Globally, 123 patients have been reported in the literature; we are aware of 20 cases in the US. There is variable phenotypic severity, with death in the first decade in the more severe cases. Burden-of-illness (BOI) and medical resource utilization (MRU) are important considerations in evaluating impact of novel therapies on disease.
METHODS: Informed consent was obtained to abstract detailed MRU data from medical records of AADC patients available for the prior two years (number/ type of visits, diagnoses, specialists, procedures, and medications). Caregivers completed the BURQOL, AQOL, and Visual Analogue Scales; effects on the caregivers' QOL, health, and vocational opportunities were examined.
RESULTS: Data were available for 5 (25%) US cases (3M, 2F; age 2-24y, median 5y). Number of appointments, specialists, therapy sessions, and medications varied greatly (Table). Four patients required caregiver assistance for mobility; one patient utilized a walker. Four did not develop head control, sitting or standing. Three did not develop speech. Patients required on average 7 healthcare professionals and 6 different medications. Caregivers described profound QOL effects including inability to maintain regular employment.

CONCLUSIONS: This BOI analysis shows significant variability in MRU required by AADC patients, and consistently high caregiver burden. This is likely the case in other rare neurometabolic conditions for which targeted novel therapeutics are in development. Quantifying natural history, MRU, and associated costs is essential for assessing value of innovative, targeted therapies, including gene therapies.
KEYWORDS: Rare Diseases, Neurometabolic Disorders, Movement Disorders (including Cerebral Palsy)

579. Disparities in Geographic and Specialty Access in U.S. Pediatric Leukodystrophy Diagnosis
Bonkowsky Josh (Salt Lake City, UT, United States) Grineski Sara, Morales Danielle, Collins Timothy, Wilkes Jacob

OBJECTIVE: Rare diseases affect 25 million individuals in the U.S. alone. Diagnosis in pediatric rare diseases is critical but up to 50% of patients are not diagnosed. Leukodystrophies, a well-studied group of rare pediatric neurogenetic diseases, have been found to have significant under-diagnosis in minority patients. The goal of our study was to examine disparities in diagnosis of leukodystrophies including geographic factors and access to specialty centers.
METHODS: Retrospective study of pediatric patients admitted to Pediatric Health Information System hospitals. Leukodystrophy patients were identified with ICD-10-CM diagnostic codes for any of four leukodystrophies (X-linked adrenoleukodystrophy, Hurler disease, Krabbe disease, and metachromatic leukodystrophy). We used three-level hierarchical generalized logistic modeling to predict diagnosis of a leukodystrophy based on distance travelled for hospital, neighborhood composition, urban/rural context, and access to specialty center.
RESULTS: We identified 501 leukodystrophy patients. Patients seen at a leukodystrophy center of excellence (COE) hospital were 1.73 times more likely to be diagnosed than patients at non-COE hospitals. Patients that travelled farther were more likely to be diagnosed than those who travelled shorter. Patients living in a Health Professionals Shortage Area (HPSA) Zip Code were 0.86 times less likely to be diagnosed than those living in a non-HPSA Zip Code.
CONCLUSIONS: We identified geographic disparities in the diagnosis of leukodystrophies in pediatric patients, in particular correlated with access to a center with expertise in leukodystrophies. Our findings suggest a need for improving access to pediatric specialists or for considering broadly deployed diagnostic testing used as a primary test.
KEYWORDS: Rare Diseases, Demyelinating Disorders

580. GRM7 as a novel neurodevelopmental disease-causing gene: report of 2 cases with insight into pathogenesis
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OBJECTIVE: The metabotropic glutamate receptors are a class of G protein coupled receptors that act to modulate neurotransmission . Mutations in *GRM7*, the gene that encodes for metabotropic glutamate receptor 7 ($mGlu_7$), have been associated with different neurodevelopmental disorders. $mGlu_7$ knockout mice exhibit abnormal behaviors consistent with clinical neurodevelopmental syndromes, including a higher susceptibility to seizures.

However, *GRM7* is not yet labelled as a neurodevelopmental disease-causing gene. Here in, we will report 2 Saudi siblings with neurodevelopmental disorder and a *GRM7* p. I154T variant.
METHODS: N/A
RESULTS: Cases description: We present 2 siblings born to a consanguineous marriage. The eldest, an 8 year old girl, presented with a seizure disorder (mainly nocturnal myoclonic), intellectual disability, deficits in language and stereotyped hand movements. On exam she was found to have microcephaly, strabismus, hypotonia, and ataxic gait. EEG showed the presence of frequent focal independent centrotemporal epileptiform discharges activated by sleep. The younger sister is 4 years old with the same clinical phenotype. Both children have a positive homozygous variant in *GRM7*, c.461T>C (p.I154T), verified by whole exome sequencing. Functional studies show that, when expressed in HEK293A cells, the I154T-mGlu$_7$ receptor exhibits weakened dimerization and reduced trafficking to the cell surface. Despite reduced expression, the activity of I154T-mGlu$_7$ can be potentiated by small molecule positive allosteric modulators.
CONCLUSIONS: We report two siblings with the *GRM7* p.I154T variant with a host of symptoms that parallel those observed in mGlu$_7$knockout mice. Functional investigation of I154T-mGlu$_7$ reveals that decreased receptor expression/function likely underlies these disease phenotypes.
KEYWORDS: Rare Diseases, Genetics, Translational/Experimental Therapeutics

581. Gamma Suppression on Somatosensory Evoked Potentials in Patients with Succinic Semialdehyde Dehydrogenase Deficiency (SSADHD), a hyper-GABAergic Condition
Papadelis Christos (Boston, MA, United States) Ntolkeras Georgios, DiBacco Melissa, AlHilani Michel, Nunes Deivid, Roullet Jean-Baptiste, Gibson K. Michael, Pearl Phillip

OBJECTIVE: SSADHD is a rare disorder of GABA degradation. Physiological fluids show elevation of GABA and GHB, and flumazenil (FMZ) PET imaging studies indicate down-regulation of brain $GABA_A$ receptors ($GABA_AR$). Gamma and beta oscillations depend on GABAergic neurotransmission and $GABA_AR$ activity.
METHODS: Somatosensory evoked potentials (SEPs) were recorded from 17 patients and 10 controls using high-density electroencephalography (HD-EEG) (64 channels). The SEPs were obtained after stimulation of both left and right extremities using a pneumatic stimulator (800 trials each). Time-frequency analysis was performed on the averaged data of each participant using Morlet wavelet analysis for all frequency bands on bipolar montage of all the channels. A permutation independent t-test was applied to time-frequency magnitude estimates comparing the two groups. Significance values ($p<0.05$) were corrected for multiple comparisons by controlling the false discovery rate.
RESULTS: Wavelet analysis revealed suppressed gamma and beta activity in the SSADHD cohort compared to controls contralateral to the stimulated side at bipolar channels F3-C3 ($p=0.002$, $t=-3.216$, time=103 ms) and Cz-C3 ($p=0.001$, $t=-4.2234$ time=100 ms) for right side stimuli, and at F4-C4 ($p=0.003$, $t=-3.278$ time=96ms) and Cz-C4 ($p=0.001$, $t=-4.115$, time=92 ms) for left side stimuli using non-parametric two-tailed t-test (Figure).
CONCLUSIONS: We observe for the first time suppressed gamma and beta activity in SEPs elicited from tactile stimulation of upper and lower extremities of patients with SSADHD compared to healthy controls. Decreased gamma activity is consistent with downregulation of

$GABA_AR$ activity previously demonstrated using clinical FMZ-PET and animal slide electrophysiology and immunohistochemistry.
KEYWORDS: Rare Diseases, Neurometabolic Disorders

582. Natural History of CLN3 (Batten) Disease: An 18 Year Ongoing Study
Masten Margaux (Rochester, NY, United States) Vermilion Jennifer, Beck Christopher, Adams Heather, Vierhile Amy, Zimmerman Grace, Mink Jonathan, Erika Augustine

OBJECTIVE: CLN3 disease is the classic juvenile-onset form of Neuronal Ceroid Lipofuscinosis (NCL). CLN3 disease begins in early childhood and results in premature death in the third decade of life. Our objective was to quantify the age-at-onset of core NCL symptoms and change in severity over time.
METHODS: We used the Unified Batten Disease Rating Scale (UBDRS), a disease-specific NCL rating scale consisting of 4 domains: physical impairment, seizures, behavior problems, and capability impairment. It also captures parent-reported age-at-onset of core NCL symptoms. Information from 126 individuals with CLN3 disease was analyzed. Some individuals had multiple annual evaluations giving a total of 380 evaluations. Age-at-onset was compared across clinical features and sexes. Severity scores were compared to age cross-sectionally and longitudinally. For cross-sectional data, the most recent data point for each individual was used. For the longitudinal data, individuals with 2 or more evaluations were included for evaluation.
RESULTS: The onset of symptoms followed a characteristic pattern, with initial vision loss, followed by cognitive decline and behavior problems, then seizures, then sleep and motor disturbances, and then feeding problems (figure 1). The severity of physical and capability impairment increased with age (figure 2). Seizure severity had a weak correlation with age. Behavior problems did not correlate with age.
CONCLUSIONS: CLN3 disease has a characteristic onset and progresses with age in a manner that can be quantified. These results have high potential to inform clinical trial design and to serve as a comparator data set for interventional trials.
KEYWORDS: Rare Diseases, Genetics

583. Pancreatic Neuroendocrine Tumors in young patients with Tuberous Sclerosis Complex
Toelle Sandra (Zurich, Switzerland) Geiger Julia, Kroiss Sabine, Steinfeld Robert

OBJECTIVE: To describe the association of pancreatic neuroendocrine tumors (p-NETs) in children with tuberous sclerosis complex (TSC) and imaging characteristics of the tumor.
METHODS: We present two female teenagers at the age of 14 and 15 years with TSC and the incidental finding of a pancreatic tumor. The abdominal MRI scans were performed to monitor renal angiomyolipomas.
RESULTS: Both lesions were located in the tail of the pancreas. The lesions were well demarcated, had a diameter of 4.8 cm (patient 1) and 1 cm (patient 2) and demonstrated post-contrast enhancement and diffusion restriction on MRI, were hypointense on T1 and heterogeneously hyperintense on T2. In patient 1 diagnosis was confirmed by endoscopic needle biopsy. DOTATATE-PET-MRI showed uptake in both tumors and revealed a parapancreatic lymphnode metastastis in patient 1. Surgery included pancreatic tail resection and in patient 1 lymphadenectomy and splenectomy. On histopathology the lymphnode metastasis was

confirmed, both tumors were completely resected, proliferation rates 1-5% (G2). The tumors were non-functional. Patient 1 was treated with mTOR inhibitor (Everolimus) afterwards. There was no relapse in the first year of follow-up.
CONCLUSIONS: p-NETs are the most common pancreatic lesion in patients with TSC. Small tumors can be surgically resected with excellent prognosis. Hence in case of metastatic disease prognosis is unfavorable, although new treatment options are emerging. The international TSC consensus group recommended 2012 to obtain MRI of the abdomen every 1 to 3 years for surveillance of renal angiomyolipomas. *As early detection is crucial, the awareness for pancreatic tumors should be increased.*
KEYWORDS: Rare Diseases, Brain Tumors/Oncology, Genetics

584. Cerliponase alfa for the treatment of atypical phenotypes of CLN2 disease: a retrospective case series
Wibbeler Eva (Hamburg, Germany) Wang Raymond, de los Reyes Emily, Specchio Nicola, Gissen Paul, Guelbert Norberto, Nickel Miriam, Schwering Christoph, Lehwald Lenora, Trivisano Marina, Lee Laura, Cohen-Pfeffer Jessica, Shediac Renee, Leal-Pardinas Fernanda, Schulz Angela

OBJECTIVE: The classic phenotype of CLN2 disease typically manifests between ages 2-4 years and has a predictable clinical course marked by epilepsy and rapid psychomotor decline. Atypical phenotypes exhibit variable time of onset, symptomatology, and progression. Intracerebroventricular (ICV)-administered cerliponase alfa (rhTPP1 enzyme) has been shown to stabilize motor and language function loss in patients with classic CLN2 disease, but its impact on patients with atypical phenotypes has not been described.
METHODS: Chart review was conducted of 14 patients (8 male, 6 female) with atypical phenotypes who received cerliponase alfa. Pre-and post-treatment CLN2 Clinical Rating Scale Motor and Language (ML) domain scores were compared.
RESULTS: Median age at first presenting symptom was 5.9 years. First reported symptoms were language abnormalities in 6 (43%) patients, seizures in 4 (29%), ataxia and language abnormalities in 3 (21%), and ataxia alone in 1 (7%). Median age at diagnosis was 10.8 years. Thirteen (93%) patients showed a decline in ML score prior to treatment. Median age at treatment initiation was 11.7 years; median duration of treatment was 1.5 years. From start of treatment, ML score remained stable in 11 patients (treatment duration 11-43 months), improved 1 point in one patient after 13 months, and declined 1 point in two patients after 15 and 58 months, respectively. There were 13 device-related infections in 8 (57%) patients and 10 hypersensitivity reactions in 6 (43%).
CONCLUSIONS: Cerliponase alfa is well-tolerated and has the potential to stabilize motor and language function in patients with atypical phenotypes of CLN2 disease.
KEYWORDS: Rare Diseases, Genetics

585. Transcranial Magnetic Stimulation in SSADH Deficiency (SSADHD): A Measure of Maturational Trajectory of Cortical Excitability
Tsuboyama Melissa (Boston, MA, United States) Liu Jingjing, Kaye Harper, DiBacco Melissa, Roullet Jean-Baptiste, Gibson K. Michael, Pearl Phillip, Rotenberg Alexander

OBJECTIVE: SSADHD is a rare disorder of GABA degradation with use-dependent downregulation of postsynaptic $GABA_{A/B}$ receptors based on prior flumazenil-PET and TMS studies. We report TMS data from our natural history study to measure cortical excitability and GABAergic tone longitudinally.
METHODS: Resting motor threshold (rMT) was measured by single pulse TMS (sp-TMS) in 18 SSADHD subjects, 9 age-matched healthy controls, and 44 age-matched patients with focal epilepsy. Separately, spTMS measures of cortical silent period (CSP), and paired pulse TMS (pp-TMS) measures of long-interval intracortical inhibition (LICI) were obtained in 8 SSADHD subjects and 7 controls. One-way ANOVA comparisons were done between subjects and controls and patients with focal epilepsy.
RESULTS: rMT was significantly higher in the SSADHD cohort compared to controls ($p=0.005$), but lower than rMT in either hemisphere of patients with focal epilepsy. The rate of rMT decline as a function of age did not differ between SSADHD and control groups. While there was no statistically significant difference in LICI between SSADHD and control groups, CSP was increased in SSADHD subjects compared to controls ($p=0.047$).
CONCLUSIONS: Given that rMT declines throughout childhood in normal subjects, the elevated rMT in SSADHD patients compared to age-matched healthy controls suggests a dysmature corticospinal tract physiology. However, a retained capacity for maturation in SSADHD is indicated by the trajectory toward lower rMT with age. Contrary to findings from prior studies, no significant difference was found in LICI, and CSP was increased in our cohort, indicating a trend toward increased GABAergic tone, particularly in the very young patients.
KEYWORDS: Rare Diseases, Neurometabolic Disorders, Neuroscience

586. CSF characteristics in a multicentric cohort of late infantile neuronal ceroid lipofuscinosis type 2 (CLN2) patients in Colombia
Espitia Segura Oscar (Bogota, Colombia) Bedoya Morales Ana, Perez Cardenas Sofy, Naranjo Florez Ricardo, Tavera Saldaña Lina

OBJECTIVE: Describe cytochemical characteristics of cerebrospinal fluid (CSF), of a cohort of colombian patients with CLN2 treated with cerliponase alfa.
METHODS: Retrospective cross-sectional study of CSF from patients with CLN2 treated with cerliponase alfa, administered via intracerebroventricular infusion (ICVI) in two institutions. CSF white-cell, glucose, protein, gram stain, culture were studied before ICVI.
RESULTS: 4 patients were included, females 50%. Phenotype was typical in 50%. Mutations identified in typical phenotypes: heterozygous c.471C>A, c.1076-2A>T; heterozygous c.1076-2A>T, c.616C>T; 2 atypical: heterozygous c.622C>T, c.887-10A>G; c.1076-2A>T, c.887-10A>G. Age at treatment start was from 4 to 16 years, mean 8.5 years, 4y for typical cases, 13y for atypical. 91 CSF samples were included, in 3 to 42 ICVI/patient, mean 23. No white-cells were found in 63%, pleocytosis (>10WBC) was found in 5.5%. Atypical cases presented a mean 6.81WBC, typical 0.71, p=.000. 26 (28.9%) had normal CSF protein, increased CSF protein in 56 (62.2%) and decrease in 8 (8.9%), mean 17.9mg/dl in typical and 22.8 in atypical patients, p=0.346. 90 samples included. Mean glucose was 53.7mg/dl; in 2.2% was <40mg/dl. No device-related adverse events, including infections, were found.
CONCLUSIONS: This is the first description in Colombia of CSF in patients treated with cerliponase. In atypical patients significant pleocytosis was found, and a tendency for hyperproteinorrachia, having in mind that normal values in ventricular CSF are lower than in

lumbar CSF. The genotype-phenotype role in hypersensitivity responses must be studied. This study highlights the need to determine a new normality range in this population.
KEYWORDS: Rare Diseases, Genetics, Epilepsy

587. Caregiver insight on the core domains in Angelman syndrome
Adera Mathews (New York, NY, United States) Tansy Aaron, Kolevzon Alex

OBJECTIVE: To describe relevant and challenging features of Angelman syndrome (AS) according to caregivers. AS is a rare, genetic, neurodevelopmental condition characterized by a broad range of symptomatology, including communication and motor impairment, aberrant behaviors, and sleep disturbance. This clinical heterogeneity poses a significant challenge in selecting appropriate outcome measures in clinical trials. Improving understanding of the most relevant and challenging aspects of AS for patients and their caregivers is essential to successful evaluation of new treatments.
METHODS: Interviews with AS caregivers were conducted assessing the relevance of four clinical domains derived from features described in the AS literature: Communication, Behavior, Motor, and Sleep. Qualitative assessment of interviews was conducted based on transcripts.
RESULTS: Communication: the inability to express physical or emotional pain was a primary concern for caregivers. Behavior: physical aggression and potential injury to self or others were considered most concerning. Motor: severe gross motor deficits significantly impact quality of life, particularly among older children who are difficult to carry. Sleep: challenges varied in type and consistency, with nighttime awakenings having the most adverse impact on quality of life.
CONCLUSIONS: Success of clinical trials in heterogeneous patient populations relies on the utilization of outcome measures that effectively capture clinical domains relevant to care and quality of life. To address this critical need, we adapted two global measures, the Clinical Global Impression-Improvement AS (CGI-I-AS) and the Clinical Global Impression-Severity-AS (CGI-S-AS) scales by anchoring them to relevant and challenging features of AS based on caregiver's guidance and feedback.
KEYWORDS: Rare Diseases, Cognitive/Behavioral Disorders (including Autism)

588. STARS a Phase 2 Safety, Tolerability, and Exploratory Efficacy Study of Gaboxadol in Adolescents and Adults with Angelman Syndrome: Seizure and EEG outcomes
Wang Sonya (Minneapolis, MN, United States) Tansy Aaron, Parry Tom, Thibert Ronald

OBJECTIVE: Angelman syndrome (AS), a genetic, neurodevelopmental condition with impaired expression of *UBE3A,* causes aberrant increases in the uptake of ɣ-aminobutyric acid (GABA). AS commonly presents with epilepsy and EEG abnormalities (>80% prevalence). Gaboxadol (OV101) is a highly selective extrasynaptic $GABA_A$ receptor agonist that restores deficits in tonic inhibition in an AS mouse model. The STARS Phase 2 Study (randomized, double-blinded, placebo-controlled) evaluated safety and tolerability of two dosing gaboxadol regimens and explored changes in EEG findings after 12 weeks of treatment.
METHODS: 88 subjects (13-49 years) with AS were randomized 1:1:1 to receive gaboxadol QD (placebo morning, 15mg evening); gaboxadol BID (10mg morning, 15mg evening) or placebo BID. Safety and tolerability including seizures and EEG at baseline and Week 12 were evaluated. Neurophysiological interpretations were performed for all EEGs.

RESULTS: One subject had one seizure (unrelated) and one subject had two seizures (possibly related). Delta rhythmicity (an AS-related EEG signal) improved by 57% in the QD cohort vs 8% in the BID cohort. Delta EEG improvements were observed in central/parietal, temporal and occipital lobes at 78, 82 and 36% in the QD cohort vs 21, 0 and -6% in the BID cohort, respectively.
CONCLUSIONS: Given the high prevalence of epilepsy in AS, gaboxadol was found to be generally safe and well tolerated, with only one subject experiencing two seizures possibly related to gaboxadol. Improvements seen in the EEG delta frequencies support further evaluation of their electrophysiological significance.
KEYWORDS: Rare Diseases, Cognitive/Behavioral Disorders (including Autism), Translational/Experimental Therapeutics

589. Vitamin D Levels and Neurological Status in Sturge-Weber syndrome
Smegal Lindsay (Baltimore, MD, United States) Germain-Lee Emily, Comi Anne

OBJECTIVE: Literature suggests vitamin D, important for bone health, may have neurologic implications. In Sturge-Weber syndrome (SWS) a somatic mosaic R183 mutation in GNAQ causes abnormal leptomeningeal blood vessels, seizures and brain injury. This study aimed to investigate the relationship between vitamin D levels and neurological scores in patients with SWS.
METHODS: 33 subjects (63.6% female, 60.6% Caucasian, 21.2% African American, 9.1% Asian, 6.1% Hispanic or Latino, 3.0% multi-racial, ages 1 to 36 at most recent visit) with informed consent, SWS brain involvement, and two vitamin D levels were studied. Spearman bivariate correlations evaluated relationships between change in vitamin D levels (highest-lowest) and change in SWS score, AED number, and SWS neurological score.
RESULTS: Mean lowest level was 23.88 ng/mL ±10.19 ng/mL and vitamin D deficiency/insufficiency occurred in 25/33 subjects. In subjects with bilateral brain involvement and age of seizure onset <12 months (n=7), increased vitamin D level was correlated with improved total neurological score ($r= -.818$, $p<0.05$). This relationship was not found in the whole cohort, nor in subjects with only age of seizure onset <12 months. However, a trend for improved neurological score with increased vitamin D level was noted in subjects with only bilateral brain involvement (n=9, $r= -.650$, $p= 0.058$).
CONCLUSIONS: Vitamin D deficiency is common in patients with SWS. Especially in patients with bilateral brain involvement and age of seizure onset <12 months, treating low vitamin D levels may be associated with improvements in neurologic status. More research is needed to investigate vitamin D supplementation in SWS.
KEYWORDS: Rare Diseases, Epilepsy, Genetics

590. Improvement of symptoms and electrophysiological findings in siblings with congenital peripheral neuropathy
Ogawa Eri (Tokyo, Japan) Mori Takayuki, Kitami Yoshikazu, Fujino Shuuhei, Suzuki Hiromi, Miyama Sahoko

OBJECTIVE: Hereditary peripheral neuropathy (HPN) generally exhibits an irreversible course. In HPN, only two neonates with congenital hypomyelination neuropathy who showed

unexpected recovery have been reported previously. We herein report a case of siblings whose symptoms and electrophysiological findings were reversible.
METHODS: Retrospective chart-review.
RESULTS: Case 1：A 4-year-old male patient presented with severe muscle weakness, hypotonia and arthrogryposis at birth requiring mechanical ventilation for 44 days due to respiratory insufficiency. Nerve conduction studies (NCS) at age 5 months showed low-amplitude CMAP/SNAP, temporal dispersion, and terminal latency prolongation. His muscle weakness gradually improved, and he achieved milestones of normal motor development with improved NCS findings at age 1 year.
Case 2： The sibling of the patient in Case 1, a 1-year-old female patient, with a history of neonatal asphyxia received therapeutic hypothermia. At birth, she showed severe muscle weakness and hypotonia with arthrogryposis multiplex and couldn't act by herself against the gravity. The level of CSF protein was not elevated. She required mechanical ventilation for 96 days. Her NCS showed severe demyelination at age 1 month. Her voluntary movements gradually appeared in the proximal, followed by the distal, upper limbs. At age 1 year, NCS showed recovery and her motor development almost normalized.
In both Cases, no inflammatory, toxic or metabolic diseases causing peripheral neuropathy were found. PMP22 gene analysis showed no abnormalities.
CONCLUSIONS: The present report is the first to document siblings with reversible congenital peripheral neuropathy although the pathogenesis remains unclear. A genetic background is suspected in this atypical HPN.
KEYWORDS: Rare Diseases, Neonatal & Fetal Neurology

591. Intrathecal adrabetadex for the treatment of Niemann-Pick disease, type C1
Berry-Kravis Elizabeth (Chicago, IL, United States) Porter Forbes, Wang Chen, VanMeter Susan, Grieco Joseph

OBJECTIVE: To reanalyze data from a Phase 2b/3 study (NCT02534844) after the co-primary endpoints, NPC-Severity Scale (NPC-SS) and the Clinician Global Impression of Change (CGIC), showed no significant difference in disease progression between the adrabetadex- and sham-treated arms.
METHODS: Data from the mITT population (all patients receiving ≥1 treatment) were reanalyzed using last observation carried forward (LOCF). Assessments included NPC-SS 4-Item (ambulation, swallow, fine motor skills, and cognition) and 5-Item (speech added) composite scores, and clinician and caregiver CGIC. Subgroups were analyzed using an ANOVA model on NPC-SS 5-Item composite controlling for baseline factors individually and simultaneously.
RESULTS: Change to LOCF showed a non-sigificant trend on all assessments, with a modest treatment effect on the NPC-SS 4-item composite (0.3) and a larger effect on the NPC-SS 5-item (0.8). Subgroups analyses revealed a directional effect favoring adrabetadex on all assessments in some subgroups (eg, no seizures). The overall result did not change for the NPC-SS 5-Item composite adjusted simultaneously for multiple factors. The largest drivers of favorable adrabetadex trends included: speech [–0.18 (adrabetadex); 0.33 (sham); difference (95% CI): –0.52 (–0.96, –0.08)]; and swallowing [–0.11 (adrabetadex); 0.11 (sham); difference (95% CI) = –0.22 (–1.01, 0.58)] suggesting potential benefit in key neurologic manifestations of NPC1.

Available longer-term data also support previous safety conclusions and a positive benefit/risk profile of adrabetadex.
CONCLUSIONS: Although the overall Phase 2b/3 study results were not statistically significant on NPC-SS, post-hoc analyses suggest a potential treatment benefit overall, and in clinically meaningful components of NPC1.
KEYWORDS: Rare Diseases, Epilepsy, Neurometabolic Disorders

592. Novel ALDH5A1 Variants and Genotype:Phenotype Correlation in Succinic Semialdehyde Dehydrogenase (SSADH) Deficiency
DiBacco Melissa (Boston, MA, United States) Pop Ana, Salomons Gajja, Hanson Ellen, Roullet Jean-Baptiste, Gibson K. Michael, Pearl Phillip

OBJECTIVE: We report previously unpublished *ALDH5A1* variants and genotype-phenotype correlation in SSADHD.
METHODS: Patients enrolled in the SSADHD natural history study received neurological/neuropsychological evaluations and genotyping. Assignment of gene variant pathogenicity was based on *in silico* testing and *in vitro* enzyme activity after site-directed mutagenesis and expression in HEK293 cells. Phenotypic scoring used a Clinical Severity Score (CSS) designed for the natural history study.
RESULTS: Twenty-four subjects were enrolled (10M, 14F, median age 8.2y). There were 24 *ALDH5A1* variants, including seven novel pathogenic variants: two missense, three splice site, two frameshift. Four previously reported variants were identified in >5% unrelated families. There was a correlation with age and presence (p=0.001) and severity (p=0.002) of epilepsy, and with OCD (p=0.014). The median IQ score was 53 (Q25 49–Q75 61). There was no overall correlation between the gene variants to the CSS, although a novel missense variant was associated with the mildest phenotype by CSS in the only subject with a normal IQ, whereas a previously reported variant was consistently associated with the most severe phenotype.
CONCLUSIONS: Seven novel pathogenic variants in the *ALDH5A1* gene are described. There is an age-dependent association with worsening of epilepsy and presence of OCD in SSADHD. Overall, there does not appear to be a correlation between genotype and phenotypic severity in this cohort of 24 patients. We did find, however, a suspected correlation between a novel pathogenic missense variant and high functionality, and a previously reported pathogenic missense variant and maximal severity.
KEYWORDS: Rare Diseases, Epilepsy, Genetics

593. Longitudinal clinicoradiological features in three children with COL4A1 mutations
Nakamura Yuko (Yonago, Japan) Maegaki Yoshihiro

OBJECTIVE: To describe the longitudinal clinicoradiological features in three children with *COL4A1* mutations.
METHODS: We retrospectively reviewed clinical symptoms and radiological findings, especially those of brain magnetic resonance imaging (MRI) and computed tomography (CT).
RESULTS: All three patients were female. Two patients were 8 years old, and one was 6 years old. All of them had bilateral ventricular enlargement, porencephaly, and multiple brain calcifications during the fetal period. Two patients also had cerebellar hypoplasia. One had brainstem hypoplasia.

All patients had hemolytic anemia and required blood transfusion during early infancy. Global developmental delay and severe spastic quadriplegia were present in all patients. All patients could not walk or talk. Two patients needed tube feeding. Two patients needed orthopedic surgery to reduce spasticity (tendon, bone, or muscle incision) for severe spastic quadriplegia. The patient who had brainstem hypoplasia needed mechanical ventilation because of laryngomalacia since the age of 3 years. All of them had intractable epilepsy and needed more than two anti-epileptic drugs. Their brain MRI and CT consistently showed progressive white matter atrophy. We incidentally found that one patient had minor cerebral hemorrhage without symptoms.
Despite the changes in radiological findings, their clinical features had not notably changed from early childhood.
CONCLUSIONS: All patients had severe global developmental delay, severe spastic quadriplegia, and intractable epilepsy. The symptoms associated with *COL4A1* mutations vary, and patients who have had symptoms during the fetal period might account for severe cases. As the radiological findings may progress after birth, follow-up examination is important.
KEYWORDS: Rare Diseases, Genetics, Neuroimaging

594. The Public Health Impact of Rare Childhood Neurological Diseases
Masten Margaux (Rochester, NY, United States) van Wijngaarden Edwin, Augustine Erika, Mink Jonathan

OBJECTIVE: Rare diseases collectively affect ~350 million people worldwide. Approximately 1/3 involve a neurologic component, and most are genetic with onset in infancy or childhood. Our goal was to examine the public health impact of rare childhood-onset neurologic diseases through a literature search in combination with our own work on the Neuronal Ceroid Lipofucinoses (NCLs).
METHODS: We conducted a literature search of rare childhood neurologic diseases (figure 1). We then investigated incidence and prevalence of the NCLs using data on 733 individuals from a registry established in 1987 provided by the Batten Disease Support and Research Association.
RESULTS: Several methods have been used to estimate rare disease prevalence. Many of these are tailored to specific diseases, to unique communities, or both. Methodologies differ depending in part on the existence of unified health care systems or nationwide surveillance systems. Results differ based on genetic and cultural factors among others. For example, the prevalence estimates of NCLs ranges from a high of 10 per million to a low of 0.08 per million. US estimates are approximately 1.37 per million.
CONCLUSIONS: There is no universal method for estimating the public health impact of rare diseases either as a whole or for any individual disease. Methods should be tailored to the disease, local public health system, and to demographic factors. The public health impact of rare diseases is substantial. In the changing landscape of individualized therapeutics for rare diseases, the need for valid and rigorous assessments of public health impact has never been greater.
KEYWORDS: Rare Diseases, Genetics

595. Cu(e) the balancing act: Copper hemostasis explored in 5 siblings with variable clinical course
Varghese Sonia (Chapel Hill, NC, United States) Shiloh-Malawsky Yael

OBJECTIVE: To present a unique variation of phenotype and course in siblings with Menkes Disease (MD)
METHODS: We present a literature review of the current evidence about both conditions, then apply this knowledge to the case of a family with five affected siblings.
RESULTS: MD and Wilson's disease are both disorders that result from disruption of copper transport, but affect different tissues resulting in their respective phenotypes. In each case the homeostatic copper balance is lost, with mutations in ATP7A resulting in copper deficiency (Menkes disease) and ATP7B resulting in copper overload (Wilson disease). As such, the two conditions require different therapies. Patients with MD typically present with neurodegeneration, kinky hair, and epilepsy with classic MRI brain findings. Patients with WD often present with abnormal movements such as tremor, dystonia, and ataxia. Current evidence has highlighted cases that exhibit phenotypic convergence despite genotypic and physiologic differences of Menkes Disease and Wilson's disease. We discuss the clinical course of 5 siblings with MD, including a unique course, not previously described, in two of them.
CONCLUSIONS: Recognizing the unique clinical course in our patients is important in guiding management and providing appropriate genetic counseling. Future research is indicated to clarify the affected common pathways and their resulting phenotypic similarities. Our case further raises questions about the nosology of a genetically similar entity with a distinct phenotype.
KEYWORDS: Rare Diseases, Genetics, Epilepsy

596. Facial palsy and disordered chromatin remodeling: the lessons from the chromodomain helicase DNA-binding protein 7 mutation spectrum and clinical presentation of two Tunisian cases
Bouayed Nouha (Sfax, Tunisia) Abdelmoula Balkiss, Abid Fatma, Kammoun Sonda, Aloulou Samir, Louati Rim

OBJECTIVE: Mutations in epigenetic genes are frequently associated with neurodevelopmental diseases. The chromodomain helicase DNA-binding protein 7 (CHD7) protein belongs to a family of proteins implicated in the chromatin organization. Cranial nerve dysfunction, including facial nerve dysfunction and facial palsy, are characteristic of CHARGE syndrome in which 60% of patients harbor CHD7 mutation. Here, we report two Tunisian patients complaining for syndromic facial palsy and in who mutations in CHD7 were confirmed.
METHODS: Two Tunisian males from Sfax (Tunisia) have been managed in our genetic counselling at the medical University of Sfax.
RESULTS: In their history, they complained for a facial palsy at infancy. Facial dysmorphic features of CHARGE syndrome were evident for a patient but not for the other in who the diagnosis of Kallman-Morsier syndrome was suspected because of hypogonadism associated to anosmia. CHD7 screening revealed two mutations respectively at exon 3 and exon 8 of the gene.
CONCLUSIONS: In literature, facial asymmetry was observed more often in the *CHD7* mutation-positive group of CHARGE patients. Despite, the different location of the altered coding sequence of CHD7 in our patients, the two identified microdeletions lead to a loss of function of the gene. Facial palsy as a shared defect in the two distinct syndromes with overlapping features in our patients need to be more studied. CHD7 should be considered in Bell's palsy because it may play a role in neuronal migration, either directly or through its interaction with various partners, particularly those involved in the epigenomic signatures.
KEYWORDS: Rare Diseases, Genetics, Neuroscience

597. Slovenian childhood narcolepsy registry

Gnidovec Strazisar Barbara (Celje, Slovenia)

OBJECTIVE: To evaluate clinical and polysomnographical characteristic of Slovenian pediatric narcolepsy cases.
METHODS: Retrospective study of childhood narcolepsy patients, referred to National Sleep Disorders Centre at University Medical Centre Ljubljana and National Centre for Paediatric Sleep Disorders at General Hospital Celje from 2000 to 2019. In all patients whole-night polysomnography was performed, followed by 5 multiple sleep latency tests and HLAanalysis.
RESULTS: 7 children (2 boys and 5 girls) have been diagnosed with narcolepsy type 1 in the observed period. Their age ranged from 7.5 to 17.5 years. The average duration of the symptoms before the diagnosis was 26 months. All narcolepsy patients had HLA DQB1*0602. Three patients were obese, 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 sleep onset REM (SOREM) at the MSLT testing. They all reported cataplexy. Two patients were treated with stimulant medication, one with combination of modafinil and venlafaxine and two with sodium oxybate. They all reported significant improvement of the symptoms. In two patients the parents declined any treatment.
CONCLUSIONS: With 7 diagnosed cases in the last 19 years narcolepsy type 1 remains severely underdiagnosed neurological disease in Slovenian children. Better recognition of symptoms of excessive daytime sleepiness and cataplexy is essential for early diagnosis and proper treatment promoting cognitive development and social integration of the affected children.
KEYWORDS: Rare Diseases

598. Efficacy of dietary protein restriction in a mild case of molybdenum cofactor deficiency with MOCS1 mutation

Uematsu Mitsugu (Sendai, Japan) Abe Yu, Aihara Yu, Endo Wakaba, Numata-Aemats Yurika, Kure Shigeo

OBJECTIVE: Molybdenum cofactor deficiency (MoCD) is clinically characterized by intractable seizures and severe, rapidly progressing neurodegeneration leading to death in early childhood in the majority of known cases.
METHODS: A 3-year-old girl showed severe neurodevelopmental delays and hypertonia. At 9 months of age, she suffered febrile illness followed by dystonic movement together with opisthotonos. We performed a blood and urine test and brain MRI.
RESULTS: T2 and diffusion weighted image of MR imaging showed increased signal intensities of bilateral basal ganglia. Blood and urine chemistry test showed remarkably low serum and urinary uric acid levels. Urine sulfite test was positive. Specific diagnostic work-up showed elevated levels of xanthine and hypoxanthine in serum with increased levels of urinary SSC (sulfocysteine). Genetic analysis revealed a homozygous missense mutation at c.1525C>T (p.504R>W) in exon 10 of the *MOCS1* gene. At the age of 1yaer 4 months the patient was put on a low protein diet (1.25g/kg/day) to reduces cysteine load and reduces accumulation of sulfite and SCC in tissues. At the 3 months after introduction of protein restriction, urine sulfite test turned negative and SCC level in urine was decreased. She grew up along the normal growth

curve after the start of protein restriction. After starting the protein restriction diet, improvement of dystonic movement was observed, and the patient progressed without regression and seizures.
CONCLUSIONS: This finding demonstrates that the dietary protein restriction suppresses disease progression in mild case of MoCD and suggests the effectiveness of dietary therapy in MoCD.
KEYWORDS: Rare Diseases, Neurometabolic Disorders, Translational/Experimental Therapeutics

599. CLINICAL SPECTRUM OF ATAXIA TELANGIECTASIA (A T) , EVALUATIONAND WORKUP
Mansour Lobna (Cairo, Egypt) Kotb Magd, Kamel Mona, Tawfik Lamia

OBJECTIVE: To highlight clinical manifestations of A T & investigations for proper diagnosis and management
METHODS: 35 cases with A T (3- 14years) enrolled with analysis of clinical, laboratory data :alpha fetoprotein, (AFP), serum IgA, E ,MRI brain.,EMG & n c: 4 cases. Whole exome sequencing (WES) :2 cases
RESULTS: Ataxia all 100%, static during early life , telangiectasia 91.2%, nystagmus 28.5% , oculomotor apraxia 28.5%,strabismus 17.1% , dysarthria 62.7%, lost facial expression , drooling ,dystonia (23.8% each) ,dysphagia 19.95%.Second decade, Peripheral Consanguinity 57%,similarly affected sibling 3 families ,one sibling death with leukemia . Ataxia neuropathy 8.55% ,postural scoliosis & progressive foot deformity 11.4% . Autoimmune Vitiligo 2.85%.Sinopulmonary infections 42.75% :recurrent pneumonia 25.65%& bronchiectasis 17.1% .Brain abscess one .Cancer :Acute lymphoblastic leukemia (ALL 17.1% : 6 cases , 3 preceded A T) .Elevated AFP 100% . Low IgA ,E 68.4%, 74.1% respectively . MRI :cerebellar atrophy 54.15% , cerebral abscesses one:, 2.85% .EMG & n c : Axonal neuropathy 8.55% .WES : homozygous ATM variant c. 2250 G>A p in two cases
CONCLUSIONS: A T shows variability in severity of manifestations and at different ages .A T is considered in DD of ataxic CP in first 4 years .Absence of telangiectasia is not against A T diagnosis.Peripheral neuropathy , dysphagia , postural scoliosis were common in second decade .Elevated AFP is important marker .Neoplasm encountered was ALL,it can precede A T diagnosis .WES confirms ATM variant and carrier detection
KEYWORDS: Rare Diseases

600. PHACE Syndrome in a Nigerian Newborn: Case Report
Jimoh Ademike (Zaria, Nigeria) Ekedigwe John, Shehu Maryam, Shehu Hassan, Gargadi Sunday, Yakubu Alhassan

OBJECTIVE: The report highlights the clinical presentation of this rare neurocutaneous disorder
METHODS: An hour old term baby presented to our Special Care Baby Unit with a large midline facial mass. On examination, he was pale, had a midline facial haemangioma measuring 6.5cm x 4.5cm, cleft lip and palate, right microphthalmia and absent left eye, rudimentary left pinna with no external auditory meatus. Telangiectatic areas were over the extensor surfaces of both upper and lower limbs. Pulse rate was 120beats per minute but with radio-radial delay. He also had microcephaly and absent anterior fontanelle. The respiratory and digestive systems were

stable. Brain CT scan showed intracranial abnormalities. The patient was diagnosed as having PHACE syndrome and multidisciplinary management was implemented. In addition, parents were counselled.
RESULTS: The facial haemangioma spontaneously decreased daily over 3 weeks. However, due to financial constraints parents signed against medical advice. Patient was reported to have died 3 days after.
CONCLUSIONS: PHACE is an uncommon neurocutaneous disorder requiring multidisciplinary management. This can be challenging in low resource setting where patient may be contending with financial constraint. However, there is a need to be aware of the clinical condition.
KEYWORDS: Rare Diseases

601. Clinical Presentation of Early Onset Huntington Disease in Two Children
O'Rourke Dana (Los Angeles, CA, United States) Luc Quyen

OBJECTIVE: We describe the clinical presentation of two patients with early onset Huntington disease (HD). This rare progressive disorder begins before age 20 and results in movement disorder, cognitive and emotional disturbances. Early onset HD represents only 5-10% of cases and presents differently from adult HD.
METHODS: Case report
RESULTS: Patient 1 had gait and speech regression at age four. There was continued deterioration in language, cognitive, and motor skills with development of dystonia, parkinsonism (bradykinesia, rigidity, and tremor), and epilepsy. MRI Brain demonstrated caudate nuclei and putamen hyperintensity with caudate head volume loss. There was no family history of HD, but father was diagnosed with schizophrenia. Initial testing showed no detectable PCR expansion. Repeat testing using repeat primed and fluorescent fragment length PCR assays identified one HTT allele with 115 CAG repeats. Patient 2 developed dystonia at age four followed by progressive language, cognitive, and motor regression along with intractable epilepsy. MRI Brain demonstrated volume loss involving the caudate nuclei and putamen and thinning of the corpus callosum. The patient was found to have 86 CAG repeats. Father was diagnosed with HD the year before with 40 CAG repeats.
CONCLUSIONS: Although adult and early onset HD both display severe language, motor, and cognitive regression, the clinical presentation differs. Chorea is less prominent and other movement disorders are common. Epilepsy can be seen in 30-50% of early onset HD before age 10 (1). Two testing techniques are recommended if there is concern for a high number of CAG repeats.
KEYWORDS: Rare Diseases, Movement Disorders (including Cerebral Palsy)

602. Methods for Quantitative Gait Analysis in CLN3 Disease
Zimmerman Grace (Rochester, NY, United States) Vierhile Amy, Adams Heather, Masten Margaux, Mink Jonathan, Augustine Erika

OBJECTIVE: CLN3 disease is a neurodegenerative disorder of childhood. Motor symptoms, primarily characterized by parkinsonism, begin between 10-12 years of age and progress to non-ambulation and eventually a bedridden state. Our objective was to evaluate the reliability of 2D gait analysis to characterize motor dysfunction in individuals with CLN3 disease.

METHODS: Spatiotemporal gait analysis was conducted in individuals with CLN3 disease, using a 16-foot pressure sensing gait analysis system. Each participant made 4-6 passes across the mat, at a self-selected natural walking speed. We compared spatiotemporal gait analysis data to two measures using bivariate correlation: UBDRS score (a validated disease-specific measure of progression) and age, a surrogate for disease duration.
RESULTS: 12 subjects completed the assessment (mean age 11 years, range 2-22 years, female n=6). Higher UBDRS gait scores (worse function) were associated with a wider base of gait (stride width r=0.78, p=0.003) and slower speed (velocity r=-0.67, p=0.02). Older age was associated with a wider base of gait (stride width r= 0.81, p=<0.01), higher time in stance phase (stance% r=0.88, p=<0.01) and slower speed (velocity r=-0.71, p=<0.01).
CONCLUSIONS: Initial comparison of gait analysis data to age and UBDRS gait scores suggest that this may be a valid approach. Positive correlations between velocity, stance % and stride width with known surrogates for disease duration (age) and/or motor dysfunction (UBDRS score) may represent disease-associated gait instability. Certain associations may also be related to expected age-related growth and development. Larger, longitudinal studies are warranted to further assess the value of this approach.
KEYWORDS: Rare Diseases, Movement Disorders (including Cerebral Palsy)

603. Cataplexy-Free Days Following Sodium Oxybate Treatment in Children and Adolescents With Narcolepsy With Cataplexy
Mignot Emmanuel (Palo Alto, CA, United States) Rosen Carol, Wang Y. Grace, Profant Judi, Dauvilliers Yves

OBJECTIVE: To determine the number of cataplexy-free days/week experienced by children/adolescents with narcolepsy with cataplexy treated with sodium oxybate (SXB).
METHODS: In SXB-naive participants, dose was optimally titrated before a 2-week stable-dose period (SD); participants taking SXB at study entry entered a 3-week SD at their usual dose. After a 2-week, placebo-controlled, double-blind, randomized withdrawal period (DB), participants entered an open-label safety period (OL; total duration ≤1 year).
RESULTS: Of 106 participants, 74 (69.8%) were SXB-naive and 32 (30.2%) were taking SXB at study entry. In SXB-naive participants, median (Q1, Q3) cataplexy-free days/week increased during titration: week 1 (0.0 [0.0, 2.0]), week 2 (1.0 [0.0, 3.0]), and last 7 days (4.0 [1.0, 6.0]); n=71. During the last 14 days of SD, cataplexy-free days/week remained stable and were similar in participants who were SXB-naive or taking SXB at study entry: 4.3 (1.0, 5.8), n=66, and 4.8 (0.8, 6.5), n=32, respectively. During the last week of DB, cataplexy-free days/week decreased to 0.0 (0.0, 2.7) in participants randomized to placebo (n=32) but remained 4.0 (1.0, 6.0) in participants continuing SXB (n=31). During the last week of observation for each participant in OL, median cataplexy-free days/week was 5.0 in both SXB-naive participants (n=63) and those taking SXB at study entry (n=32). Common adverse events (>10%) in the safety population (n=104) were enuresis, nausea, vomiting, headache, and decreased weight.
CONCLUSIONS: SXB treatment increased cataplexy-free days/week in children/adolescents with narcolepsy with cataplexy. The overall safety profile was consistent with previous studies in adult and pediatric narcolepsy.
KEYWORDS: Rare Diseases, Neuroscience

604. Targeting Gys1 by CRISPR-Cas9 Decreases Abnormal Glycogen Formation in Lafora Disease Mouse Models

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OBJECTIVE: Lafora Disease (LD) is a fatal, autosomal recessive, glycogen storage disorder, and is a rare form of progressive myoclonus epilepsy. LD typically starts in previously healthy adolescents, and symptoms rapidly evolve into progressive refractory epilepsy, cerebellar ataxia, and respiratory failure which lead to death within about a decade. Currently, there is no treatment available for LD. LD is caused by loss of function mutations in *EPM2A* or *NHLRC1*, which encode proteins laforin or malin respectively. Both laforin and malin are involved in regulating glycogen metabolism by an unclear mechanism. The absence of either protein results in aberrant cytoplasmic glycogen inclusions (Lafora bodies). Studies indicate that these intracellular inclusions are a principal driver of the disease pathology and, partial or full reduction of glycogen synthase in mouse models prevents LD. We hypothesized that inhibiting *Gys1* with CRISPR-Cas9 will provide therapeutic benefit. We tested this hypothesis as a proof of principle study, in two different LD mouse models.
METHODS: We packaged the SaCas9 and a *Gys1* targeting sgRNA in a recombinant adeno-associated virus (rAAV2/9). We injected neonatal mice with the rAAV-SaCas9 vectors via bilateral intracranial ventricular (ICV) injections. And, we aged mice to 3 months and harvested brain tissue for biochemical and histopathological analysis.
RESULTS: Our results show that targeting *Gys1* by CRISPR-Cas9 provides therapeutic benefit by decreasing abnormal glycogen formation in LD mouse models.
CONCLUSIONS: This study highlights the potential of *in vivo* CRISPR/Cas9 gene editing as an important path forward for the treatment of Lafora Disease.
KEYWORDS: Rare Diseases, Epilepsy, Translational/Experimental Therapeutics

605. Sodium Oxybate Treatment Effects on Sleep Architecture in Pediatric Patients With Narcolepsy With Cataplexy

Mignot Emmanuel (Palo Alto, CA, United States) Bogan Richard, Black Jed, Parvataneni Rupa, Wang Y. Grace, Dauvilliers Yves

OBJECTIVE: Evaluate sodium oxybate (SXB) effects on sleep architecture in study participants 7–17 years of age with narcolepsy with cataplexy.
METHODS: SXB-naive participants titrated SXB dose to an optimal level and entered a 2-week stable-dose period (SD; Figure). Participants already taking SXB entered a 3-week SD at their usual dose. After SD, participants received placebo or continued SXB treatment in a 2-week, double-blind, randomized withdrawal period (DB), then entered open-label (OL) treatment for ≤47 weeks (Part 1). SXB-naive participants underwent polysomnography at screening (before initiating SXB), end of SD (optimal dose), and end of study (optimal dose). Participants taking SXB at study entry underwent polysomnography at screening and end of study (taking SXB).
RESULTS: Of 106 participants, 85 completed Part 1. In SXB-naive participants, changes from screening to end of SD included arousals/night (median [Q1, Q3] change, −43.0 [−58.0, −17.0]), N1% (−4.6% [−7.5, −0.6]), and N3% (12.6% [7.1, 20.9]). These changes were maintained through end of study. In participants taking SXB, sleep architecture remained similar from

screening to end of study. Treatment-emergent adverse events (TEAEs) >10% during Part 1 were enuresis, nausea, vomiting, headache, and decreased weight.
CONCLUSIONS: Open-label SXB treatment in children with narcolepsy was associated with reduced arousals, reduced stage 1 (N1) sleep, and increased stage 3 (N3) sleep, consistent with improvement in disrupted nighttime sleep. Treatment effects and TEAEs were consistent overall with adult studies.
KEYWORDS: Rare Diseases, Neuroscience

606. Prevalence of Diagnosed Pediatric Narcolepsy in the United States
Morse Anne (Danville, PA, United States) Licholai Greg, Bron Morgan, Profant Judi, Yang Mo

OBJECTIVE: To estimate the prevalence of diagnosed narcolepsy among pediatric patients in a large US healthcare claims database.
METHODS: Prevalence of diagnosed narcolepsy was estimated from medical/prescription claims (Symphony Health) from 2013-2016. Data collected included age (0-6, 7-11, 12-17 years), sex, insurance type, and presence of cataplexy. Included cases had either ≥2 claims with a narcolepsy diagnosis ≤6 months apart, or ≥1 narcolepsy claim with ≥1 claim for a multiple sleep latency test or maintenance of wakefulness test ≤6 months prior.
RESULTS: In 2016, the majority of pediatric patients diagnosed with narcolepsy were aged 12-17 years (79.0%), female (51.6%), commercially insured (62.8%), and diagnosed with narcolepsy without cataplexy (56.4%). Standardized prevalence of diagnosed pediatric narcolepsy was 8.9 (95% confidence interval [CI] 8.3-9.5) per 100,000 persons in 2013 and 10.0 (95% CI 9.3-10.6) per 100,000 persons in 2016. Extrapolated US prevalence of diagnosed pediatric narcolepsy increased from 6780 persons in 2013 to 7606 in 2016. Estimated diagnosed prevalence increased by age category from 0.7 per 100,000 for 0-6 years to 6.9 for 7-11 years and 24.0 for 12-17 years. Percentage of narcolepsy with cataplexy claims was 32.6% (2013) to 43.6% (2016), indicating a standardized prevalence of diagnosed pediatric narcolepsy with cataplexy of 2.9 per 100,000 in 2013 and 4.4 in 2016.
CONCLUSIONS: Prevalence of diagnosed pediatric narcolepsy was 8.9 to 10.0 per 100,000 during 2013-2016, with 2.9 to 4.4 per 100,000 diagnosed with narcolepsy with cataplexy. Analyses were limited to diagnosed and insured patients seeking care, and thus may underestimate prevalence.
KEYWORDS: Rare Diseases, Neuroscience

607. Seizures as the initial manifestation of central nervous involvement in Parry-Romberg Syndrome Associated with Localized Scleroderma.
Di Luca Daniel (Miami, FL, United States) Alfaris Basma, Lopez- Alberola Roberto

OBJECTIVE: To describe a rare case of seizures in the setting of Parry-Romberg syndrome associated with localized Scleroderma.
METHODS: Here we present an observational case report of new onset focal seizures with complete workup performed, including electroencephalography (EEG), neuro-imaging and treatment.
RESULTS: A 12-year-old girl with a history of localized scleroderma initially presented to our emergency department after a first-time seizure at home. Semiology was characterized as involuntary movements of the left upper extremity followed by loss of awareness and secondary

generalization. Examination on arrival was remarkable for hemiatrophy of the left arm and face with forehead involvement "en coup de sabre". CT brain revealed scattered punctate calcifications and vasogenic edema and subsequent MRI Brain demonstrated confluent areas of hyperintense FLAIR signal changes in the bilateral cerebral hemispheres with irregular areas of enhancement, suggestive of CNS involvement of scleroderma. EEG was remarkable for frequent electrographic seizures, mostly located in the left occipital region. She was started on high dose steroids for 3 days followed by IVIG and Cyclophosphamide with good response. Events were initially not responsive to Keppra therefore patient was started on Vimpat, with good control of clinical and electrographic events.
CONCLUSIONS: We report an unusual central nervous system manifestation of linear scleroderma and Parry-Romberg syndrome, presenting as new-onset seizure. To our knowledge, this is one of the few cases reporting focal seizure as the initial manifestation of localized scleroderma. Clinical recognition and initiation of therapy are critical.
KEYWORDS: Rare Diseases, Epilepsy

608. Phenotypic Clustering in Tuberous Sclerosis Complex-Associated Neuropsychiatric Disorders
Alperin Samuel (Cincinnati, OH, United States) Krueger Darcy, Capal Jamie

OBJECTIVE: Tuberous sclerosis complex (TSC) is an autosomal-dominant genetic disease affecting multiple organs. TSC-associated neuropsychiatric disorders (TAND) are cognitive, psychiatric and neurodevelopmental problems, that affect 90% of TSC individuals, but only 20% receive assessment and treatment. The TAND Checklist was created in 2013 to improve detection of TAND-related symptoms. Using this Checklist, our objectives were to 1) investigate TAND symptom prevalence and stability over consecutive visits 2) identify natural symptom clusters, and 3) identify phenotypic presentations based on symptom clusters.
METHODS: TSC patients seen at Cincinnati Children's Hospital between 2015-2018 completed the Checklist via iPad at clinic visits. Cluster and factor analyses were conducted to identify naturally-occurring symptom groups in TAND. K-means cluster analysis was used to characterize phenotypic profiles based on factor scores. All statistical analyses were performed using R, an open-source platform.
RESULTS: 1545 Checklists were completed by 668 patients over the 3-year period. Mood swings (52%), anxiety (53%), and attention difficulties (57%) were most common symptoms. Symptoms tended to be stable, changing only 5-20% of the time, in individuals completing multiple visits. A seven-cluster solution was found, including "scholastic", "behavioral dysregulation", "mood/anxiety", "neuropsychological", "restless" and two "ASD-like" clusters. Seven clinically-unique profiles were found, ranging between high- and low-symptom burden.
CONCLUSIONS: Our study is consistent with TAND symptom prevalence and clusters found in previous studies. Clinically-meaningful symptom profiles were found that may be useful for developing treatment interventions for specific TSC subpopulations. The TAND Checklist is easily integrated into clinic visits, providing a method for monitoring symptoms on subsequent visits.
KEYWORDS: Rare Diseases, Cognitive/Behavioral Disorders (including Autism)

609. Wolf in Sheep's Clothing: Case of Spinal Muscular Atrophy with Respiratory Distress Type 1 (SMARD1) presenting as Brief Resolved Unexplained Event (BRUE)

Ojha Kshama (Louisville, KY, United States) Lakhotia Arpita

OBJECTIVE: To describe a case of SMARD1 secondary to mutation in IGHMBP2 gene, presenting as BRUE in an infant.
METHODS: Chart review
RESULTS: A 4-week-old term male, presented with an episode of apnea and cyanosis after crying. Complete sepsis evaluation, including CSF studies, was unremarkable. Patient was discharged home with diagnosis of GERD. He re-presented with another episode of apnea requiring rescue breaths. He had further work up for BRUE, including cardiology, pulmonology and neurology evaluations. He continued with episodes of apnea and bradycardia in the hospital, ultimately requiring intubation. Neurological exam was normal except bilateral 3-4 beats of ankle clonus. EEG and MRI imaging were normal. Bronchoscopy showed severe bilateral bronchomalacia and had tracheostomy placed. As part of work up, whole exome sequencing was sent, which showed two pathogenic mutations in IGHMBP2 gene in trans, associated with SMARD1. Over time, he developed weakness, hypotonia and loss of reflexes, more characteristic of the condition. He was discharged home on a ventilator.
CONCLUSIONS: SMARD1 is an autosomal recessive, motor neuron disorder, which presents with diaphragmatic and progressive muscular weakness, neuropathy and autonomic dysfunction. BRUE may be secondary to neurological etiologies in less than 10% cases, predominantly seizures. Neuromuscular etiologies form a small subset of neurological BRUE. SMARD1 has not been described previously as an etiology. As in case described, SMARD1 can have a seemingly benign early presentation leading to delayed or missed diagnosis. It is important to consider SMARD1 and other neuromuscular etiologies in the differential for neurological etiologies for BRUEs.
KEYWORDS: Rare Diseases, Neuromuscular Disorders, Teaching of Child Neurology

610. Novel homozygous missense mutation in the ERCC5 gene leading to psychomotor delay and evolving spastic paraparesis with milder phenotype and overlap with cerebro-oculo-facio-skeletal syndrome type 3 (COFS3).
Chandratre Saleel (Ajman, United Arab Emirates)

OBJECTIVE: To describe the phenotype of a novel homozygous missense mutation in the ERCC5 gene.
METHODS: Retrospective review of medical records.
RESULTS: A 3-year-8-month old boy presented with psychomotor delay during infancy. He was the only child born at term to healthy consanguineous parents (first cousins), weighing 2.5 kg. Mother had pregnancy induced hypertension. He had moderate psychomotor delay (walked independently around 2 years, unable to walk fast or run at 3-years-8-months, fine motor and speech delay. There was no reported sun-sensitivity or loss of skills. He had subtle facial dysmorphology (low-set protruding ears, pre-axial tag), wide-based crouched gait, central hypotonia, lower limb spasticity and hyperreflexia. There was no microcephaly or growth failure. Eye examination was normal. Magnetic resonance imaging of the brain done when 14-months-old showed partial agenesis of corpus callosum, mild global cerebral atrophy, paucity of white matter and delayed myelination. Comparative Genomic Hybridization Microarray, skeletal survey, abdominal ultrasound, auditory brainstem evoked responses, ophthalmology assessment

were normal. Trio whole genome sequencing detected a novel homozygous missense variant in the ERCC5 gene inherited from both parents. The variant alters a highly conserved tryptophan residue and is most probably pathogenic.
CONCLUSIONS: Previous reported cases of COFS3 have all been secondary to truncating mutations in the ERCC5 gene. Our case further expands the phenotype of the ERCC5 gene leading to milder phenotype and overlap with COFS3. Further functional studies are needed to determine the effect of this variant at the protein level and the relation with the phenotype.
KEYWORDS: Rare Diseases, Genetics, Neuroimaging

611. Phenotype Variation in a Mother and Son with ATP1A3 Mutation.
Lax Daniel (Bronx, NY, United States) Patel Puja

OBJECTIVE: ATP1A3-related disorders consist of distinct but overlapping phenotypes which include alternating hemiplegia of childhood (AHC), cerebellar ataxia, areflexia, (pes cavus), optic atrophy, sensorineural hearing loss (CA(P)OS), rapid-onset dystonia-parkinsonism (RDP), and intermediate phenotypes. Fever-Induced Paroxysmal Weakness and Encephalopathy (FIPWE) was more recently described as a separate ATP1A3 phenotype. We present a child and his mother with the same ATP1A3 mutation but different clinical phenotypes.
METHODS: Proband is a 22-month-old boy with speech delay presenting with fever, flaccid paralysis, and encephalopathy. Four months prior, he had a one-week-long episode of flaccid paralysis and encephalopathy, but with persistent areflexia; nerve conduction studies with electromyogram (NCS/EMG) was normal and an etiology was not discovered.
RESULTS: Video electroencephalogram (EEG) was normal. NCS/EMG was notable for acute dysfunction of the anterior horn cells or nerve roots (Figures 1 & 2). Testing for the ATP1A3 gene showed c.2425G>A (p.Glu818Lys), a pathogenic heterozygous variant. The patient developed choreoathetoid movements, dysautonomia, and remained profoundly hypotonic. His 31-year-old mother was found to have the same genetic mutation and had all the clinical manifestations of CA(P)OS syndrome, except for pes cavus.
CONCLUSIONS: ATP1A3 syndromes are rare disorders for which separate genotype-phenotype relationships have been recognized, however it is evident that there is a phenotypic continuum. We describe a mother and child with the same genetic mutation but with clinically different phenotypes. This is the first pediatric case report to demonstrate acute dysfunction of the anterior horn cells or nerve roots in an ATP1A3-related disorder. More research is necessary to characterize these syndromes.
KEYWORDS: Rare Diseases, Genetics, Movement Disorders (including Cerebral Palsy)

STROKE

612. Incidence of Feeding and Swallowing Impairment in Children After Stroke
Sherman Victoria (Toronto, Ontario, Canada) Moharir Mahendranath, Bhathal Ishvindar, Thorpe Kevin, Martino Rosemary

OBJECTIVE: Stroke occurs across the lifespan and is becoming increasingly recognized in childhood. Dysphagia is common after stroke in adults; however, few studies have explored

dysphagia in children post stroke. This study assessed incidence and predictors of dysphagia in children following stroke.
METHODS: The Canadian Pediatric Ischemic Stroke Registry for a tertiary hospital was used to identify consecutive patients aged 1mo-18yrs, admitted with arterial ischemic stroke (AIS) or cerebral sinovenous thrombosis (CSVT) over five years (Jan/13-Nov/18), and included demographic and stroke details. Two independent raters reviewed medical charts to capture in-hospital feeding and swallowing impairment. Bivariate analysis and simple logistic regression derived incidence and odds ratios with respect to select variables such as type, severity and laterality of stroke.
RESULTS: There were 106 children: 73(68.9%) AIS, 35(33.0%) CSVT; 57(53.8%) male; and, median age 5.5 years (1.3-11.2). There were 26(25.0%) with severe neurological deficit at stroke presentation, 12(11.3%) at discharge. Hemiparesis was present in 52(49.1%), 26(50.0%) left sided. Across the entire sample, the incidence of feeding impairment was 20(18.9%), and swallowing was 38(35.8%). Of those with feeding and swallowing impairment, the majority were AIS (17, 85.0% and 33, 86.8%) and had a right sided or bilateral neurological deficit, 12(60.0%) and 27(71.1%) respectively. Of those with swallowing impairment, 11(28.9%) had severe neurological deficit. There were 43(40.6%) children who had either feeding and/or swallowing impairments.
CONCLUSIONS: These findings suggest that dysphagia is a consequence of stroke in children, with up to 40.6% affected. Due to study design limitations, these estimates are likely conservative leaving the true incidence unknown.
KEYWORDS: Stroke (including other Vascular Disorders)

613. CLINICAL PROFILE AND OUTCOME OF CHILDREN WITH STROKE AT A TERTIARY CARE CENTRE: A DESCRIPTIVE STUDY
Patel Smruti (Vellore, India) Thomas Maya, Yoganathan Sangeetha, Muthusamy Karthik, Selvi Bernice, Yadav Bijesh

OBJECTIVE: To describe clinical profile, radiological findings and outcome of children and adolescents with stroke.
METHODS: Clinical details and outcome of children (1 month to 16 years of age) with acute stroke from July 2014 to July 2019 under Pediatric Neurology Unit was extracted from the electronic database. Children with stroke mimics, transient ischemic attacks, Todds paralysis and Sturge Weber syndrome were excluded. The outcome was assessed at discharge and follow-up using Modified Rankin Scale.
RESULTS: A total of 91 children diagnosed with stroke during this 5 year period had a male female ratio of 1.4:1. The mean age at presentation was 73.6 ± 58.36 months. The etiologies identified were mineralising angiopathy(25.3%), moya-moya disease(18.7%), dissection(14.3%), infectious or parainfectious arteriopathy (11%), prothrombotic state(7.7%), cerebral venous thrombosis(3.3%) and iron deficiency anemia (2.2%). The common manifestations were focal motor deficits (90.1%), seizures (29.67%), change in mental status (20.9%), headache (35.2%), vomiting (34%), aphasia (15.4%) and fever prodrome (19.8%). History of trivial or non-trivial trauma was found in 38.4% of dissection and 100% of mineralising angiopathy. A total 59 (64.1%) had anterior circulation stroke, 23(25%) had posterior circulation stroke, 3(3.26%) had both anterior and posterior circulation stroke, 20(21.7%) had watershed infarcts. Motor deficits

were present in 82 out of 90 children (91%) at discharge. Three children succumbed. Persistent deficits were seen in 43 out of 74 (58.1%) on follow-up.
CONCLUSIONS: The etiology of stroke in children is diverse. Pediatric stroke subtypes have typical clinical presentation that aids diagnosis.
KEYWORDS: Stroke (including other Vascular Disorders), Neuroimaging

614. Outcomes of Paediatric Stroke associated with Systemic or Central Nervous System Infection

Choong Chew Thye (Singapore, Singapore) Thomas Terrance, Tan Grace Soo Woon

OBJECTIVE: Infection is a significant factor in strokes. We evaluated the outcome of a cohort of childhood stroke associated with systemic or central nervous system infection. Understanding the role of infection can permit more specific intervention and suitable preventive measures.
METHODS: We conducted a 15- year (1997-2010) Institution Review Board approved retrospective case-note review of childhood strokes managed at the KK Women's and Children's Hospital, Singapore. A sub-group of children with preceding infection or evidence of acute concomitant infection, and no other demonstrable stroke etiology, was identified, and outcomes analysed.
RESULTS: Of 103 children with stroke: Female: male 49: 54, age range 1 month to 18 years, infection contributed to stroke in 20. Apart from neurological deficits, clinical presentation was varied including seizures, vomiting, flu-like symptoms and neck stiffness. Bacterial infections (pneumococcal meningitis, TB meningitis, sepsis , respiratory infections) accounted for the majority. Two children had underlying immunodeficiency; one had aspergillosis. Epstein Barr, Herpes simplex and Influenza B infections were the three identifiable viral infections. Overall outcome in the infection associated cohort was extremely poor: Mortality 9 of 20; eight acutely. Of the 11 survivors, 7 had poor outcome (epilepsy, cognitive deficits, hemiplegia, quadriplegia). Only 4 had reasonably good outcome. In contrast, good outcome was seen in 44 (53 %) patients with stroke without associated infection.
CONCLUSIONS: Infection is associated with mortality and poor long-term outcome in paediatric stroke.
KEYWORDS: Stroke (including other Vascular Disorders), Infections/Neuroimmunology

615. A NEW KIND OF BLEED - A CASE SERIES OF SUBPIAL HEMORRHAGES IN A NEONATAL INTENSIVE CARE UNIT

Dabrowski Ania (Baltimore, MD, United States) Carrasco McCaul Melisa, Façanha Barreto André, Tekes Aylin, Sun Lisa

OBJECTIVE: Subpial hemorrhages (sPH) in infants were first described in 1972 but remain underrecognized on neuroimaging. This study aims to describe clinical presentations, risk factors, imaging findings, and outcomes of sPH in neonates.
METHODS: An Institutional Neonatal Intensive Care Unit database was queried for sPH. Infants with intracranial hemorrhage on MRI were reviewed by a pediatric neuroradiologist. Data on perinatal history, comorbidities, and outcomes was collected through retrospective chart review.
RESULTS: Twenty infants with sPH were identified: 10 (50%) were preterm, 7 (35%) had low birthweight. Comorbidities included hypoxic-ischemic encephalopathy (n=7, 35%), birth trauma

(n=6, 30%), cardiopulmonary disease (n=5, 25%), disseminated intravascular coagulation (n=3, 15%), ventricular shunt (n=3, 15%), and severe congenital brain anomalies (n=1, 5%). All children with sPH had another form of hemorrhage and/or ischemic stroke: subdural (n=14, 70%), intraparenchymal (n=12, 60%), intraventricular (n=9, 45%), subarachnoid hemorrhage (n=7, 35%), ischemic stroke (n=6, 30%). Eleven infants with sPH (55%) had seizures. 6 patients (30%) had follow-up MRIs; adjacent encephalomalacia developed in children with large subpial hemorrhages. Of the 20 patients, at least 14 (70%) received outpatient neurodevelopmental monitoring, 9 (45%) patients required outpatient therapies, and 7 (35%) were followed by an outpatient neurologist for evaluation and/or management of seizures, infantile spasms, perinatal stroke, or hemiplegia.
CONCLUSIONS: sPH are associated with multiple comorbid medical conditions, other types of intracranial hemorrhage, and ischemic strokes. Further studies to understand prognostic implications of sPH are needed.
KEYWORDS: Stroke (including other Vascular Disorders), Neonatal & Fetal Neurology, Neuroimaging

616. LONG-TERM FUNCTIONAL AND COGNIVE OUTCOMES AFTER PEDIATRIC STROKE

Shamansurov Shaanvar (Tashkent, Uzbekistan) Shamansurova Barno, Tulyaganova Nodirakhon, Nazarova Sadokat

OBJECTIVE: To determine of long-term functional and cognitive outcomes in stroke patients from birth to 7 years.
METHODS: 38 children from birth to 7 years (Me±16,2 months) who had stroke were examined with the PSOM (Pediatric Stroke Outcome Measure).
RESULTS: Hemiplegic motor deficiency are observed - 33 (86.8%) and tetraplegic - 5 (13.2%) cases. Right side motor deficiency observed in 14 (36.8%), left side - in 19 (50%) and on both sides – in 5 (13.2%) patients. Scores on the PSOM sensorimotor subscale shows that deficiency identified at right side – in 15 (39.5%), at the left side – in 18 (47.4%) and on both sides – in 5 (13.2%) cases. The Spearman correlation analysis showed, a moderate positive correlation to the high level of significance between movement abnormality (hemiplegia, quadriplegia) and the side of the motor deficit ($r=0.64$ at $p<0,001$). Likewise, we detected strong positive correlation with the high level of significance between speech deficit (understanding) and speech production deficit (exception dysarthria) ($r=0,93$ at $p<0,001$).
CONCLUSIONS: The PSOM is a valid and reliable outcome measure for pediatric stroke. It is useful for retrospective scoring from health records and prospective serial longitudinal outcome assessments and is ideally suited for prospective clinical trials in pediatric stroke.
KEYWORDS: Stroke (including other Vascular Disorders)

617. Long-term neurologic outcomes following neonatal arterial ischemic stroke

Slim Mahmoud (Toronto, Ontario, Canada) Aziz Aly, Dlamini Nomazulu, MacGregor Daune, Moharir Mahendranath, deVeber Gabrielle

OBJECTIVE: To evaluate long-term neurologic outcomes after Neonatal Arterial Ischemic Stroke (AIS).

METHODS: Neonates with acutely diagnosed AIS were prospectively enrolled in a single-center outcome study from November 1993 to August 2015. Children underwent serial neurologic assessments using the Pediatric Stroke Outcome Measure (PSOM). We included children assessed at or beyond 4 years age. Neurologic deficits were scored within sensorimotor, language and cognitive/behavioral domains as 0 (no deficit), 0.5, 1, 1.5 or 2 (maximal deficit). The PSOM severity classification scheme was used to classify overall neurologic outcome as normal, mild, moderate or severe. Predictors of poor neurologic outcomes (moderate or severe deficit) were assessed using univariate logistic regression models.
RESULTS: A total of 105 neonates were included (54% males) and followed for a median of 7.7 years (interquartile range [IQR]:5.5-10.5 years). Normal, mild, moderate and severe neurologic outcomes were seen in 55.2%, 22.9%, 15.2% and 6.7%, respectively. Sensorimotor outcomes deficits were the most common (52%) followed by cognitive/ behavioral (38%) and language (15%) deficits. Predictors of poor neurologic outcomes included cardiac risk factors (odds ratio [OR]= 8.7, 95% confidence interval [CI]: 1.08-69) and prothrombotic disorders (OR=5, 95% CI: 1.1-22.8). A trend toward significance was found for abnormal consciousness at presentation in predicting poor outcomes (OR=2.9, 95% CI: 0.9-8.9).
CONCLUSIONS: Although most neonates have favorable outcomes four years post-stroke onset, nearly half demonstrate deficits in motor, cognition or language acquisition. Neonates with comorbid cardiac or prothrombotic disorders appear to be at increased risk for poor outcomes.
KEYWORDS: Stroke (including other Vascular Disorders)

618. Circadian rhythms, stroke risk and outcome in pediatric stroke
Balut Fernanda (Santiago, Chile) Slim Mahmoud, Moharir Mahendranath, MacGregor Duane, Pulcine Elizabeth, deVeber Gabrielle, Dlamini Nomazulu

OBJECTIVE: Adult studies in arterial ischemic stroke (AIS) suggest an association between circadian rhythms, stroke incidence and neurological outcome. We aimed to determine the association between circadian rhythms and childhood stroke incidence and outcomes.
METHODS: Children aged 29 days-18 years diagnosed with AIS were prospectively enrolled in a single-center study from 1992 to 2018. Parent/caregiver-reported time of stroke symptom onset or last known well was classified into one of four time intervals (TINTs): TINT1: 6:01–12:00; TINT2: 12:01–18:00; TINT3: 18:01–00:00; TINT4: 00:01–6:00. The Pediatric Stroke Outcome Measures was used to classify neurologic outcomes as normal/mild or moderate/severe at discharge.
RESULTS: A total of 215 children (62.8% males; median age at diagnosis: 5.9 years, interquartile range [IQR]: 2.3-10.4) were included. Incidence of AIS was most common in TINT2 (32.6%) followed by TINT1 (27.4%), TINT3 (24.7%) and TINT4 (15.3%). Children aged 1-4 years were more likely to experience AIS in the TINT2 (37.5%) compared to children aged 4-8 years who were more likely to experience stroke in TINT1 (36%), p=0.09. Children aged≥8 years with cardiac risk factors were more likely to experience AIS in TINT2 (30%, p=0.04). Children with moyamoya experienced AIS in TINT2 or TINT3 only (p=0.01). Favorable neurologic outcomes (normal/mild), assessed at a median of 6 years (IQR:3-9.5) post-stroke, did not vary significantly between TINTs.

CONCLUSIONS: Age-of-stroke and stroke sub-type may be associated with time related factors including circadian rhythms. However, larger studies are warranted to further evaluate this potential association.
KEYWORDS: Stroke (including other Vascular Disorders)

619. SPECTRUM OF PEDIATRIC ARTERIAL ISCHEMIC STROKE
Sultan Tipu (Lahore, Pakistan)

OBJECTIVE: To determine the causes of arterial ischemic stroke and neuroimaging findings in children. Its an observational, prospective, cross-sectional study.
METHODS: From Jan 2019 to Dec 2019. Children from 1 month to 18 years of age with radiologically confirmed arterial ischemic stroke, occurring 1st time in life, were included in the study. Arterial ischemic stroke (AIS) was confirmed on the basis of history, examination and neuroimaging findings of the brain. Further investigations were done according to the cause of arterial ischemic stroke and neuroimaging
brain findings.
RESULTS: A total of 72 patients of arterial ischemic stroke were identified over a period of 6 months. Among these, male predominance was found in 53 (73 %) children. Outpatient department patients outnumbered the indoor patients with stroke in 38(53%) children. Children between 1-5 years of age were the most affected ones (65%). Hemiplagia, fits, hemiparesis and aphasia were the most common presenting features affecting 60(83%), 27(38%),14(19%) and 8(11%) children respectively. The commonest cause of arterial ischemic stroke was iron deficiency anemia, found in 30%(n=22) of the children followed by anemia due to other causes in 27%(n=20) and congenital heart diseases in 8.3%(n=6) of the children. On neuroimaging studies, parietal lobe was the most affected part of the brain in 23% of the children (n=16). Middle cerebral artery was the major artery affecting 57% (n=12) of the patients.
CONCLUSIONS: Iron deficiency anemia and anemia due to other causes and congenital heart diseases were common etiologies in children with arterial ischemic stroke in our study.
KEYWORDS: Stroke (including other Vascular Disorders)

620. Cerebral Small Vessel Disease and Intracerebral Hemorrhage Recurrence Risk Among US Minority Individuals
Senthil Priyanka (Reno, NV, United States)

OBJECTIVE: Black and Hispanic survivors of Intracerebral Hemorrhage (ICH) are at higher risk of recurrent intracranial bleeding when compared to their white counterparts. While established differences in hypertension severity after ICH play a role, they do not fully account for this disparity. We sought to investigate whether differences in Cerebral Small Vessel Disease (CSVD) subtype and/or severity exist among race/ethnicity groups.
METHODS: We utilized data from the MGH-ICH and ERICH-L studies. We collected MRI-based CSVD markers using cerebral microbleeds (CMBs). We conducted univariable and multivariable analyses for presence of CMBs, differentiating on the basis of two primary CSVD subtypes: Cerebral Amyloid Angiopathy (CAA) and Arteriolo-Sclerosis (AS).

RESULTS: We analyzed data for 2192 ICH survivors (MGH-ICH study: 991 and ERICH-L: 1201). Of these, 1245 self-identified as white, 460 as black, 392 as Hispanic, and 67 as other race/ethnicity. We found that minority ICH survivors were more likely to have CMBs on MRI scan at time of ICH compared to white participants (54% vs. 41%, $p < 0.001$). Minority ICH survivors had higher burden of AS-associated CMBs (median: 1, Inter-Quartile Range [IQR] 1-2 vs. median 0, IQR 0-1, $p = 0.016$). Burden of CAA-associated CMBs did not differ between white and minority participants (median: 0, IQR 0-2 vs. median 0, IQR 0-1, $p = 0.12$).
CONCLUSIONS: Minority ICH survivors presented with greater CSVD burden on MRI scan, especially as it pertains to the AS-subtype. Given the known association between AS and hypertension, our findings may reflect disparities in primary stroke prevention long pre-dating ICH.
KEYWORDS: Stroke (including other Vascular Disorders)

621. Not Just Coincidence: Basal Ganglia Infarction Post Childhood Head Injury
Ram Dipak (Manchester, United Kingdom) Pavaine Julija

OBJECTIVE: Infarction is a very unusual consequence of head injury in children. We describe a rare case of basal ganglia infarction in an infant, likely to represent mineralising angiopathy of childhood.
METHODS: A seven month old male infant presented with right sided weakness 30 minutes after a trivial accidental head injury. He had a background of hypoxic ischaemic encephalopathy at birth. A full septic screen was negative and extensive cardiac, haematological, immunological and metabolic work-up was normal. He made rapid recovery over two weeks and was discharged on aspirin with no significant neurological deficits. He remains well at his one year follow-up.
RESULTS: *Figures 1&2: CT and MRI findings. (A, B) CT Head: Bilateral basal ganglia calcifications in the region of lenticulostriate arteries, hypodensity in the left striatocapsular region. (C, D) MRI Brain: Restricted diffusion in the left caudate, lentiform nuclei and internal capsule confirmative for acute infarction. MRA of head and neck was normal.*
Basal ganglia stroke is rarely reported as a consequence of head injury in children. However, this presentation is recognised in a particular cohort of children, most of whom have had previous calcification of the lenticulostriate arteries, which may represent mineralising angiopathy. In our case, this could have occured secondary to birth-related hypoxia, and may have increased the risk of spasm or thrombosis of these arteries during a head injury, leading to ischaemic stroke.
CONCLUSIONS: Young children presenting with basal ganglia infarction after minor head injury should be more carefully investigated for mineralising angiopathy of childhood using dedicated imaging modalities.
KEYWORDS: Stroke (including other Vascular Disorders)

622. Cerebral Thrombectomy in a Pediatric Patient
Fain Daniel (Grand Rapids, MI, United States) Singer Justin, Krueger Jena

OBJECTIVE: Thrombectomy for the treatment of arterial ischemic stroke is an effective treatment for adult patients but efficacy in pediatric patients is currently under investigation.
METHODS: We report a previously healthy 14-year-old female who presented with acute left face, arm, and leg weakness. She was transferred to our institution for neuroprotective measures, thrombectomy, and neurocritical care monitoring.

RESULTS: At school, a 14-year-old girl became acutely weak and fell with no loss of consciousness nor sensory deficits. Her symptoms resolved after presentation to an outside ED. She had no history of illness, nor prior known hypercoaguable state, nor injury. She did have left calf pain for a few weeks with increased intensity the morning prior to her acute event. CTA of head and MRA of brain confirmed right MCA clot. She underwent mechanical thrombectomy with clot removal from the right distal M1 segment without complications. Initially 4 extremity venous dopplers showed no evidence of thrombus, but a follow up venous doppler identified a superficial muscular branch thrombus. Hypercoaguable work up was negative. The patient began low molecular weight heparin and is currently awaiting PFO closure.
CONCLUSIONS: This patient suffered a stroke due to thrombotic occlusion of the right M1 segment. Prompt, appropriate imaging led to the identification of thrombus and subsequent removal. It is postulated that this was caused by a DVT. This case illustrates the need for a pediatric stroke protocol utilizing rapid and appropriate imaging even following resolution of symptoms. Finally, repeating venous doppler should be considered when thrombus etiology is unknown.
KEYWORDS: Stroke (including other Vascular Disorders), Neuroimaging, Critical Care

623. Spinal Cord Infarctions in Children: A Case Series
Avallone Jennifer (Saint Petersburg, FL, United States) Geller Thomas, Bhatt Ashmit

OBJECTIVE: In the pediatric population, spinal cord infarction is an uncommon pathology. There is limited existing literature on prognosis. This case series describes clinical presentation, neuroimaging, and neurologic outcomes of three pediatric patients with spinal cord infarction. The study explores the challenges in recognition of this diagnosis and focuses specifically on long-term outcomes.
METHODS: This retrospective case series is based on three previously healthy pediatric patients between the ages of 5 to 12 years old who presented with spinal cord infarction at a tertiary children's hospital between 2017-2019. These patients went on to receive rehabilitative therapy and were followed months after the inciting event in a pediatric multidisciplinary stroke clinic.
RESULTS: Diagnosis of all three patients was based on acute onset of loss of neurologic function in the setting of MRI spine findings consistent with spinal cord ischemia. Clinically, all three cases initially presented with significant neurologic deficits including monoplegia, hemiplegia, and quadriplegia depending on spinal cord level and extent of the infarction. Acute trauma played a role in two of the patients. None of the patients had known stroke risk factors prior to the inciting event. With intensive rehabilitative therapy over the course of one year, there was significant neurologic recovery in all patients.
CONCLUSIONS: Spinal cord infarction is an uncommon diagnosis in the pediatric population. Given the potential severity of initial neurologic insult and otherwise limited literature, long term prognosis is unknown and challenging to predict. This case series provides some insight into the potential significant recovery of these patients.
KEYWORDS: Stroke (including other Vascular Disorders), Neurorehabilitation, Neuroscience

624. Feasibility and Tolerability of BCI Activated FES in Children with Perinatal Stroke
Jadavji Zeanna (Calgary, Alberta, Canada) Zewdie Ephrem, Metzler Megan, Kirton Adam

OBJECTIVE: Perinatal stroke (PS) causes most hemiparetic cerebral palsy (CP) and lifelong disability for 10000 Canadian children. Unfortunately, children with severe hemiparesis have limited rehabilitation options. Brain Computer Interface (BCI) is a technology that may change this. Research suggests that BCI activated functional electrical stimulation (BCI-FES) of target muscles may enhance upper extremity function in adults. We aimed to complete the first study combining BCI-FES in children with hemiparetic CP to assess tolerability and feasibility of this approach.
METHODS: Thirteen participants (mean age=12.2 years, 31% female) were recruited through the Alberta Perinatal Stroke Project (APSP), a population-based cohort. Inclusion criteria were: (1) MRI-confirmed PS, (2) hemiparetic CP, (3) age 6-18 years, (4) informed consent/assent. Exclusion criteria were: (1) neurological comorbidities, (2) unstable epilepsy. Participants attended two sessions and wore an EEG headset with two electrical stimulation electrodes attached to each forearm. Participants imagined wrist extension of their left or right hand continuously in random order. Muscle stimulation and visual feedback were provided when the correct visualization was detected.
RESULTS: Data from ten participants included in Table 1. No serious adverse effects occurred. Most common complaints were mild headache and headset discomfort (7/10). Some participants reported mental fatigue and frustration (50%) affecting their ability to continue. No children ranked the experience as unpleasant.
CONCLUSIONS: Preliminary results suggest that BCI-FES is feasible in this population. BCI-FES has the potential to afford a new therapy for young patients with limited options. Clinical trials can now be modeled to optimize approaches and test efficacy.
KEYWORDS: Stroke (including other Vascular Disorders), Movement Disorders (including Cerebral Palsy), Neurorehabilitation

625. Rare case of a child with recurrent posterior circulation infarcts due to anatomic abnormalities in Klippel-Feil Syndrome
Thamann Anna (Louisville, KY, United States) Barton Chris, Lakhotia Aprita

OBJECTIVE: Klippel-Feil Syndrome (KFS) is an uncommon genetic disorder characterized by bony deformities of the spine. Stroke is a rare complication, with less than ten reported cases. Here we describe a case of recurrent pediatric stroke due to vascular occlusion secondary to KFS-associated vertebral abnormalities.
METHODS: Detailed chart review and literature search.
RESULTS: A 12-year-old-right-handed female with a known history of KFS with cervical spine deformity and scoliosis presented with headache, dizziness, and vomiting without report of trauma. Exam showed ataxia and dysarthria. MRI/MRA brain and neck revealed right > left cerebellar infarction, right non-occlusive vertebral and proximal basilar artery thrombi, with hypoplastic left vertebral artery (Figure 1). She was found to
have MTHFR mutation (heterozygous), mild elevation of anticardiolipin and antiphospholipid antibodies and echocardiogram revealed PFO. While etiology of cryptogenic stroke was worked up, anticoagulation was started. Over the next year, serial vessel imaging
showed progressive worsening of vertebral occlusion and basilar
narrowing. Conventional cerebral angiogram showed vertebral artery compression by the skull base due to underlying cervical spine subluxation (Figure 2). Cervical decompression/fusion were performed with improvement in flow without recurrence of stroke to date.

CONCLUSIONS: Pediatric stroke is often difficult to diagnose and treat in the absence of obvious risk factors. This case demonstrates that KFS-associated cervical spine vertebral abnormalities may increase risk of stroke due to biomechanical stress on surrounding vessels. Careful evaluation of spine and vascular anatomy is imperative when stroke occurs in the setting of KFS in order to properly prevent further events.
KEYWORDS: Stroke (including other Vascular Disorders), Rare Diseases, Neuroimaging

626. Delayed Internal Carotid Dissection after Roller Coaster ride: Potential role of SMAD-4 and SKI gene variants as causative factors.
Tamrazian Eric (Torrance, CA, United States) Mehta Bijal, Chen Agnes, Langille Megan, Panosyan Eduard, Gotesman Moran

OBJECTIVE: Cervical Artery Dissections are an important cause of strokes in the pediatric age group. Most cases are reported to be sporadic, however there have been increasing reports of pediatric dissections as a result of acceleration-deceleration injuries such as those experienced in Roller-Coaster rides. Classical risk factors for pediatric strokes have generally been attributed to connective tissue disorders such as Marfan's syndrome and Ehlers-Danlos. The use of genetic sequencing techniques has allowed clinicians to screen for multiple genes.
METHODS: Case Report:
RESULTS: A healthy 8-year-old boy presented to the ED with sudden painless vision loss of his right eye while at school. He had visited an amusement park 15 days prior which included various roller coaster rides. Imaging with an MRA of the head and neck showed a Right ICA dissection above the carotid artery bifurcation (See Figure 1). Patient was kept on anticoagulation for 4 months and on Aspirin for over a year. Genetic screening using a 43 gene panel showed a heterozygous mutation for SMAD4 (c.535A>G) and SKI (c1048G>A). Although clinically the role of this mutation is unknown, both are involved in the signaling pathways for TGF-Beta.
CONCLUSIONS: While most pediatric strokes due to acceleration-deceleration injuries are idiopathic, genetic sequencing has allowed clinicians to screen wider varieties of genes. Given the overwhelming evidence of the role of TGF-beta with vessel wall integrity and its role in aneurysm formation, dissections and strokes, it is worthwhile to elucidate the role of genetic anomalies associated with TGF-beta
KEYWORDS: Stroke (including other Vascular Disorders), Neuroimaging, Trauma

627. Ischemic stroke in the setting of arterial thoracic outlet syndrome, case report and literature review
Kerashvili Nino (St. Louis, MO, United States) Galardi Maria, Noetzel Michael

OBJECTIVE: A cervical rib is an uncommon congenital anatomical variation, rarely causing neurogenic, venous and rarely arterial manifestations. Arterial thoracic outlet syndrome (TOS) can result in ischemic stroke. After encountering a patient with an ischemic stroke in the setting of TOS, we wanted to better understand the pathophysiologic mechanisms by which this condition can result in stroke.
METHODS: Case report and literature review.
RESULTS: We describe the case of a 17-year-old female with no significant past medical history who presented with left-sided face, arm, and leg weakness and headache. She was

diagnosed with right middle cerebral artery ischemic stroke, and her workup revealed a right M1 occlusion, as well as a right subclavian artery thrombus. Imaging demonstrated bilateral cervical ribs causing R>L TOS. No other causes for stroke were identified. The pathophysiology of stroke in arterial TOS is thought to be from retrograde embolization, mechanism of which is poorly understood, but the compression of the subclavian artery (SCA) resulting in stasis, intimal trauma with or without post stenotic dilatation and thrombus formation are commonly accepted as inciting events. Transient retrograde flow within the SCA can be identified on ultrasonography in some patients with TOS associated stroke and retrograde SCA flow can be induced experimentally, thus leading to cerebral embolization. Another hypothesis centers on the concept of retrograde clot propagation from the SCA and subsequent embolization into the cerebral circulation.
CONCLUSIONS: Ischemic strokes in the setting of arterial TOS have been described, but the mechanism, while it most likely involves retrograde embolization, remains obscure.
KEYWORDS: Stroke (including other Vascular Disorders), Headache/Migraine, Neuroimaging

628. Treatment of Reversible Cerebral Vasoconstriction Syndrome with intra-arterial Nifedipine
Fain Daniel (Grand Rapids, MI, United States) Mazaris Paul

OBJECTIVE: Reversible cerebral vasoconstriction syndrome (RCVS) is a group of disorders involving cerebral constriction and dilation often associated with nonaneurysmal subarachnoid hemorrhage (SAH). Although more common in adults, numerous pediatric cases have been reported. The pathophysiology in the pediatric population is unknown but may be due to a dysregulation of vascular tone. Presenting signs and symptoms include severe headache, vomiting, focal neurologic deficits and stroke.
METHODS: We describe a previously healthy 3-year-old boy with a diagnosis of B-cell ALL who developed SAH, right hemipariesis and multiple evolving left frontoparietal infarcts. He was transferred from an outside hospital for treatment of evolving stroke with suspected RCVS.
RESULTS: RCVS was confirmed by catheter angiography. He was treated with intra-arterial nifedipine and monitored in the pediatric ICU with strict neuroprotective measures observed. Serial intracranial dopplers showed stable velocities for the first 24 hours, but then increasing velocities suggesting worsening vasoconstriction. This patient stabilized after a second dose of intra-arterial nifedipine and showed improving velocities on IV nicardipine. He remained stable with no evidence of subsequent stroke and was transferred to a rehabilitation facility on oral nimodipine
CONCLUSIONS: This patient suffered stroke associated with RCVS without a clear etiology. Possible causes are multifactorial and include SAH, chemotherapy, and hypertension. We present a role for aggressive treatment of pediatric patients with RCVS and stroke that emphasizes: adherence to pediatric neurocritical care guidelines, efficacy and tolerability of intracranial vasodilating agents, and intracranial doppler to monitor RCVS progression and assess therapeutic intervention.
KEYWORDS: Stroke (including other Vascular Disorders), Neuroimaging, Critical Care

629. Basal Ganglia Hemorrhage? – Think Metabolic. Leigh's Syndrome Presenting with Intracerebral Hemorrhage
Philbrook Bryan (Atlanta, GA, United States) Keller Stephanie

OBJECTIVE: Leigh's Disease (LD) is a well know mitochondrial disorder (MD) causing necrotizing encephalomyelopathy. Certain MD's have small vessel predilection leading to ischemic stroke (defects in Complex I and IV), and intracerebral hemorrhage (ICH) in Complex IV dysfunction. We report a child with gene defect Complex I presenting with left hemiplegia due to ICH.
METHODS: Literature review searching PubMed.
RESULTS: An adopted male, family history unknown, with language delay, one syncopal episode, and cleft lip presented with acute hemiplegia at 28 months old. Neuroimaging revealed ICH involving the putamina (right > left), and signal abnormalities in surrounding tissues including caudate nuclei and cerebral peduncles. Non-contrast MRA/MRV was unremarkable. Subsequent MR spectroscopy demonstrated a lactate peak in the left basal ganglia. Hematologic and rheumatologic work-up was unremarkable. Initial metabolic testing was normal. Gene testing revealed two defects in the NADH: Ubiquinone Oxidoreductase Complex Assembly Factor 5 gene (NDUFAF5 c.718-1G>A splicing, and p.F147L), resulting in Complex 1 Deficiency. We have continued to follow the patient, and at 8 years old he has had slow, but step-wise decline in motor and language functions more typical of LD.
CONCLUSIONS: Intracerebral hemorrhage is a known but uncommon presentation of MD's, but this case illustrates ICH as a presenting problem attributable to Complex 1 dysfunction; deficiency due to NDUFAF5 mutation. Our case emphasizes the need for a high level of vigilance in unexpected ICH in young children, especially with basal ganglia involvement.
KEYWORDS: Stroke (including other Vascular Disorders), Neurometabolic Disorders, Genetics

630. Fevers and Aches and Weakness—Oh My!: A Case Series of Acute Ischemic Stroke With Concurrent Influenza
Lin Jenny (Atlanta, GA, United States) Elkins Kathryn, Philbrook Bryan

OBJECTIVE: To highlight a case series of three patients who presented with acute ischemic stroke (AIS) in the setting of influenza.
METHODS: Retrospective chart review was performed.
RESULTS: Ages of patients were 23 months old (patient 1), 2 years (patient 2), and 4 years (patient 3). Two patients had Trisomy 21 and trivial cardiac septal defects (1 and 3), and one was previously healthy (2). All patients tested positive for influenza within a week of symptoms. Patients presented with acute hemiparesis (1 and 3) or focal status epilepticus (2). Neuroimaging showed AIS involving right deep grey matter structures and bilateral posterior cortex (1), acute left parietal infarct (2), and multifocal bilateral acute cerebral infarcts (3) (Figure 1). Vascular abnormalities include moyamoya disease in two patients confirmed by diagnostic angiography and a focal arteriopathy in one patient. Patients 2 and 3 had active fevers with influenza and were started on clopidogrel given concern for Reyes syndrome with aspirin. Patient 1 did not have active infectious symptoms and was started on aspirin.
CONCLUSIONS: Case series highlights three pediatric patients with AIS with concurrent influenza. Two patients had comorbid moyamoya disease, further increasing risk for AIS. Literature has shown that influenza-like illnesses increase risk of AIS in the adult population. Bacterial infections and viruses such as VZV and HIV have been linked to increased risk for AIS

in children, but influenza has not been well described. There is some evidence to suggest that vaccination against such illnesses may be protective for AIS.
KEYWORDS: Stroke (including other Vascular Disorders), Infections/Neuroimmunology, Neuroimaging

631. Risk factors for recurrent stroke in Childhood: A Prospective Study in Bangladesh
Fatema Kanij (Dhaka, Bangladesh) Rahman Md Mizanur, Akhter Shaheen

OBJECTIVE: Stroke is relatively rare in children, but can lead to significant morbidity and mortality. Strokes present differently in children than adults and often present with unique risk factors. Understanding the risk factors will optimize outcomes in children. Published cohorts of children with stroke recurrence rates are variable. This study has been done to determine rates and predictors of recurrent stroke in a developing country.
METHODS: We prospectively enrolled 98 children with stroke, 16 children were excluded due to incomplete investigations and lost in follow up. This study has been done in a tertiary care hospital in Dhaka, Bangladesh from 2016 to 2019. Detail history, investigations including MRI of brain, MRA and MRV was done if needed. Each children were followed up minimum 3 months and outcome were studied.
RESULTS: We studied 82 patients , among them 52 presented with first attack and 30 with recurrent attack of stroke . Age range of onset was 4.78±3.90 and 5.30±4.25 in first and recurrent stroke respectively. Recurrence rate was 57% (37% in infarction, none in hemorrhagic stroke). Commonest cause of recurrent stroke was intracranial vusculopathy (66.7%) most common being vascular narrowing and Moya Moya syndrome. In follow up the commonest outcome was motor deficit. No significant difference was found in risk factors of first and recurrent stroke.
CONCLUSIONS: In children with recurrent stroke most common cause was vasculopathy. Thus targeted investigation and treatment should be done in these cases and follow up should be done.
KEYWORDS: Stroke (including other Vascular Disorders)

632. The role of growth hormone in a pediatric case of transient ischemic attack
Sandweiss Alexander (Houston, TX, United States) Farrier David, Bartlett Brittnie, Abid Farida

OBJECTIVE: Growth hormone is often prescribed in pediatric populations with short stature and is associated with a number of potential adverse events. One underrecognized potential adverse event is its effect on intracerebral vasculature. Multiple studies have linked the use of growth hormone in pediatric patients with hemorrhagic stroke in early adulthood. The objective is to present a pediatric case of presumed transient ischemic attack (TIA) in the setting of chronic growth hormone administration.
METHODS: NA
RESULTS: A 10-year-old right-handed female with a past medical history of idiopathic short stature syndrome on growth hormone treatment—with a recent increase in dose two weeks prior—developed sudden-onset aphasia, right sided facial droop, right arm numbness and weakness while at school. Symptoms lasted 5-10 minutes before resolving spontaneously prior to arriving to the emergency room. Brain imaging in the ER demonstrated no acute abnormalities;

hypercoagulable labs revealed no obvious cause of TIA and echocardiography was normal with no PFO. She was started on aspirin 81 mg per day and discontinued GH due to presumed TIA.
CONCLUSIONS: The presentation was most consistent with a TIA of the left MCA without other appreciable stroke risk factors. Therefore, we felt the role of GH should be examined. Previously reported, GH administration in children increases the risk of hemorrhagic stroke in early adulthood (average stroke at 24.2 years old). This may be due to microscopic changes in intracranial vasculature induced by GH directly or IGF-1 indirectly. We feel endocrinologists and neurologists alike should be aware of this potential adverse event of GH.
KEYWORDS: Stroke (including other Vascular Disorders)

633. Pushing Boundaries: The Paediatric Neurovascular Service of Northwest England
Ram Dipak (Manchester, United Kingdom)

OBJECTIVE: There is a strong need for more robust paediatric neurovascular services internationally. In the UK, new paediatric stroke guidelines were published in 2017. Despite this, there is no single centre in the UK which is currently able to deliver solid hyperacute stroke therapy in children. We aim to highlight a unique model of service delivery for paediatric neurovascular disorders.
METHODS: With the aim of setting up a more cohesive neurovascular service for children living in the North West of England, discussion took place between two large tertiary paediatric hospitals in Manchester and Liverpool. The idea of using pooled expertise across both sites was exchanged and agreed. Using strengths across both sites meant that service delivery across the North West was significantly enhanced.
RESULTS: After forming a core team in 2019, regular multidisciplinary team (MDT) meetings now occur on a monthly basis, involving paediatric neurologists, neurosurgeons, neuroradiologists and specialist nurses. Dedicated haematologists and geneticists were involved in the MDT as required. An MDT clinic has also been setup on a monthly basis and feedback from patients and families have been overwhelmingly positive, and this clinic now accepts quaternary referrals from across the country.
CONCLUSIONS: The paediatric neurovascular service in Northwest England is currently a lot more robust and is able to deliver MDT-orientated care to patients in the region. However, there is still more work to be done nationally and internationally for paediatric stroke in terms of hyperacute management. Pooling resources nationally may be a way forward to achieve this next vision.
KEYWORDS: Stroke (including other Vascular Disorders)

634. Use of anticoagulation does not increase hemorrhagic transformation following cardioembolic stroke in childhood
Ko Pin-Yi (Seattle, WA, United States) Khalatbari Hedieh, Wainwright Mark, Amlie-Lefond Catherine

OBJECTIVE: Delayed anticoagulation is recommended in adults with cardioembolic stroke to minimize risk of hemorrhagic transformation, but in children, who may be at higher risk of recurrent stroke and/or suffer delays in procedures requiring anticoagulation, the benefit of delayed anticoagulation is unknown. The objective of this study was to characterize the risk of

hemorrhagic transformation, in relation to early anticoagulation, following pediatric cardioembolic stroke.
METHODS: We reviewed the clinical course and neuroimaging in a retrospective cohort of 67 children (age 1 month – 18 years) with cardioembolic arterial ischemic stroke at our institution between 1/1/2009 and 1/1/2019. Chi-square test was used for statistical analysis, with p-value <0.05 considered statistically significant.
RESULTS: Hemorrhagic transformation (HT) occurred in 11 of 67 children (16%), over half of which (55%) were petechial, and the majority of which (73%) occurred within the first two days after stroke. There was no significant difference in HT between patients who were and were not anticoagulated (19% vs. 16%, p=0.62). Furthermore, there was no significant difference in HT when comparing patients who had their anticoagulation adjusted after a diagnosis of stroke was made (Figure 1).
CONCLUSIONS: The incidence of hemorrhagic transformation after pediatric cardioembolic stroke was 16%, which was not increased with the use of anticoagulation. On serial imaging, some children suspected of having HT were found to have laminar necrosis and other mimics, supporting the need for careful neuroimaging review (Figure 2). Most hemorrhagic transformations occurred early, suggesting a short time window of maximal risk, regardless of anticoagulation therapy.
KEYWORDS: Stroke (including other Vascular Disorders), Critical Care, Neuroimaging

635. Application of a Childhood Stroke Guideline at a Tertiary Care Center: A Brief Case Series
Sauer Ryan (Lexington, KY, United States) Lightner Donita

OBJECTIVE: Childhood stroke is an area of study with many challenges. Rare outside the perinatal timeframe, it has significant morbidity and mortality. Due to low incidence and delayed recognition, experts must utilize limited or adult-driven data for recommendations. Some centers do not have standard guidelines, but this is changing due to recognized need for rapid evaluation and treatment. We present two cases wherein pediatric stroke guidelines were applied and prompted management.
METHODS: We reviewed our stroke database and found two patients who received early evaluation and intervention.
RESULTS: A 15-year-old female presented with aphasia and right hemiparesis, last known normal 14 hours prior. Following stroke alert activation, CTA head identified thrombus in the left middle cerebral artery (Figure 1) which prompted mechanical thrombectomy. Post-procedurally, the child's National Institute of Health Stroke Scale (NIHSS) decreased from 13 to 2 without complication.
A 14-year-old female presented with symptoms of confusion, right facial droop and right hemiparesis, with last known normal 4 hours prior. Rapid imaging revealed stenoses in multiple vascular territories (Figure 2) suspicious for underlying vasculitis. Further intervention was deferred. Imaging prompted rheumatologic workup and led to the diagnosis of Takayasu Arteritis. The child was treated with immunosuppression.
CONCLUSIONS: Through utilization of multi-departmental pediatric stroke guidelines, each child in our series received prompt intervention. We believe cases such as these support development of stroke protocols and underscore potential impact on outcomes. Lastly, we

believe there is potential for greater research and development into inter-facility networking for acute childhood stroke management.
KEYWORDS: Stroke (including other Vascular Disorders)

636. Sturge-weber syndrome unmasked by traumatic brain injury
Sah Jeetendra (Brooklyn, NY, United States) Balucani Clotilde, Abrams Aaron, Velayudhan Vinodkumar, Pavlakis Steven

OBJECTIVE: To describe the clinical characteristics of a patient with Sturge-Weber syndrome (SWS) who developed neurological deficits following traumatic brain injury (TBI), to review similar cases described in the literature and to explore the underlying pathophysiology.
METHODS: The clinical presentation and radiographic findings of a patient are described. A descriptive literature review was conducted, with 6 additional cases taken into consideration.
RESULTS: A 13-year-old boy with no prior neurological symptoms or facial angioma presented after sustaining a minor head trauma with fluctuating mental status, emesis and unsteady gait. He later developed right-sided hemiparesis, aphasia and focal motor seizure with status epilepticus. A contrast-enhanced brain MRI revealed abnormal leptomeningeal enhancement of left cerebral hemisphere that led to diagnosis of SWS. Six cases with SWS have been described in literature who had worsening neurological symptoms following TBI.
CONCLUSIONS: SWS is a neurocutaneous disorder characterized by angiomas involving the face, choroid vessels and leptomeninges. Our patient with a rare SWS with exclusive leptomeningeal angiomatosis developed neurodeficits with TBI similar to other published cases. There is altered cerebral arterial regulation secondary to congested venous system in SWS. Impaired cerebral autoregulation has also been documented in TBI. We postulate that impaired cerebral autoregulation in TBI triggers further hemodynamic changes exhausting already compromised venous system leading to neuronal dysfunction and consequent manifestation. Further observations are needed to confirm that a TBI can exhaust the compromised cerebrovascular autoregulation and alter cerebral perfusion in patients with SWS. Therefore, it is reasonable to suggest to avoid head trauma in children with SWS.
KEYWORDS: Stroke (including other Vascular Disorders), Genetics, Epilepsy

637. A rare presentation of perinatal spinal cord infarct
Muth Gilad (Teaneck, NJ, United States) Segal Devorah

OBJECTIVE: A case of perinatal spinal cord infarct.
METHODS: Perinatal stroke is a common pathology affecting 1/2300 to 1/5000 newborns. It is defined as a neurologic issue that occurs between the 20th week of gestation and 28 days postnatally. The challenge of diagnosis lies in the fact that stroke in the neonate presents with signs and symptoms of seizure, often delaying the diagnosis. Spinal cord infarct is extremely rare, accounting for approximately 1% of all strokes.
RESULTS: A woman presented at 40 weeks gestation for decreased fetal movement. The baby was delivered via C-section and was noted to be apneic, floppy, and cyanotic. APGAR scores were 2, 7, and 8 at 1, 5, and 10 minutes, respectively. The baby displayed hypotonia, greater in the arms, and was moving both legs and left arm, with brisk reflexes in the legs. MRI showed edema in the cord at C2-C3 to C7-T1 that was concerning for tumor. MRI was repeated and demonstrated resolution of the enhancement. There was focal hyperintense T2 signal in the right

lateral cord at C3 level and left lateral cord at C4 level and possible myelomalacia. These findings were consistent with spinal cord infarct. Over the subsequent months, the patient received PT and regained near-normal strength in his legs but continued to have hypotonia, decreased DTRs, and weakness in the arms. Repeat imaging demonstrated evolution of myelomalacia but no new lesions.
CONCLUSIONS: The case is an unusual presentation of perinatal spinal cord infarct, which needs to be considered in neonates with quadriparesis.
KEYWORDS: Stroke (including other Vascular Disorders), Neonatal & Fetal Neurology, Neuroimaging

638. Pediatric Stroke: Time to Treatment Starts Before You Reach the Hospital
Jacob Cerin (Memphis, TN, United States) Caron Elena

OBJECTIVE: Pediatric arterial ischemic stroke (AIS) is associated with a 10-25% mortality rate and more than 50% of children will have persistent deficits or develop subsequent disorders including epilepsy or learning disabilities.[1]In addition, given the onset of impairment in childhood, the effect on quality of life is amplified. AIS requires prompt diagnosis due to a narrow therapeutic window. Consequently, we reviewed AIS in the emergency department (ED) and intensive care unit (ICU) to understand how the therapeutic window could be optimized and thus improving outcomes.
METHODS: We conducted a retrospective chart review of children aged 1 month to 18 years of age with diagnosis of AIS evaluated in the ED and ICU at our institution from January 2015 to December 2019. Stroke cases were screened by ICD-10 codes. We extracted data on age, sex, clinical presentation, National Institutes of Health Stroke Scale (NIHSS), time of clinical onset to time to ED evaluation, neurology consultation, obtaining neuroimaging studies, and intervention.
RESULTS: Over the 5-year period, a total of 18 patients with AIS were identified. Of the 18 patients, 11 presented outside of the window for tissue plasminogen activator (tPA) administration. However, of these patients, 1 received mechanical thrombectomy and 2 received continuous heparin infusions for arterial occlusions. All 7 patients who presented within the therapeutic window received tPA and/ or mechanical thrombectomy.
CONCLUSIONS: Significant pre-hospital delay exists in diagnosing pediatric AIS. More than half of our patients presented outside the therapeutic window. Efforts to reduce diagnostic delays can optimize the management of pediatric AIS.
KEYWORDS: Stroke (including other Vascular Disorders)

TEACHING OF CHILD NEUROLOGY

639. Telephonic helpline and consultation for chronic childhood neurological disorders: a novel initiative
Gulati Sheffali (New Delhi, India) Sinha Rahul, NM Shruti, Panda Prateek, Jossy Mable, Yousaf Jyoti, Bhardwaj Mitesh, Parmar Balwinder, Thapliyal Nikita, Pandey Ravindra

OBJECTIVE: To evaluate the usefulness of a comprehensive teleconsultation service by trained nursing officers, supplemented with toll free 24X7 telehelpline in providing appropriate clinical follow up advice and identifying critical clinical events requiring face-to-face consultation for

children with neurodevelopmental disorders in a tertiary center with long waiting list for appointment
METHODS: Based on successful results of four prior studies in epilepsy, muscular dystrophy and neurocysticercosis analyzing about 700 children over last 15 years and 80% sensitivity/specificity by nurses, this pan-India 24X7 telehelpline was launched in April 2018. Four trained nursing officers addressed the queries round the clock, helped by Pediatric Neurology Fellows and faculties. Teleconsultation for individual disorders are performed according to separate standardized protocol. Those requiring Face-to-face consultation were given priority appointment.
RESULTS: Besides addressing telephonic inquiries by caregivers and general population satisfactorily, between April 2018 and January 2020, teleconsultation was successfully completed for 587 patients (neuromuscular disorder-143, autism-193, neurocysticercosis-150, epilepsy-74, rest miscellaneous disorder). Only 99 subjects (17%) were advised Face-to-face consultation. All of these were subsequently found to be essential, when evaluated by Pediatric Neurologist during Face-to-face consultation. No untoward emergency events occurred in rest of the patients till their next routine appointment. Minor technical glitches were observed in 57 (10%) cases, but none of them led to failure of teleconsultation. About 95% caregivers were found to be satisfied with the teleconsultation.
CONCLUSIONS: Teleconsultation is a novel and to reduce clinician's burden and travel expenses and school absenteeism for children and work absenteeism for parents.
KEYWORDS: Teaching of Child Neurology

640. Impact of Annual Educational Sessions on Clinical Management of Pediatric Seizures in Guatemala
Kammeyer Ryan (Aurora, CO, United States) Gomez Reynoso Henry, Martinez Martinez Elisa, Casillo Reyna Josseline, Racancoj Sac Matilde, Huix Ramos Eugenia, Molina Wolfre, Henriquez Alicia, Knupp Kelly, Walleigh Diana

OBJECTIVE: To evaluate the effectiveness of annual educational sessions on the clinical management of status epilepticus (SE) and pediatric seizures at a regional hospital in Coatepeque, Guatemala
METHODS: A partnership was formed between National Hospital Juan Jose Ortega (NHJJO) and the Children's Hospital Colorado in 2016, to provide pediatric neurology expertise at this location that was not previously available. Educational sessions occurred in-person annually. A retrospective chart review was performed of all pediatric patients presenting to NHJJO with seizure from 2016-2018, including demographics, and seizure etiology, length, and treatment. Similar data was collected prospectively in 2019. Statistical analyses were performed using single-tailed Fisher's exact tests for proportions, and two sample t-tests for continuous variables.
RESULTS: A total of 148 patients (127 retrospective and 19 prospective) participated. An increase in the use of benzodiazepines for treatment of SE (9% vs 100%, $p < 0.001$), and a decrease in the median duration of SE (30 vs 17 min, $p=0.48$) were seen comparing the retrospective and prospective study periods. A decrease in new prescriptions of daily anti-seizure medications for diagnoses not related to epilepsy or brain injury (22% vs 0%, $p=0.039$), and an increase in the prescription of home rescue medications (1% vs 16%, $p=0.007$) were also noted.
CONCLUSIONS: There was a trend suggesting an improvement in management consistent with standards of care after annual educational initiatives. This quality improvement study faced

several limitations, however, including low sample size (although collection is ongoing), potential confounders, and a potential Hawthorne effect, making strong conclusions difficult.
KEYWORDS: Teaching of Child Neurology, Epilepsy

641. Increasing Comfort of Resident Physicians Treating Patients with Intellectual and Developmental Disabilities (IDD) by Facilitating Meaningful Interactions
Johnson Hannah (Boston, MA, United States) Sanders Jessica, Chiujdea Madeline, Fialkow Alexandra, Williams Kathryn, Urion David

OBJECTIVE: To describe resident physicians' discomfort with patients with intellectual and developmental disabilities (IDD) and evaluate the impact of an interactive conference session on resident physicians' comfort with people with IDD.
METHODS: During interactive conferences with 2 pediatric and 4 adult residency programs, individuals with IDD employed at a nearby art studio demonstrated their artwork and worked collaboratively on art projects with the residents. Before and after the conferences, residents completed surveys assessing their comfort with individuals with IDD, including the validated "Interactions with Disabled Persons Scale." The main outcomes were residents' ratings of their own comfort in interacting with and treating individuals with IDD (6-point scale: very uncomfortable = 1, very comfortable = 6).
RESULTS: 69 out of 537 (13%) residents completed both pre- and post-conference surveys. Although 92% of residents responding reported they had treated individuals with IDD, 75% reported they had no formal education about IDD. The mean level of comfort interacting with and treating individuals with IDD were 3.8 and 3.7, respectively, before the intervention, and 4.5 and 4.2, respectively, after the intervention ($p<.001$ and $p<.01$, respectively).
CONCLUSIONS: Our results suggest the high frequency with which resident physicians care for patients with IDD while highlighting resident's discomfort in caring for this population. Our data suggest that providing physicians with real-life connections and experiences with people with IDD can increase comfort in treating this population.
KEYWORDS: Teaching of Child Neurology, Cognitive/Behavioral Disorders (including Autism)

642. A Bibliometric Analysis of Publication Patterns in Child Neurology
Doja Asif (Ottawa, Ontario, Canada) Wilson Mitch, Sampson Margaret

OBJECTIVE: To examine the publication patterns of child neurology articles in general pediatric, general neurology, and neurology subspecialty journals using a bibliometric approach.
METHODS: The top 5 journals in general pediatrics, general neurology and neurology subspecialties were identified using the 2017 Journal Citations Report (JCR). For general pediatric journals we selected 4 pediatric subspecialties for comparison of publication patterns with neurology: immunology, endocrinology, gastroenterology, and respirology. For general neurology and neurology subspecialty journals we searched both the top 5 neurology and neurology subspecialty journals for pediatric articles. Using OVID Medline, we identified articles published between 2009-2019.
RESULTS: With regards to child neurology-based articles, 1611 were published in general pediatrics journals, 648 in general neurology journals and 740 in neurology subspecialty journals. Examination of the top pediatric journals (Table 1) revealed that *JAMA*

Pediatrics published the most neurology-based articles. Neurology-based studies were published more frequently than other pediatric subspecialty studies. Of the top general neurology journals (Table 2), *Neurology*published the most child neurology-based articles,
while *Epilepsia* published the most child neurology-based articles out of the neurology subspecialty journals. Cohort studies were the most frequent study type across all journals.
CONCLUSIONS: Our study revealed that child neurology articles are published more often in pediatric journals as opposed to general neurology and neurology subspecialty journals. We also found that in general pediatric journals, neurology-based articles are published more frequently compared to other specialties. Our results provide guidance to authors when considering submission of their pediatric neurology research.
KEYWORDS: Teaching of Child Neurology, History of Child Neurology

643. Age at Presentation to a Neurodevelopmental Clinic in a Low Income Country.
Offiong Uduak (Gwagwalada, Nigeria) Fashi Andrew

OBJECTIVE: Early recognition of a delay is critical. In many low and middle income countries e routine developmental screen or surveillance are not carried out thus presentation of children with developmental delays to healthcare facilities is dependent on caregivers' recognition and response. This study was undertaken to determine the age at which parents became concerned about their child's development, the first symptom that draw their attention to a possible problem with their child's development and the average age of children at first presentation to a neurodevelopmental clinic.
METHODS: A cross-sectional study of children 0-60months who presented with their mothers over a 3 month period. Children had no prior heralding disease/disorder except a delay in development. Data on sociodemographic characteristic, age of first recognition, type of delay and health seeking behavior of mothers were obtained.
RESULTS: Forty-nine children presented. The average age of first presentation was 25 months. The average age at caregivers' recognition of delay was 9.1months. Motor delay was the main type of delay (81%) with an average age at presentation of 21.2 months and first concern of 6.8months. Speech delay presented in 16.3% and the age at presentation was 44.1 months and first concern 21.6 months. 52% of mothers sought medical attention but only 28.5% were referred for further evaluation.
CONCLUSIONS: The results show that there is disparity between first concern and first presentation. To improve the long-term outcome of children in LMIC, strategies to improve both parental and health worker's knowledge of child development is advocated.
KEYWORDS: Teaching of Child Neurology, Cognitive/Behavioral Disorders (including Autism)

644. Project Neurotransmission: Improving Neurology Communication and Teaching
El-Hallal Maria (New York, NY, United States) Fisler Grace, Karkare Shefali, Pavkovic Ivan, Kothare Sanjeev

OBJECTIVE: To improve communication and education between the neurology team and pediatrics residents, we instituted multidisciplinary rounds with pediatric residents and implemented a novel rounding script.

METHODS: Pediatric residents completed a survey that used Likert scales to assess their satisfaction with communication and education by the neurology team for each patient encounter. They also indicated if they were present for rounds. This was followed by mandating pediatric resident attendance on rounds and the implementation of a rounding script with a section specific for teaching. A second data collection period then occurred. Likert score means were compared using a two-sample t-test with $p<0.05$ as being statistically significant.
RESULTS: In the first data collection period, 80 surveys were completed by pediatric residents who were present on rounds 45% (n= 36) of the time. Pediatric residents present during rounds were more satisfied with communication and teaching than pediatric residents absent during rounds (communication mean [M]=4.3 vs. M=2.7, $p<0.001$; teaching M=3.8 vs M=2.4, $p<0.001$). Figure 1. After mandating pediatric resident attendance at rounds and implementation of the rounding script, 95 surveys were completed by residents who were present on rounds 92% (n= 86) of the time. After controlling for resident presence during rounds, resident satisfaction with education improved after implementation of the rounding script (M=3.8 vs M=4.4, p = 0.01). Figure 2.
CONCLUSIONS: Multidisciplinary rounds with pediatric residents and the neurology team achieves good communication for shared patients. Additionally, by implementing a rounding script with a section specific for teaching, education is guaranteed with each patient encounter.
KEYWORDS: Teaching of Child Neurology

645. Length of Stay Patterns in Pediatric Neurology Hospital Admissions
Hong Annie (New Hyde Park, NY, United States) Talreja Sushil, Shah Yash, Stringel Virginia, Kothare Sanjeev

OBJECTIVE: Hospital length of stay (LOS) is an important health care quality measure that is not well studied in pediatric neurology. Two pilot quality improvement studies were implemented in 2017 to identify factors associated with discharge before noon and improve interdisciplinary communication, in order to reduce overall hospital LOS. The purpose of this study was to describe inpatient LOS patterns for pediatric neurology patients following these quality improvement initiatives.
METHODS: This was a retrospective review of patients <19 years old admitted with a principal neurological diagnosis to our hospital between 01/2017-07/2019. Scheduled admissions and hospital admissions lasting >30 days were excluded from analysis. LOS was obtained in addition to demographic characteristics, principal admission diagnosis, multispecialty care, use of multiple antiepileptic drugs (AED), and PICU admission for unplanned admissions and 7- and 30-day hospital readmissions.
RESULTS: There were a total of 1488 unplanned admissions. The most common reasons for admissions were seizure (n=941), headache (n=160), other neurological diagnosis (n=133), and behavioral (n=60). Children admitted to the hospital for a neurological condition have an average LOS of 2.8±5.0 days for unplanned admissions, 4.5±7.4 days for 7-day readmissions, and 5.2±7.5 days for 30-day readmissions. Demographics, LOS, and readmission information from 2017 to 2019 are displayed in Table 1. Linear regression for factors impacting length of stay are displayed in Table 2.
CONCLUSIONS: PICU admission, multispecialty care, readmission, multiple AEDs and behavioral diagnosis prolong overall LOS. LOS for unplanned hospital admissions and

readmissions, and overall readmission rates were similar from 2017-2019, suggesting that LOS may be relatively immutable.
KEYWORDS: Teaching of Child Neurology

646. Humanities in Neuropediatrics. Results of an experience in the training of pediatricians
Campbell Oscar (Hermosillo, Mexico) Figueroa-Duarte Ana Silvia

OBJECTIVE: As a complementary activity to the Neuropediatric course, a series of activities were carried out aimed at improving the teaching-learning of neuropediatrics disorders from a social and humanistic approach. The objective is: Improve the teaching-learning of neuropediatrics disorders from a social and humanistic approach.
METHODS: Held in Hermosillo, Sonora, with first-year pediatric residents of the Children's Hospital of the State of Sonora (MEXICO). Strategies employed: a) Reading of texts on neuropediatrics disorders and preparation of an essay. b) Review of five books of Art in Medicine and descriptive-explanatory work. c) Discussion about what was reported in his previous works. d) Final questionnaire. A qualitative methodology was used to analyze the results.
RESULTS: The students identified the need for better physician preparation; a teaching with values and ethics. For this, those in charge of their training today must emphasize the preservation and transmission of this type of knowledge. In addition, understand the students themselves their own limitations and ask for help when they need it.
CONCLUSIONS: It is necessary that the training not only focuses on the biomedical field, but also that it takes into account the social and human context of the patients, in terms of the teaching-learning of the clinic. It represents a great responsibility and moral commitment to train academically and humanistically the new generations of doctors; Above all, foster a teaching and learning environment that does not harm in principle, if the changes in the medical and institutional culture are not previously given.
KEYWORDS: Teaching of Child Neurology

647. Diagnostic yield of capilar, compared to venous glucose in the diagnosis of hypoglycorrhachia in children: a prospective, observational study
Farfan-Albarracin Juan (Bogotá, Colombia) Ramirez-Sierra Christina, Espitia-Segura Oscar, Perez-Cardenas Sofy, Tellez-Prada Hugo, Rueda-Rodriguez Maria, Lemus-Espitia Ingrid, Bedoya-Morales Ana

OBJECTIVE: The ratio of cerebrospinal fluid (CSF) glucose and blood glucose is of major relevance, conducting to the diagnosis of hypoglycorrhachia, which is a sign of neuroinfection, as well as of a number of neurological diseases of genetic or neoplastic etiology. Glucose in capillary sample (glucometry) is a low cost, readily available technique as compared to venous glucose. This study aims to compare glucometry to venous glucose in the diagnosis of hypoglycorrhachia in pediatric population.
METHODS: Prospective cross-sectional study, based on data obtained from lumbar punctures in the period from february 2017 to january 2019 in a specialized pediatric institution in Colombia.

RESULTS: 97 patients were analyzed, aged 1 month to 17 years old, mean 7.67 years, 52 (53.61%) were female. 26 (26.8%) were diagnosed with hypoglycorrhachia. Pearson correlation coefficient for absolute venous and capillary glucose was 0.54 (Figure 1), and for the ratios of CSF glucose/venous glucose and CSF glucose/glucometry, it was 0.55, which support a linear correlation between the variables in both, absolute values and ratios. Intraclass correlation coefficient was calculated for both, the venous glucose and glucometry ratios, which was 0.515 (Figure 2), revealing a moderate agreement among the tests. Sensitivity and specificity of CSF glucose/glucometry, as compared to gold standard are 73.1% and 60.6% respectively; whereas predictive positive value (PPV) and negative predictive value (NPV), were 40.4% and 86.0%.
CONCLUSIONS: Glucometry cannot replace the glucose in venous sample in the diagnosis of hypoglycorrhachia in children.
KEYWORDS: Teaching of Child Neurology

648. Pediatric Neurology in Developing Countries: Challenges and Opportunities
Ali Shaila (Lahore, Pakistan) Sultan Tipu

OBJECTIVE: Pediatric neurology is one of the largest super-speciality of pediatrics. History dates back to the Hippocratic description of seizures and other neurologic conditions in children. However, remarkable advances in pediatric neurology starts during last decade.
METHODS: Pediatric neurology evolved into a specialty early in the 20th century .In Pakistan, a lot of work is being done in the past 5 years to establish and furnish this superspeciality. Advancesments in the field of pediatric neurology particularly genetics ,immunology and neurometabolic disorders have allowed new therapeutic approaches like immunoglobulin's and immunomodulating drugs in epilepsy, neurodegeneration, demyelinating and neuromuscular disorders.
RESULTS: Fellowship:Pediatric Neurology has recently been established as a separate discipline with full training program by College of Physicians and Surgeons of Pakistan (CPSP). At present, there are three accredited departments of pediatric neurology in the country for second fellowship in Paediatric Neurology by CPSP. In 2018 , another milestone was achieved when first examination of Pediatric neurology was conducted and 6 candidates passed their examination. Meetings:Annual meetings are being held for past few years where Pediatric Neurologists from within and outside the country give their talks and expert advise. Research drug trails:Due to the active participation and research work by Pediatric Neurologists of Pakistan in internationl meetings, they are now part of research drug trials .
CONCLUSIONS: There is remarkable impact in teaching, training and patient care as this superspeciality is progressing for past couple of years.The present day status of pediatric neurology and suggestions for the future development of the specialty are very promising
KEYWORDS: Teaching of Child Neurology, History of Child Neurology

649. Online education can be an effective tool for distributing knowledge about basic neurologic assessment and epilepsy to primary care providers in low-resource setting.
Kielian Agnieszka (Boston, MA, United States) Hayes Leslie, Sham Lauren, Patel Archana

OBJECTIVE: According to the WHO, nearly 80% of people with epilepsy live in low- and middle-income countries. With proper diagnosis and treatment, up to 70% of patients can become seizure-free. In limited resource countries, 75% of people with epilepsy do not receive

adequate. In most of the developing world, epilepsy is managed by general practitioners with limited neurology consultation. The objective of this project is to create a scalable online course for primary health care practitioners in low resource settings to enhance knowledge regarding basic pediatric neurologic assessment and epilepsy.
METHODS: In partnership with Open Pediatrics, we created an online course composed of 4 videos surrounding the following topics: pediatric neurologic assessment, introduction to seizures and epilepsy, management of epilepsy, and status epilepticus. The videos were developed based on feedback from the in-person training in Zambia and Rwanda and will be piloted in those two countries in conjunction with in-person training and as a standalone online training. Pre-test and post-test will be conducted at various times intervals.
RESULTS: Pre- and post- test will be filled out by all participants with the first training to be rolled out in the Spring of 2020 in Zambia and Rwanda.
CONCLUSIONS: Online education can be an effective tool for distribution of knowledge about basic neurologic assessment and epilepsy to primary care providers in low-resource settings. We will evaluate the feasibility of constructing an online curriculum that is generalizable to two sub-Saharan African audiences, which suggests this model can be scaled to across other countries with similar resources.
KEYWORDS: Teaching of Child Neurology, Epilepsy

650. Daily Dose of Development: Feasibility of an app-based spaced education curriculum of normal child development
Goldstein Jessica (Cleveland, OH, United States) Wiznitzer Max

OBJECTIVE: Pediatric resident education in child development is historically not taught in a formalized manner despite identification by pediatricians as a priority for education. Residents must master child development to provide developmentally appropriate care. Spaced education is centered on repeated presentation of core concepts in small increments over time. This pilot study evaluated feasibility of using an app-based spaced education curriculum, Daily Dose of Development, to teach normal child development to pediatric residents.
METHODS: Participating pediatric residents were randomized to control and intervention (app) groups. The curriculum cycled over 3 months and consisted of multimedia questions presenting a developmental milestone, pushed to the learner's mobile device daily. They responded and received immediate feedback. Self-reported comfort with developmental care was collected at baseline, mid and post study. Mid- and post-study data was gathered on perceived curriculum effectiveness and usability. Pre and post difference scores were calculated for comfort level and mean differences compared using t-tests.
RESULTS: 56.7% (17/30) of residents completed all 3 study tools: 8/17 (47%) from the app and 9/17 (53%) from the control group. 100% of the app group endorsed it as an effective tool for learning child development. 88% accessed the app daily. 50% of the app group reported an improvement in their clinical developmental assessment compared to 33% in controls ($p=0.49$). Self-reported comfort with developmental care showed improvement in ability to recall and evaluate milestones and identify children with developmental delay ($p<0.01$).
CONCLUSIONS: A novel app-based longitudinal spaced-education curriculum teaching fundamental concepts in child development was well-received by pediatric residents.
KEYWORDS: Teaching of Child Neurology

651. Pediatric Neurology Research in the 21st Century: Status, Challenges, and Future Directions Post-COVID-19

Bonkowsky Josh (Salt Lake City, UT, United States) deVeber Gabrielle, Kosofsky Barry

OBJECTIVE: The field of pediatric neurology is undergoing a radical transformation. A historically unprecedented research effort has advanced the ability to diagnose, treat, and even cure developmental brain disorders. However, research funding limitations; corporate goals vs. academic research missions; and increasingly costly research technologies; present obstacles to future research in pediatric neurology. Our objective was to evaluate the current status of pediatric neurology research; identify barriers and challenges; and make suggestions as to future directions and efforts in the post-COVID-19 era.
METHODS: In response to a Request for Information from the NIH/NINDS, Strategic Planning Process (NOT-NS-19-079), the Research Committee of the Child Neurology Society evaluated by coordinated and step-wise consensus-building teleconferences, current and future status, challenges, and opportunities in pediatric neurology research across the designated themes of science, training, communication and work force culture.
RESULTS: Although significant obstacles were noted, unique opportunities were identified including improving research data infrastructure achievable by capitalizing on electronic health record data and data element standardizations; increasing relative underfunding across all areas of pediatric neurology research; recognizing design aspects unique to pediatrics in trials and natural history studies; engaging and synergizing across patient advocacy groups; enhancing minority research trainee pathways; addressing disparities in research and treatment gaps; adjusting funding mechanisms to reflect work-life balance realities of 21st century physician-scientists with family obligations; and committing to a sustainable work-force in pediatric neurology research.
CONCLUSIONS: We identified key priorities in pediatric neurology research that can best be accomplished through focused involvement by NIH and other funding stakeholders post-COVID-19.
KEYWORDS: Teaching of Child Neurology, Translational/Experimental Therapeutics, Neuroscience

652. Qualitative Analysis of Neurology Consulting Services in a Pediatric Emergency Department

Hiller Matthew (Denver, CO, United States) Martin Jan, Hanson Janice

OBJECTIVE: Based on preliminary survey data from our institution, there is room for improvement in effective use of an already highly utilized neurology consult service. We sought to construct a grounded theory describing barriers to effective use of the neurology consult service in the pediatric emergency department and explore interventions to address these barriers.
METHODS: We interviewed providers from neurology and emergency medicine, including residents, fellows, NPs/PAs, and attending physicians. The interviews were semi-structured, with iterative data analysis as emergent themes informed future interviews. Interview questions focused on common reasons for requesting consults, areas for educational interventions, and ideas for implementation.

RESULTS: We performed 14 interviews with 6 neurology providers, and 8 emergency room providers. Several common themes emerged. First, there is wide variation in education around the neurological exam. Both groups expressed an interest in an educational curriculum focusing on "red flag" neurological signs, specifically those with high inter-observer reliability. Second, many emergency providers feel uncomfortable independently determining initial workup of common neurological complaints, such as new-onset seizure, headache, and weakness. Much of this discomfort stems from a lack of confidence in their initial assessment of the patient.
CONCLUSIONS: Based on our interview data, we propose that improving neurological examination skills of emergency providers will result in more efficient use of neurology consult services. The next step is designing an educational intervention which improves emergency providers' skills in the initial assessment of a child with a neurological complaint.
KEYWORDS: Teaching of Child Neurology

653. Current Practice Habits and Educational Opportunities in the Evaluation and Management of Pediatric Seizures in Guatemala
Racancoj Sac Matilde (Guatemala City, Guatemala) Huix Ramos Eugenia, Molina Wolfre, Henriquez Alicia, Kammeyer Ryan, Walleigh Diana

OBJECTIVE: To evaluate current practice habits and identify topics of education for optimizing the care of pediatric patients presenting with seizure to National Hospital Juan Jose Ortega (NHJJO), a regional hospital in Coatepeque, Guatemala
METHODS: A retrospective chart review of pediatric patients presenting to NHJJO with seizure from 2016-2018 was performed. A "most likely" retrospective clinical diagnosis (RCD) based on history/presentation alone was created for each patient, to allow determination of appropriateness of subsequent diagnostic and management strategies. RCDs of interest included first time unprovoked seizure (FTUS), simple febrile seizure (SFS), and complex febrile seizure (CPS).
RESULTS: A total of 127 pediatric patients presented with seizure during the study interval. 8% of patients in status epilepticus received a benzodiazepine. 60% of patients presenting with a single seizure received an acute anti-seizure medication (ASM) load. The concordance of an RCD with the given diagnosis ranged from 53% to 65%. For an RCD of SFS and FTUS, respectively, early EEG was obtained in 14% and 47%, and head CT in 6% and 18% of patients. Four patients with a febrile seizure at <2 months old did not receive a lumbar puncture. 35% of patients presenting with an RCD of FTUS were prescribed a daily ASM, with phenytoin most commonly prescribed.
CONCLUSIONS: Using this study of practice habits, a curriculum was developed focusing on common seizure presentations, yield of various diagnostic/management strategies, and indications for prescribing daily ASMs. The RCD framework will be used to determine effectiveness of the intervention on future practice habits.
KEYWORDS: Teaching of Child Neurology, Epilepsy

654. Using Telemedicine platform to train Neurology residents in clinic
Menon Deepa (Baltimore, MD, United States) Shapiro Bruce, Leppert Mary

OBJECTIVE: Innovative electronic platforms can be used to train resident physicians in the neurodevelopmental evaluation and to incorporate just in time didactic instruction to enhance the learning experience of the trainee.

METHODS: The Zoom platform embedded within EPIC and HIPPA protected , allows the resident and preceptor to access medical records ,to connect with the patients and family remotely . Prior to the clinic visits the preceptor and resident discuss the cases allocated to them , do a quick record review to view relevant labs and imaging The resident then conducts the evaluation of the patient ,discusses the patient in the Zoom breakout room with the attending who then interact with the family . Standardized neurological evaluation and comprehensive Neurodevelopmental evaluation was conducted . Preceptors used in time didactic brief presentations (10-15 min) to educate the resident
RESULTS: high satisfaction with families , residents and attending physicians demonstrated using satisfaction surveys done at the time of the visit
Residents preferred multimodal learning opportunity, just in time learning and ability to learn from multidisciplinary team members. Teaching Attendings preferred clinic efficiency, , ability to use standardized curricular material to provide just in time teaching to residents and families
CONCLUSIONS: Telehealth to teach residents in a Neurodevelopmental clinic was effective. The multimodal method of interacting and learning from patients in the safety of their homes , and in time learning valued by the millennial learners
KEYWORDS: Teaching of Child Neurology

TRANSLATIONAL/EXPERIMENTAL THERAPEUTICS

655. Transpher B, an open-label, multicenter, single-dose, dose-escalation, Phase 1/2 Clinical Trial of gene transfer of ABO-101 in Sanfilippo Syndrome type B (Mucopolysaccharidosis IIIB)

Flanigan Kevin (Columbus, OH, United States) de Castro Maria, Heron Benedicte, Couce Maria, Truxal Kristen, McBride Kim, Ravelli Claudia, McNally Kelly, Simmons Tabitha, Rinaldi Federica, Giraudat Kim, Lopez Luisa, Siffert Joao, Oreiro M, Ruiz Juan

OBJECTIVE: Study the safety and efficacy of intravenous ABO-101 (AAV9-based gene vector expressing the human *NAGLU* gene) in children with Sanfilippo syndrome type B (MPS IIIB).
METHODS: Transpher B is a Phase 1/2 of ABO-101 in children with MPS IIIB receiving 1 X 10^{13} vg/kg (Cohort 1, n=2), 5 X 10^{13}vg/kg (Cohort 2, n=5), and 1 X 10^{14} vg/kg (Cohort 3, up to 5). Evaluations include serial measures of general safety, biomarkers, liver and brain volumes and neurodevelopment.
RESULTS: 8 patients have been treated. Follow-up is 13-26 months in Cohort 1, 2.3-9 months in Cohort 2 and 7 days in Cohort 3. No serious drug-related adverse events have been found. *NAGLU* plasma enzyme activity showed a dose-dependent normalization, lasting up to 3 months in Cohort 2. A rapid reduction in CSF heparin sulfate (HS) was observed in all patients treated, up to 79% decrease at month 12 (longest follow-up, Cohort 1, n=1). Abdominal MRI showed a rapid decrease in liver volume, sustained at months 6 (n=2) and 12 (n=1) in Cohort 1. Limited follow-up duration to date preclude adequate assessment of neurological outcomes.
CONCLUSIONS: Intravenous administration of ABO-101 in children with MPS IIIB was well tolerated with no treatment-related SAEs. ABO-101 showed a biologic effect, including a dose-dependent normalization of enzyme activity in plasma up to month 3, decreased CSF HS levels (maintained up to month 12 in Cohort 1) and diminished liver volume. A longer follow-up is needed to evaluate neurodevelopmental changes.

KEYWORDS: Translational/Experimental Therapeutics, Rare Diseases, Neuromuscular Disorders

656. Early-Onset Efficacy and Safety Pilot Study of Amphetamine Extended-Release Oral Suspension (AMPH EROS) in the Treatment of Children with Attention-Deficit/Hyperactivity Disorder

Pardo Antonio (Monmouth Junction, NJ, United States) King Thomas, Kando Judith, Dansie Lorraine

OBJECTIVE: Determine if AMPH EROS has an onset of effect at 30 minutes post-dose in children with ADHD.
METHODS: Randomized, double-blind, 2-treatment, 2-sequence, placebo-controlled crossover pilot study enrolled subjects 6-12 years with ADHD. A dose of 5-20 mg/day of AMPH EROS was optimized during a 1-week open-label phase based on medication history, symptom control, and tolerability. Subjects completed a practice laboratory classroom then received one day of double-blind AMPH EROS or placebo each in sequence during 2 double-blind laboratory classroom days. Subjects completed the first double-blind laboratory classroom, returned to open label drug for 5 days then crossed over on day 6 during a second double-blind laboratory classroom. Double blind dose was AMPH EROS 15, 17.5, or 20 mg. Primary endpoint was change from predose in SKAMP-C score measured at 30 minutes on two double blind days. Key secondary endpoint was change from predose in SKAMP-C after 3 hours for AMPH EROS vs placebo. Safety included vital signs and adverse events.
RESULTS: Eighteen subjects enrolled (14 males); mean age of 9 years. At 30 minutes and 3 hours postdose, changes from baseline in SKAMP-C for AMPH EROS vs. placebo were statistically significant ($p<0.01$ and $p=0.0002$, respectively) with corresponding effect sizes of 0.96 and 1.57. Adverse events (>10%) during the open-label phase included upper respiratory tract infection, fatigue, upper abdominal pain, headache, decreased appetite, and affect lability.
CONCLUSIONS: AMPH EROS was effective in reducing ADHD symptoms at 30 minutes postdose. AEs were mild and consistent with those of other ER amphetamines.
KEYWORDS: Translational/Experimental Therapeutics

657. Anxiolytic Dosing of Oral Midazolam Reduces General Sedation Need in Patients Receiving Intrathecal and Intra-Port Therapeutic Medications

Shea Stephanie (Aurora, CO, United States)

OBJECTIVE: Children's Hospital Colorado (CHCO) has a Complex Drug Program to coordinate care for patients receiving treatment with therapies including gene therapy, enzyme replacement, and ASO mediated treatments such as Zolgensma, Brineura, and Spinraza. This program coordinates care, scheduling, and insurance approval for treatment. Spinraza is administered intrathecally every three months on maintenance therapy while Brineura is administered via intraventricular every two weeks on maintenance therapy. Regularly repeated therapies such as these in pediatric patients raise complicating issues related to anxiety surrounding treatment. This prompted our program to further consider sedation needs as part of a desire to avoid repeated use of sedation in these patients.
METHODS: As part of this program and in consultation with anesthesia, we began the use of anxiolytic dosing (0.5 mg/kg up to 20 mg maximum) oral Midazolam to avoid repeated general

sedation. This improved comfort with the dosing as it is outside of typical Neurology experience. This dosing is provided in a controlled setting with specialized nurse support, vital sign monitoring, and post-procedure monitoring.
RESULTS: Of the 35 Spinraza patients and 2 Brineura patients currently in treatment at CHCO, 14 receive local anesthesia only, 11 receive local and general anesthesia, and 10 receive local and anxiolytic oral midazolam. The oral midazolam allows for significant improvement in procedural anxiety, pain reduction, and the added benefit of reduced sedation exposure.
CONCLUSIONS: Anxiolytic oral midazolam dosing is beneficial to avoid repeated general sedation while providing a marked reduction in procedure-related anxiety and improved comfort in pediatric patients.
KEYWORDS: Translational/Experimental Therapeutics, Neurometabolic Disorders, Neuromuscular Disorders

658. A Novel, Modified Release Drug Delivery Technology Containing Amphetamine-Ion Exchange Complexes
Pardo Antonio (Monmouth Junction, New Jersey, United States) King Thomas, Dansie Lorraine, Kando Judith

OBJECTIVE: The proprietary immediate/extended drug delivery technology LiquiXR™ utilizes an ion-exchange resin that complexes with any protonated, water-soluble active moiety. LiquiXR™ technology allows for customized, sustained release of active drug for ~24 hours. Mechanistically, drug particles enter the gastrointestinal (GI) tract. As positively-charged ions from GI fluids diffuse across the coating, ionically-charged drug diffuses through the coating, into the GI fluids. As the coating is of variable thickness, some drug takes longer to diffuse+absorb, providing for programmable delayed release.
METHODS: The active drug complexes with ion-exchange polymers in the resin, which is then formed into micron-sized particles. Some particles are coated with an aqueous, pH-independent polymer for immediate or sustained release. The coating applied to the ion-exchange resin particles is of varying thickness for programmed, extended release. Solid, coating-free particles provide for immediate release. The micron-sized particles are formulated into solid or chewable tablet, suspension, orally disintegrating tablet, film, or capsules. Active drug is subsequently released in millions of particles, driven by ion exchange and diffusion. After release, the ion-exchange resin is excreted.
RESULTS: The LiquiXR™ drug delivery technology is utilized in Dyanavel® XR (amphetamine extended-release oral suspension; AMPH EROS), indicated for ADHD. It comprises 2.5 mg/mL amphetamine base complexed with the technology for immediate release followed by an extended release, with onset of effect demonstrated at <1 hour after dosing and efficacy observed through 13 hours.
CONCLUSIONS: The efficacy reported for AMPH EROS provides an example of the clinical application for other active drug products requiring an immediate release and extended release profile.
KEYWORDS: Translational/Experimental Therapeutics

TRAUMA

659. Amygdala Hypoconnectivity and Emotional Blunting in Pediatric TBI

Sheridan Christopher (Los Angeles, CA, United States) Bickart Kevin, Olsen Alexander, Dennis Emily, Babikian Talin, Asarnow Robert, Giza Christopher

OBJECTIVE: In survivors of pediatric traumatic brain injury (TBI), socioemotional dysfunction often remains undetected and undertreated. We hypothesized that limbic circuits are particularly vulnerable to TBI, which may underlie such dysfunction.
METHODS: We studied 19 patients (mean age: 17±2) 13-19 months after moderate/severe TBI recruited from 4 pediatric intensive care units as well as 44 well-matched healthy controls (HC). Resting-state fMRI and T1 images were processed and analyzed in the CONN Toolbox. We leveraged three previously published large-scale resting-state networks of the amygdala to compare connectivity across groups and determine whether connectivity strength correlates specifically with disruptions in emotion and behavior but not cognition in the TBI patients.
RESULTS: Compared to HCs, patients with TBI demonstrate weaker connectivity within a medial amygdala network, which includes structures involved in both reward- and goal-based behavior (Figure 1, t=2.02, p<0.05, Effect size 0.56). Patients with the weakest connectivity showed the lowest emotional and behavioral reactivity ratings on the BRIEF (r=0.55, p=0.05) and CBCL (r=0.47, p<0.05), respectively (Figure 2), but no difference in working memory ratings on the BRIEF.
CONCLUSIONS: Medial amygdala resting-state circuitry may be particularly vulnerable to TBI in adolescents. Hypoconnectivity in this resting-state network could be a useful biomarker specific to emotional and behavioral impairments after TBI and could be a target for therapies that modulate the function of these connections.
KEYWORDS: Trauma, Neuroimaging, Cognitive/Behavioral Disorders (including Autism)

660. USE OF SPACE TECHNOLOGIES IN REHABILITATION OF CONSEQUENCES OF TRAUMATIC BRAIN INJURY IN ADOLESCENTS

Nemkova Svetlana (Moscow, Russian Federation)

OBJECTIVE: Study of the effectiveness of system of neurodynamic correction (SNC) using space suit “Adeli” into the rehabilitation of adolescents with the consequences of traumatic brain injury (TBI).
METHODS: 297 adolescents were examined in the long-term period of TBI. Vertical body stability (VBS) using computer stabilography, hand movements (HM), cognitive testing (Raven's Progressive Matrices), as well as speech, the ability to self-service and training were studied before treatment, after course of conventional treatment (CT) and after a course of SNC.
RESULTS: VBS was reduced after the MTBI in 5 times and after STBI in 12 times. After SNC the VBS was improved in patients with MTBI by 66 %, STBI by 54%, exceeding the results of CT (p<0,05).
SNC efficiency in restoring HM was 2 times higher than the results of CT (p<0,05). Cognitive test results were reduced in patients with LTBI by 20 %, MTBI by 54 %, STBI by 70 %. After SNC cognitive functioning in patients with LTBI was enhanced by 19%, MTBI by 37 %, STBI by 43 % (p<0,05). After the use of SNC, clinical improvement was observed in 95 % of patients with LTBI, 82 % with MTBI and 54 % with STBI, with restoration of ability of self-care in 67

% of patients after MTBI and 63% after STBI, ability to study in 83% and 72%, respectively, as well as speech function in 56% and 45%.
CONCLUSIONS: SNC using space suit "Adeli" is a highly effective method of rehabilitation of the consequences of TBI in adolescents
KEYWORDS: Trauma, Neurorehabilitation

661. A Novel Pediatric TBI Clinic Model
Otallah Scott (Winston Salem, NC, United States)

OBJECTIVE: Patients seen in a pediatric TBI Clinic focused on non-sports injuries between 2018 and 2020 were reviewed with the goal of identifying areas where neurology involvement altered/improved care.
METHODS: In 2017 a Pediatric TBI clinic was established at Wake Forest with a focus on TBIs sustained by a significant mechanism of injury or mild TBIS with prolonged post-concussive symptoms (PPCS). All charts with ICD10 diagnoses of concussion, post-concussion headache, post-concussion syndrome, and traumatic brain injury were reviewed.
RESULTS: 84 cases were reviewed. In 49 cases, management was altered from the initial course taken by the ER physician, PCP, or sports medicine provider with resultant positive symptom trajectory or symptom resolution. In 43 cases, pre-existing risk factors played a significant role in prolonged post-concussive symptoms (>1 month). Small SAH, SDH, epidural hemorrhages, or skull fractures were present in 20 patients and lead to differential counseling. There was an association between more mild mechanism of head impact and more prolonged symptoms in this cohort (often mediated by pre-existing PPCS risk factors). 14 patients had other neurologic diagnoses (tics, seizure-like-activity, etc.) that were addressed.
CONCLUSIONS: Pediatric Neurologists are steadily becoming more involved in the diagnosis and management of concussion/TBI. Sports neurology is a burgeoning field. Non-sports mild TBI has a higher prevalence than sports concussion in many studies. Given the greater forces involved in accidental injuries such as motor vehicle collisions and resultant co-morbidities (intra-cranial hemorrhage, seizure, etc.) the skill set of a child neurologist is even more relevant for these children than in sports participants.
KEYWORDS: Trauma, Headache/Migraine, Neurorehabilitation

662. A Glimpse into the Concussion Specialty Clinic: When to Refer
Baham Michael (Los Angeles, CA, United States) Sheridan Christopher, Kang Kaylee, Choe Meeryo, Pearson Rachel

OBJECTIVE: Pediatric concussion has been identified as a key public health concern and common presentation to outpatient settings. While most patients recover within 4 weeks, a subset develop persistent post-concussive symptoms and benefit from referral to a specialized pediatric concussion clinic. We aimed to characterize this subset of patients.
METHODS: Retrospective chart review of patients presenting between May 2016-May 2019. We included consented 7-25 year old patients diagnosed with concussion/mild traumatic brain injury (TBI) in our clinic registry. We excluded patients with moderate-severe TBI and/or significant missing data. Demographics, injury characteristics, past medical and family history data were extracted.

RESULTS: 332 patients (50.3% female, mean age 15.9 years) were included. Median time to presentation was 45 days post-injury. 16 (4.8%) patients had intracranial injuries and 44 (13.3%) loss of consciousness. 154 (46.4%) had at least one prior concussion. Pre-existing comorbidities included: 122 (36.7%) headaches, 93 (28.0%) anxiety, 60 (18.1%) depression, 43 (13.0%) ADHD and/or learning disability, and 57 (17.2%) sleep disturbance. 154 (46.4%) had family history of migraine/headaches, 67 (20.2%) ADHD/learning disabilities, and 110 (33.1%) depression, anxiety, or other psychiatric diagnosis.
CONCLUSIONS: While overall concussion incidence is higher in males, our patient population has a disproportionately high female prevalence, notably presenting >4 weeks from injury. In addition, there was a high prevalence of patients with history of concussion and other pre-existing comorbidities or pertinent family history. These are factors that should lead clinicians to consider early referral to a specialized pediatric concussion clinic.
KEYWORDS: Trauma

663. Not Your Typical POTS: Prevalence of Post-Concussive Orthostatic Tachycardia in a Concussion Specialty Clinic
Pearson Rachel (Los Angeles, CA, United States) Sheridan Christopher, Kang Kaylee, Baham Michael, Choe Meeryo

OBJECTIVE: Postural orthostatic tachycardia syndrome (POTS) occurs in some patients after concussion/mild traumatic brain injury (mTBI); mTBI is the second most common trigger preceding POTS. There is significant overlap between POTS and post-concussive symptoms which may lead clinicians to overlook POTS and miss opportunities for targeted interventions. We hypothesized that a substantial proportion of patients presenting to pediatric concussion clinic exhibits orthostatic tachycardia (OT) and that females and adolescents would be most likely to have post-concussive OT.
METHODS: Retrospective review of 343 patients presenting from May 2016-May 2019. We included 7-25 year olds with mTBI/concussion diagnosis and orthostatic vitals measured on their initial visit, excluding patients with pre-existing POTS and/or moderate-severe TBI. OT was defined as orthostatic heart rate change ≥30 bpm. Sex and age group (7-12 vs 13-25 years) differences between patients with and without OT were analyzed using Chi-squared tests with p-value<0.05 for significance.
RESULTS: 291 patients (51.9% female, median age 15.8 years) met inclusion criteria. 15.8% were <13 years. Median time to presentation was 46.4 days post-injury. 59 (20.3%) patients had OT: 26 (44.1%) females and 49 (83.1%) ≥13 years. There was no significant association between OT presence and sex (X^2 [1, N=291] =1.8, p=0.178) or age (X^2 [1, N=291] =0.07, p=0.778).
CONCLUSIONS: While POTS literature describes female and adolescent predominance, we found that post-concussive OT occurs with similar prevalence between sexes and pre/post-pubertal ages. Clinicians should screen for OT after concussion as this may inform treatment strategies, including increasing hydration/salt, graded exercise programs, medications, relaxation/meditation protocols, and cognitive behavioral therapy.
KEYWORDS: Trauma, Neurorehabilitation

664. The Need for Occupational Therapy in an Multidisciplinary Concussion Clinic
Harris Madison (Los Angeles, CA, United States) Rafeedie Samia, McArthur David, Babikian Talin, Snyder Aliyah, Westerberg Shannon, Polster Douglas, Giza Christopher

OBJECTIVE: Further identify the need for an occupational therapist (OT) in an interdisciplinary concussion clinic.
METHODS: A qualitative comparison of a retrospective and prospective cohort of patients seen in an interdisciplinary concussion clinic at a single academic institution were included. Patients were 12-24 y/o and referred for suspected concussion. Exclusion criteria: moderate/severe TBI diagnosis, <8 or >24y/o, or missing data. Domains of practice were identified by a single researcher using the *Occupational Therapy Practice Framework* and include occupations, client factors, performance skills, performance patterns and context. An initial evaluation note for 51 consecutive patients seen by a physician were reviewed for the retrospective cohort. The prospective cohort included patients seen with both physician and OT present. Research published in 2019 included 121 consecutive patients. 71 additional prospective patients have been included in this cohort.
RESULTS: 49 retrospective patients, and 139 prospective patients meet inclusion criteria. Average time since injury (TSI) for the retrospective and prospective cohort is 188.00 days (SD 328.49) and 170.43 days (DR 297.16) respectively. There is no significant difference in TSI between the two groups (p= 0.350) and no significant difference (p=0.910) for age between the retrospective cohort (16.35 y/o, SD=3.46 y/o) and the prospective cohort (16.88 y/o, SD=3.59 y/o). Preliminary analysis shows that "performance skills" are more often identified when an OT is present during initial evaluation than when not (78% prospective, 37% retrospective).
CONCLUSIONS: Inclusion of OT in an interdisciplinary concussion clinic allows for increased identification of impacted domains, prompting more comprehensive care for concussion patients.
KEYWORDS: Trauma

665. The prevalence of sleep difficulties in pediatric concussion patients
Ronay Avy (Lake Success, NY, United States) Hogan Katherine, Pavkovic Ivan, Kothare Sanjeev

OBJECTIVE: To identify sleep difficulties after a concussion in the pediatric population, compare symptoms affecting sleep and determine co-morbid conditions augmenting sleep difficulties.
METHODS: A retrospective chart review of patients with concussions seen at a tertiary-care children's hospital was done. A 23 item questionnaire was provided to patients prior to their visit. If the patient answered yes to questions pertaining to sleep difficulties, 8 further questions reflecting sleep were asked. Data reflecting other post-concussive symptoms was also collected.
RESULTS: One-hundred-sixteen patients who suffered a concussion within two weeks of injury were included in this study. Thirty-eight-percent endorsed having difficulty falling asleep, 61% reported being more tired than usual, 34% were sleeping more than usual. Twenty-one-percent endorsed all three complaints. Thirteen-percent of patients reported sleep difficulties prior to the injury and 20% with prior history endorsed at least one of the three complaints.
CONCLUSIONS: Patients who suffered from a concussion subsequently had sleep difficulties, either involving initiation or maintenance of sleep and or general somnolence. Discussing sleep-hygiene prior to injury should be instituted in all children who are predisposed to injury. Further investigations are warranted on the use of melatonin in patients with sleep-dysregulation after a concussion.
KEYWORDS: Trauma, Neurorehabilitation

666. Spontaneous regression of an enhancing lesion in a 3 year old girl with left sixth nerve palsy

Osman Mohaned (Cambridge, MA, United States) Caruso Paul, Krishnamoorthy Kalpathy, Staley Kevin

OBJECTIVE: Sixth nerve palsy may be due to a number of causes, depending on the location along the path of the nerve. In children, the most common causes of sixth nerve palsy are tumors, trauma, increased ICP, and congenital lesions. Here we report a case sixth nerve palsy with unusual MRI finding.
METHODS: We report a case of a 3 yo F with one day of left eye eso-deviation. History was unremarkable except for mild trauma several hours prior, consistent with the car door hitting the back of her head.
RESULTS: On evaluation, patient had L sixth nerve palsy. Serum and CSF work up was unremarkable. An MRI Brain was obtained that showed an enhancing lesion along the left Dorello canal along the course of the L 6th cranial nerve. The differential diagnosis was suspected to be a blood clot in the setting of reported mild trauma. Neoplastic such as meningioma, polyclonal lymphoproliferative disorders and Chordomas, Inflammatory disorder such as as IgG related disorders, Wegner Granulomatosis and Sarcoidosis. Infectious causes such as Gradenigo syndrome and Vascular cause such as A-V fistula. She was treated with a course of steroids with no improvement.
CONCLUSIONS: MRI Brain at 2 and 3 months interval showed reduction of the mass with complete resolution of the nerve palsy favoring a resolving retroclival hematoma with small thrombus. Traumatic retroclival epidural hematoma is a rare entity, occuring in conjunction with high speed MVA [1,2]. To our knowledge, we are unaware of cases with similar imaging in the setting of mild trauma.
KEYWORDS: Trauma, Neuroimaging

667. Factors Predictive of Significant Post-Concussive Symptoms in a Pediatric Concussion Clinic

Parikh Karishma (New York, NY, United States) Duggan Ryan, Hamilton Cameron, Wascher Alexander, Catarozoli Corinne, McCarthy Matthew, Kosofsky Barry

OBJECTIVE: Persistent post-concussion symptoms (PPCS) are defined as a constellation of physical, cognitive, emotional, and/or sleep symptoms persisting ≥28 days after concussion. We aimed to identify independent predictors for PPCS based on patients' initial post-concussive symptom inventory (PCSI), medical history, and comorbidities.
METHODS: A retrospective chart review was performed on 281 patients (45% female, mean age 12.9 years) seen over a 7-year period at a single pediatric neurology concussion clinic. Factors contributing to PCSI scores ≥12 were compared for patients presenting to our clinic <28 days (n = 191) vs. ≥28 days (n = 90) following concussion.
RESULTS: Patients presenting at <28 days had significantly lower total PCSI scores than those presenting at ≥ 28 days (p= 0.003) as well lower subscores for cognitive (p = 0.006), affective (p <0.001), and sleep (p = 0.003) symptom clusters. The ANOVA/tests of association with higher PCSI score demonstrated significant main effects of female gender (p < 0.001), personal history of headache (p <0.001), and longer time to visit (p = 0.007), along with a significant three-way interaction of these (p = 0.009). Significant main effect of family history of headache (p = 0.003)

and personal history of anxiety (p = 0.007), along with a two-way interaction of personal history of anxiety and later time to visit (p = 0.007) was also seen with higher PCSI scores.
CONCLUSIONS: Physicians can prospectively identify pediatric patients with high risk of developing PPCS, which can help direct treatment and management at the time of initial evaluation.
KEYWORDS: Trauma, Neurorehabilitation, Headache/Migraine

668. Anti-seizure medication prophylaxis for children with traumatic brain injury
Surtees Taryn-Leigh (Ann Arbor, MI, United States) Kumar Ishani, Garton Hugh, Shellhaas Renee

OBJECTIVE: Prophylactic anti-seizure medications (ASMs) have been studied in adults with traumatic brain injury (TBI), but less is known about ASMs for children with TBI. We evaluated clinical features that inform decision-making regarding prophylactic ASMs in pediatric TBI.
METHODS: Retrospective, single-center study of every child (age <18 years) admitted for TBI from January to December 2019.
RESULTS: Among 66 patients (61% male; age 7.7±6.3 years), 35 (53%) received ASM prophylaxis. Most children (71%) prescribed ASM prophylaxis received levetiracetam 20mg/kg/day, 2 children >20mg/kg/day, and 8 adolescents 500mg BID (<20mg/kg/day). Five (8%) developed EEG-confirmed seizures during the acute admission; all 5 were on prophylaxis and had inflicted and/or severe TBI. ASM prophylaxis was more commonly prescribed for children with neurosurgical intervention (8/8 ASM vs 27/58 no ASM, Fisher exact p=0.006), neurology consultation (15/18 vs. 20/48, p=0.005), abnormal neuroimaging (33/46 vs 2/20, p<0.0001), and/or suspected clinical seizures (12/15 vs 23/51, p=0.02). Duration of ASM prophylaxis varied. Excluding those with EEG seizures, 8 children (27%) were prescribed ASM for <7 days, 14 (47%) 7 days, and 8 (27%) for >7 days.
CONCLUSIONS: Children with more severe TBI received prophylactic ASM most often, and the 8% post-traumatic seizure rate was consistent with the published literature. Yet, a consistent treatment approach is not equivalent to optimal evidence-based management. While some studies suggest it may be inferior to phenytoin, levetiracetam was the exclusive ASM used for prophylaxis at our center. Data from our ongoing research highlight the need for focused study of ASM prophylaxis and prevention of post-TBI seizures in children.
KEYWORDS: Trauma, Critical Care

669. Changes in Working Memory-Related Cortical Activation Following Paediatric Mild Traumatic Brain Injury: A Longitudinal Study
Stein Athena (Brisbane, Australia) Iyer Kartik, Barlow Karen

OBJECTIVE: Persistent post-concussion symptoms (PPCS) affect one in seven children for three months or longer following a mild traumatic brain injury (mTBI), with memory problems as a common complaint. We aimed to examine differences in neural responses within the dorsolateral prefrontal cortex (dlPFC) and default mode network (DMN) between one and two months post-injury in children with PPCS, during a *n*back working memory (WM) task.
METHODS: Using a prospective controlled cohort study design, we examined 29 children exhibiting PPCS (mean age 14.9 ±2.25; 48.3% male). Participants were part of a randomized, placebo-controlled, clinical trial of melatonin conducted in children with PPCS at 4-6 weeks

post-injury. Children performed the WM *n*back task during fMRI acquisition twice, at one and two months post-injury. The primary outcome was change in neural activations of the dlPFC over time. The secondary outcome was whether recovery status affected changes in neural activations over time.
RESULTS: Significant increases in dlPFC-related neural activations over time were observed at the group level (t-test, $p<0.05$, family-wise error-corrected). Thirteen participants had clinically recovered at the time of the second scan. Repeated-measures ANOVA analyses indicated no significant differences in recovery status nor response to melatonin treatment over time.
CONCLUSIONS: Neural responses in the dlPFC increased over time in children with PPCS, suggesting improved DMN deactivation during recovery. These changes, however, were not significantly correlated with recovery. Our findings contribute to understanding changes in working memory function in children with PPCS following mTBI.
KEYWORDS: Trauma, Neurorehabilitation, Neuroimaging

670. Headaches After Youth Concussion – Migrainous Phenotype Treatment and Outcome: A Study from the 4 Corners Youth Consortium
Blume Heidi (Seattle, WA, United States) Kamins Joshua, Richards Rachel, Locandro Christopher, Barney Bradley, Pacchia Nina, Cook Larry, Rivara Frederick, Gioia Gerard, Giza Christopher

OBJECTIVE: 1: Compare baseline characteristics among concussed youth with migrainous post-traumatic headache (MH) and non-migrainous post-traumatic headache (NMH) 2: Describe treatments used to manage PTH in youth 3: Compare the time to concussion symptom resolution and risk of headache after injury between those with migrainous vs. non-migrainous PTH
METHODS: Subjects were 5-18 years old and presented to participating specialty TBI clinics after concussion. Headache phenotypes were defined using the post-concussion symptom inventory as MH, NMH, or "no new headache". Outcomes were time to recovery from concussion, and presence of concussion-related-headache 3 and 6 months after injury.
RESULTS: The study included 294 concussed youth. Patient and injury characteristics were similar between MH and NMH groups (Table 1). Preventive prescription medications were prescribed to 22% of MH and 8% of NMH groups ($p=0.024$), supplements were recommended for ~37% of both groups. Time to recovery was longest for those with MH (Fig 1). Within each PTH phenotype, recovery time was not different between males and females (MH $p=0.94$, NMH $p=0.84$). At 3 months, PTH was endorsed by 25% of MH and 12% of NMH groups ($p=0.09$), and by 12% of MH and 4% of NMH groups at 6 months ($p=0.22$).
CONCLUSIONS: Migrainous PTH is associated with prolonged recovery following concussion and may have a stronger association with prolonged recovery than female gender. Further study investigating PTH phenotype will help to identify youth at risk for persistent symptoms and may provide a target for early intervention.
KEYWORDS: Trauma, Headache/Migraine

671. Clinical Definition of the Academic Effects of Concussion: Psychometric properties of the Concussion Learning Assessment and School Survey-3 (CLASS3) Self-Report
Gioia Gerard (Rockville, MD, United States) Vaughan Christopher, Sady Maegan, Cullum Munro, Didehbani Nyaz, Babikian Talin, Giza Christopher

OBJECTIVE: Define the psychometric properties of an assessment tool of academic problems post-concussion, the Concussion Learning Assessment and School Survey-3 (CLASS3)
METHODS: 791 patients (ages 10-18, mean=14.1 years, 45% male), diagnosed with concussion were administered the CLASS3 to define resulting academic problems and stresses. The CLASS3 identifies 14 academic problems, difficulties with 5 academic subjects, and 6 stress types (0-3 severity). Evidence of reliability and validity was examined.
RESULTS: Examination of scale structure (construct validity) via factor analysis revealed: 2-factor solutions for academic problems (academic skills, symptom interference) and school stress (academic, extracurricular stresses). Internal consistency reliability was excellent for academic problems (alpha=0.93) and symptom interference (alpha=0.84), and expectedly lower on the shorter stress subscales (4-item academic alpha = 0.75; 2-item extracurricular=.52). Evidence of concurrent validity was demonstrated with post-concussion symptoms (e.g., Academic problems subscale with PCSI Cognitive scale r=.65 (p<.001) and the School Stress scale with PCSI Emotional scale r=0.42 p<.01). Sex differences were not observed on the CLASS3, but higher grade level was associated with greater academic problems and stresses (p<.01).
CONCLUSIONS: Students who sustain concussions commonly experience challenges in returning to school during recovery, requiring definition of their needs to provide targeted supports. Psychometric analyses of the CLASS3 provide evidence of reliability and validity in defining the factor structure and internal consistency of its subscales, its relationships with similar measures, and grade- based differences. Overall, the CLASS3 exhibits appropriate psychometric characteristics supporting its use in defining the academic needs of concussed students.
KEYWORDS: Trauma, Neurorehabilitation

672. Defining Concussion Subtype Treatment Targets: Psychometric properties of the Concussion Symptom Subtypes Inventory (CSSI)
Gioia Gerard (Rockville, MD, United States) Vaughan Christopher, Sady Maegan, Didehbani Nyaz, Babikian Talin, Cullum Munro, Giza Christopher, Lumba-Brown Angela, Bloom Josh, Chestnutt James, Clugston Jay, Ghajar Jamshid, Leddy John

OBJECTIVE: Examine the psychometric properties of a novel symptom subtype assessment tool, the Concussion Symptoms Subtype Inventory (CSSI), to better define treatment targets.
METHODS: 27 patients (ages 12-21, mean=15.5 years; 50% male; median 38 days post injury) diagnosed with concussion completed the 116-item CSSI to define symptom status in seven subdomains (headache, cognition, emotion, vestibular, ocular-motor, sleep, cervical). RAPID (Retrospective Adjusted Post-Injury Difference) scores (0-6 unidimensional severity rating), accounting for pre-injury status, were analyzed.
RESULTS: Analysis of item-scale membership revealed appropriate item-total correlations (ITC) across the seven scales (Mean subscale ITC range 0.45-0.76), and strong internal consistency (Coefficient Alpha = 5 subscales >0.9, 2 subscales >0.80; Total CSSI=0.973). Moderate intercorrelations were found between subscales and with CSSI Total Symptom score (r's = 0.40-0.65). Symptom severity rankings were observed (highest to lowest): Cognitive, Headache, Sleep, Ocular-Motor, Emotional, Vestibular, Cervical; rank order correlated strongly with adult subtype prevalence (Spearman rho=0.99). Subscales correlated moderate-strongly with the overall rating of "difference from normal." No significant age differences in symptom ratings were found. No sex differences were seen except on sleep symptoms (p<.01).

CONCLUSIONS: Treatment of concussion requires appropriate assessment of symptom subtypes. The 7-subscale CSSI demonstrated strong psychometric properties in a sample of youth. Strong internal consistency and item-scale membership with moderate relationships among the scales were noted, suggesting unique assessment of concussion subdomains. Symptom severity ranking was consistent with published subtype literature. Future analyses are planned with larger samples and an examination of CSSI sensitivity to change over time.
KEYWORDS: Trauma

673. Comparison of Occupational Therapy Goals Identified by Patients with Concussion and Epilepsy

Westerberg Shannon (Los Angeles, CA, United States) Sheridan Chris, Harris Madison, Lerner Jason, Giza Christopher

OBJECTIVE: Systematic identification of therapeutic goals gives insight into patients' perceived dysfunction and is critical to successful occupational therapy (OT) intervention. We compared therapeutic goals identified by patients referred to OT from two pediatric neurology clinics specializing in concussion and epilepsy.
METHODS: Data was obtained retrospectively from medical records of patients referred to OT from two specialty clinics at a single academic institution between August 2018 and April 2020. Therapeutic goals were identified using the Canadian Occupational Performance Measure, a standardized OT measure used to identify client-centered goals in: self-care, productivity and leisure. Data from patients aged 12-25 with complete records who underwent OT evaluation were analyzed. Fisher's exact and Wilcoxon rank-sum tests were used for categorical and count data and $p \leq 0.05$ was taken to represent statistical significance.
RESULTS: Fifty-two patients' records were reviewed, and 38 met inclusion criteria: 19 concussion (17±3 years, 16 female) and 19 epilepsy (17±3 years, 9 female). Groups differed significantly by sex ($\chi 2$ [1,N=33]=4.209, Fisher's p= 0.04), but not age (p=0.98). Groups did not differ in total number of goals set (p=0.835, d=0.07); concussion 5[IQR=4-5], epilepsy 5[IQR=4-5]). The epilepsy group exhibited a preference for productivity goals (p=0.04, d=0.77). There were no significant differences in the number of self-care goals (p=0.44, d=0.27) or leisure goals (p=0.08, d=0.61).
CONCLUSIONS: Both groups identify goals addressable by OT. Epilepsy patients may prefer setting goals focused on productivity, such as school participation. Future work characterizing the profile of goals set by concussion and epilepsy patients can help OT professionals target interventions for these populations.
KEYWORDS: Trauma, Epilepsy, Neurorehabilitation

674. Demographics of pediatric mild traumatic brain injury and recovery in specialty clinics: A study from the Four Corners Youth Consortium.

Rosenbaum Philip (Los Angeles, CA, United States) Locandro Chris, Chrisman Sara, Choe Meeryo, Richards Rachel, Pacchia Christina, Cook Larry, Rivara Fred, Gioia Gerard, Giza Chris

OBJECTIVE: To characterize pediatric patients with mTBI presenting to outpatient clinics and describe their recovery.

METHODS: 611 patients from 5-18.99 years of age presenting with an mTBI within 11 weeks of injury were prospectively consented and enrolled from outpatient concussion specialty clinics of the Four Corners Youth Consortium with up to 12-month follow-up. Exclusion criteria included if the patient or his/her parents were unable to read or sign the consent document, an initial GCS <13, or a penetrating injury. This study utilized CDEs from NINDS including data on demographics, injury details, history, neurological and neuropsychological assessments and treatment.
RESULTS: 54% of subjects were female and 72% were of adolescent age (13-18 years old). A higher proportion of females were adolescents compared to males (250/329 (76%) vs. 192/282 (68%)). Females, compared to males, reported significantly more pre-existing anxiety (27.1% vs 18.3%), depression (13.2% vs 7.7%) and migraine (21.8% vs 14.7%). Females recovered more slowly than males (median days IQR: 73 [66, 87] vs. 57 [45, 66]; p=0.033), with 18.2% vs. 28% recovered by 4 weeks and 57% vs. 68.7% recovered by 12 weeks. Independent of gender, patients with history of migraine or anxiety/depression (mental distress) recovered more slowly than those without (Figures 1 & 2).
CONCLUSIONS: In a large consecutive cohort of pediatric patients presenting to concussion clinics, several factors (female sex, history of migraine, history of anxiety/depression) were associated with longer recovery. Identification of subgroups of pediatric mTBI patients at risk for prolonged recovery will permit better prognostication and more targeted treatment interventions.
KEYWORDS: Trauma, Headache/Migraine, Cognitive/Behavioral Disorders (including Autism)

LATE BREAKING ABSTRACTS

675. Efficacy and Safety of IncobotulinumtoxinA in the Treatment of Children and Adolescents with Chronic Troublesome Sialorrhea Associated with Neurological Disorders and/or Intellectual Disability

Berweck Steffen (Vogtareuth, Germany) Flatau-Baqué Birgit, Althaus Michael

OBJECTIVE: To investigate the efficacy and safety of incobotulinumtoxinA for chronic troublesome sialorrhea in children/adolescents.
METHODS: SIPEXI (NCT02270736) was a Phase III, prospective, randomized, double-blind, placebo-controlled, parallel-group, multicenter study with an open-label extension (OLEX). Children/adolescents (2–17 years) with chronic troublesome sialorrhea associated with neurological disorders and/or intellectual disability, and severe drooling (investigator's Modified Teacher's Drooling Scale rating ≥6), were recruited in a stepwise approach. 6–17 year olds were randomized 2:1 to incobotulinumtoxinA ~2 U/kg body weight (BW) (fixed total dose 75 U for subjects ≥30kg BW) or placebo in the main phase (MP). 2–5 year olds only received incobotulinumtoxinA. All subjects received 3 further incobotulinumtoxinA injection cycles (IC) in the OLEX. Unstimulated Salivary Flow Rate (uSFR) change from baseline and carer's Global Impression of Change Scale (GICS) score were assessed at Week 4 (co-primary efficacy endpoints) and over time. Treatment-emergent adverse events (TEAEs) were also assessed.
RESULTS: 256 subjects were randomized: 250 (97.7%) completed the MP and 247 entered the OLEX; 222/247 (89.9%) completed all 3 ICs. The incobotulinumtoxinA group showed a

statistically significant superiority over placebo in uSFR change from baseline and improvement in carer's GICS score at Week 4. Improvements were also observed throughout the OLEX with a cumulative effect after repeated incobotulinumtoxinA treatment. No major differences in TEAE incidence were observed between groups in the MP, and TEAEs did not increase with the increasing number of ICs.
CONCLUSIONS: IncobotulinumtoxinA was effective and well tolerated for the treatment of children/adolescents with chronic troublesome sialorrhea.
KEYWORDS: Neuromuscular Disorders, Neurorehabilitation

676. ROCKET Phase 2a Trial: Safety, Tolerability, and Efficacy of OV101 (gaboxadol) in Adolescents and Young Adult Males With Fragile X Syndrome (FXS)
Berry-Kravis Elizabeth (Chicago, IL, United States) Dominick Kelli, Gabis Lidia, Adams Maxwell, Adera Mathews, Huang Linda, Ventola Pamela, Tartaglia Nicole, Budimirovic Dejan

OBJECTIVE: FXS is a rare genetic condition characterized by intellectual disability and behavioral dysfunction. There are currently no approved medications for the treatment of FXS. OV101 (gaboxadol) is a δ subunit-selective extrasynaptic $GABA_A$receptor agonist that showed improvement in a mouse model of FXS and has been evaluated in a Phase II study of Angelman syndrome. Here we report safety, tolerability, and efficacy of OV101 from the ROCKET trial.
METHODS: ROCKET was a randomized, double-blind, parallel-group trial evaluating gaboxadol in males with FXS 13–22 years-of-age. Patients were randomized 1:1:1 to 5mg QD, 5mg BID, or 5mg TID OV101 for 12 weeks. The primary objective was safety and tolerability as assessed by adverse events reported. Other assessments included ABC-$C_{FXS,}$ CGI–Severity (CGI-S), CGI–Improvement (CGI-I), and ADAMS.
RESULTS: Twenty-three patients were randomized to OV101 5mg once (n=7), twice (n=8), or three times (n=8) daily dosing for 12 weeks. Treatment-emergent AEs (TEAEs) and treatment-related TEAEs were reported for 69.6% and 34.8% of patients, respectively. TEAEs occurring in ≥2 patients included diarrhea, irritability, headache, upper respiratory tract infection. All TEAEs except 1 (agitation) were mild. No serious AEs were reported. Across the dosing groups, a significant improvement from baseline to Week 12 was observed in ABC-C_{FXS} total score, CGI-S total score, ADAMS total score (see Table 1), and 60% of patients were identified as CGI-I responders. Additional analyses are ongoing.
CONCLUSIONS: OV101 was generally well tolerated at all 3 dose levels. Improvements were observed for several efficacy endpoints at 12 weeks.
KEYWORDS: Rare Diseases, Cognitive/Behavioral Disorders (including Autism)

677. Tolerability and Efficacy of ZYN002 Cannabidiol (CBD) Transdermal Gel in Children and Adolescents With Autism Spectrum Disorder: An Open-Label Phase 2 Study (BRIGHT [ZYN2-CL-030])
Heussler Helen (Brisbane, Australia) Duhig Michael, Hurst Terry, O'Neill Carol, Gutterman Donna, Palumbo Joseph

OBJECTIVE: ZYN002 is a pharmaceutically manufactured transdermal cannabidiol gel in development for the treatment of autism spectrum disorder (ASD). BRIGHT (ZYN2-CL-030) is an exploratory, single-center, open-label phase 2 study evaluating the safety and tolerability (primary objective) and efficacy of ZYN002 in children/adolescents aged 3-17 years.

METHODS: BRIGHT enrolled patients with Clinical Global Impression (CGI)–Severity score ≥4 (moderate or greater) and Aberrant Behavior Checklist-Community (ABC-C) Irritability score ≥18. Patients received ZYN002 250 or 500 mg/day for 14 weeks on top of stable standard of care (including antipsychotic agents, when prescribed). Safety assessments included adverse events (AEs), laboratory tests, and electrocardiograms (ECGs).
RESULTS: Of the 37 patients (mean age, 9.2 years) enrolled, 94% had moderate-to-severe symptoms per Autism Diagnostic Observation Schedule 2nd edition criteria; the mean baseline ABC-C Irritability score was 30.3. At week 14, significant improvement was observed for each ABC-C subscale (Table). 57% of patients were "very much improved" or "much improved" based on CGI-Improvement, and patients experienced a mean improvement of 46% in Parent-Rated Anxiety Scale-ASD score (P<0.0001). All AEs were mild (75%) or moderate (25%) and reported in 49% of patients. Treatment-related AEs were reported in 14% of patients; most were mild and transient. No serious or severe AEs or clinically significant changes in laboratory tests or ECGs were reported.
CONCLUSIONS: BRIGHT may provide initial evidence suggesting a positive risk–benefit profile for ZYN002 when added on top of stable standard of care in children/adolescents with moderate-to-severe ASD. Further studies are warranted in this difficult-to-treat population.
KEYWORDS: Cognitive/Behavioral Disorders (including Autism)

678. A Pivotal Study of ZYN002 Cannabidiol (CBD) Transdermal Gel in Children and Adolescents With Fragile X Syndrome [CONNECT-FX (ZYN2-CL-016)]
Berry-Kravis Elizabeth (Chicago, IL, United States) Erickson Craig, Hagerman Randi, Tartaglia Nicole, Cohen Jonathan, Sebree Terri, Gutterman Donna, Tich Nancy, Dobbins Thomas, Palumbo Joseph

OBJECTIVE: ZYN002 is a pharmaceutically manufactured transdermal cannabidiol gel in development for the treatment of behavioral symptoms in Fragile X syndrome (FXS). CONNECT-FX (ZYN2-CL-016) is a multinational, randomized, double-blind, 14-week pivotal study to evaluate the efficacy and safety of ZYN002 in children/adolescents aged 3 to 17 years with a full *FMR1* mutation.
METHODS: Eligible patients were randomly assigned 1:1 to receive 12-week treatment with ZYN002 (250 mg or 500 mg daily) or placebo. The primary end point was change from baseline in the Aberrant Behavior Checklist–Community FXS Specific (ABC–C_{FXS}) Social Avoidance subscale at week 12. Key secondary end points included change from baseline in the ABC–C_{FXS} Irritability and Socially Unresponsive/Lethargic subscales at week 12. Safety assessments included adverse events, laboratory tests, and electrocardiograms.
RESULTS: A total of 212 patients were randomized at investigative sites in the United States, Australia, and New Zealand. The mean age of enrolled patients was 9.7 years, and 75% were male. Mean baseline ABC-C_{FXS} subscale raw scores for Social Avoidance, Irritability, and Socially Unresponsive/Lethargic were 7.2, 28.0, and 13.1, respectively (Table). Based on Autism Diagnostic Observation Schedule, 2nd edition criteria, 46.5% of patients had "severe" autism-related symptoms and 33.3% had "moderate" symptoms at baseline (Table).
CONCLUSIONS: CONNECT-FX is anticipated to further our understanding of the efficacy and safety of ZYN002 in FXS. Topline results (anticipated in Q2 2020) will be presented at the CNS-ICNA Conjoint Meeting and may provide the basis of NDA for ZYN002 in the treatment of behavioral symptoms of FXS.

KEYWORDS: Cognitive/Behavioral Disorders (including Autism)

679. Overview and differentiation of ZYN002 (transdermal cannabidiol gel)

Hagerman Randi (Sacramento, CA, United States) Berry-Kravis Elizabeth, O'Neill Carol, Sebree Terri, Banks Stan, Agnese Wendy, Palumbo Joseph

OBJECTIVE: ZYN002 is a pharmaceutically manufactured transdermal cannabidiol (CBD) gel under evaluation in an FDA-regulated clinical development program for the treatment of behavioral symptoms in Fragile X syndrome (FXS).
METHODS: Over-the-counter CBD products are not regulated by the strict standards of the FDA and Current Good Manufacturing Practices (cGMPs) and may be prone to inconsistencies in potency, subeffective dosages and formulations, mislabelling, and suboptimal purity. The active ingredient in ZYN002 is manufactured under a highly controlled process which produces the identical structure of CBD found in the *Cannabis* plant. The final drug product is manufactured under cGMPs, with established controls for potency, uniformity, and purity.
RESULTS: ZYN002 has been evaluated in more than 650 individuals aged 3 to 78 years. Quality control testing has confirmed that tetrahydrocannabinol (THC) is not present in ZYN002 (active pharmaceutical ingredient and drug product). The permeation-enhanced gel formulation allows for transdermal delivery, avoiding first-pass metabolism in the liver and potential gastric acid degradation to THC. In addition, transdermal application may decrease the potential for gastrointestinal-related side effects. Product testing of non-FDA-regulated CBD formulations has shown the presence of THC (at levels which may be sufficient to produce euphoric effects), and reports have shown common cannabis contaminants including microbes (bacteria and fungi), heavy metals, and pesticides.
CONCLUSIONS: The highly controlled, pharmaceutically manufactured formulation as well as preclinical and clinical data, support the dosing, safety, and effectiveness profile of ZYN002 transdermal gel for continued evaluation as an investigational treatment for children and adolescents with FXS.
KEYWORDS: Cognitive/Behavioral Disorders (including Autism), Rare Diseases

ACNN ABSTRACTS

680. Neurology advanced practice provider education: A new approach to building knowledge and confidence in independent practice

Jacobson Mona (Aurora, CO, United States) Turner Scott, Shea Stephanie

OBJECTIVE: Background: Research has supported improved Advanced Practice Provider (APP) education and support to assist with transition to practice as well as ongoing job satisfaction and retention (Faraz, 2019, Barnes 2015). Our program has worked to provide newly hired APPs with a structured clinical orientation to prepare them to independently diagnose and manage common neurological problems within a specific population of patients. Some department providers raised concern that our initial approach was not fully preparing new APPs to function autonomously, confidently and efficiently in clinical practice. More experienced APPs also identified gaps in their knowledge and experience that limited their diagnostic reasoning and management skills. Based on this feedback, the program was redesigned to create

a more systematic and effective structure for APP on-boarding and a more robust ongoing educational program for APPs at all levels of experience within the specialty.
METHODS: A new on-boarding format was developed with a graduated system of integration into neurology and APP practice. Additionally, a foundational biyearly conference for all neurology APPs was instituted, supplemented with a monthly skills session on various elements of a detailed neurological examination. At the start of the educational program year, all neurology APPs completed a self-evaluation of comfort level and knowledge base using a core competency reporting form. A follow up evaluation was administered at the end of the program year.
RESULTS: Twelve APPs who participated in the redesigned APP educational program expressed improved comfort level on an objective scoring matrix. All twelve indicated movement toward manager on the RIME framework. The feedback on the biyearly conference was positive with all APPs indicating the sessions helped advance their neurology skills
CONCLUSIONS: Providing neurology APPs, a structured on boarding program, along with continued educational programming, helps increase individual comfort level and knowledge in core neurology topics.
KEYWORDS: ACNN

681. Seizues in the community: School staff knowledge and experience
Sanders Cindy (Flagstaff, AZ, United States)

OBJECTIVE: To survey school staff (RNs and others) in a rural community with regards to incidence and prevalence of epilepsy students, use of rescue medications, and comfort in treating seizures in the setting of public and charter schools.
METHODS: A questionnaire was developed and distributed to both charter and public schools in the Flagstaff community. This survey collected demographic data regarding school nurses or other staff tenure as well as prevalence of seizure disorder students present in the school. Further, the incidence of observed seizures was reported , as well as whether rescue medicine was given and seizure action plan followed.
RESULTS: The returned surveys (N=15) demonstrated a wide variation in both the prevalence of seizure disorder students within the individual schools as well as the incidence of seizures occurring in the school setting. The nurses and other staff's comfort with administration of rescue medications as part of a seizure action plan was consistently high.
CONCLUSIONS: In the setting of a rural community, there is variation in the prevalence of students with seizure disorders within the schools. Despite varying incidences of seizures and the need to administer rescue medications, the data collected demonstrated that nurses and other school staff are comfortable in following a seizure action plan. Further opportunity exist to survey other schools within the service area our neurology clinic serves.
KEYWORDS: ACNN

682. Training School Personnel: Impact of Standardized Seizure Training Programs
Schultz Rebecca (Houston, TX, United States) Shafer Patricia, Kiriakopoulos Elaine, Gilchrist Brian, Haynes-Smith LaQueisa, Kakacek Jody R.M., Owens Steven B.

OBJECTIVE: To evaluate the use and impact of the Epilepsy Foundation's standardized seizure training program for school personnel and changes in its' use since state mandates for school training in epilepsy have been implemented.
METHODS: A 1-hour training for school personnel has been available for many years. In September of 2019, the training was updated to include new terminology, rescue therapies, a simplified approach to seizure first aid, and observational learning with rich media. The training is offered in person by educators from local Epilepsy Foundation offices and online through the Foundation's Learning Management System. Users completes pre and post testing targeting knowledge and self-efficacy. Mandated training for school personnel began in Texas in December 2019 and more states will be implementing the training in 2020.
RESULTS: The updated training has been delivered in person to 2,651 school personnel via 92 programs from October through December 2019. Online programs have been completed by 3,558 people in October and November 2019. Online use increased dramatically since Texas mandated training began with 22,430 trainings completed in December 2019 and January 2020. Paired sample T-tests were used to assess change in seizure first aid knowledge and self-efficacy. There was a significant increase in knowledge from the pretest ($M = 18.8$, $SD = 7.6$) to the posttest ($M = 30.1$, $SD = 2.7$), $t(145) = -17.4$, $p = .000$). Similarly, there was a significant increase in self-efficacy from the pretest ($M = 17.6$, $SD = 8.6$) to the posttest ($M = 30.6$, $SD = 5.2$), $t(113) = -14.7$, $p = .000$).
CONCLUSIONS: The reach of the Epilepsy Foundation's training for school personnel is increasing with implementation of mandated training laws for school personnel. The online program eliminates geographic constraints of in person trainings. Results suggest increased knowledge and confidence of school personnel who care for students with seizures.
KEYWORDS: ACNN

683. High-dose prednisolone for treatment of infantile spasms after presumed perinatal stroke
Hall Kristin (Indianapolis, IN, United States) Golomb Meredith R.

OBJECTIVE: BACKGROUND: High dose prednisone and prednisolone have been increasingly studied as a lower-cost alternative to ACTH for the treatment of infantile spasms, but this treatment has not been well-studied in children with infantile spasms due to perinatal stroke.
METHODS: We identified a child with new onset infantile spasms due to presumed perinatal left middle cerebral artery stroke seen in our hospital's pediatric stroke clinic in 2019.
RESULTS: This child developed infantile spasms at 9 months of age. She had right hemiplegic cerebral palsy due to her perinatal stroke, but had been otherwise previously healthy. Modified hypsarrhythmia was confirmed on prolonged video EEG. High dose prednisolone at 8mg/kg/day was initiated on the 8th day of spasms. She was treated with this dose for 2 weeks, then tapered over 5 weeks. The girl became seizure-free after receiving her first dose of prednisolone, and suffered no significant side effects during therapy. Routine EEG after completion of prednisolone taper confirmed resolution of modified hypsarrhythmia, and no epileptiform discharges. She continued to make excellent development progress during and after treatment.
CONCLUSIONS: High-dose prednisolone should be considered for first-line therapy for children with infantile spasms due to perinatal stroke.
KEYWORDS: ACNN

684. How RN's are meeting the unmet needs of the pediatric epilepsy population

Greene Roethke Carol (Wilmington, DE, United States) Berardi Maria, Dangerfield Tia, Hersey Susan, Kotowski Mary

OBJECTIVE: Illustrate how Specialty RN's improve the unmet needs of the epilepsy population.
BACKGROUND: Children with epilepsy and their families consistently report unmet health care needs, whether epilepsy is of new onset or drug resistant/intractable. While we have many new medical therapies to offer, studies show that up to 75% of unmet needs are related to emotional or educational needs rather than medical issues.
METHODS: We are a Level IV Epilepsy Center serving the population of Delaware and surrounding regions. We have utilized a quality improvement system-based approach to identify unmet needs and to develop programs and processes that can be provided by specialty-trained epilepsy nurses, both in the hospital and in the community. Specifically, we have developed methods for instructing on medication side effects, seizure safety, use of rescue medications, seizure monitoring devices and impact on daily life. Specialty RN's meet with families in the hospital inpatient and outpatient settings to provide education, training and support, and act as liaisons to guide patients through the health care system at critical times, such as new onset epilepsy and epilepsy surgery. We have developed a social media support group for our patients to share their common experiences. We work with the local Epilepsy Foundation chapter to participate in community events.
RESULTS: The most significant unmet needs are described and strategies that were successfully utilized by Nemours RN's are provided with this presentation. Perhaps other institution will benefit as well.
KEYWORDS: ACNN

685. PEDIATRIC HEREDITARY NEUROPATHIES: PHENOTYPES, GENOTYPES, AND THE PATH TO DIAGNOSIS

Moore Allison (New York, NY, United States) Aldrich Joy, Moore Robert, Thomas Florian, Dastgir Jahannaz

OBJECTIVE: Pediatric patients diagnosed with hereditary neuropathies present with a wide spectrum of symptoms according to disease type. Age at diagnosis may contribute to prognosis because failure to identify disease pathophysiology may delay appropriate, often multidisciplinary, care needs. GRIN, the (Global Registry for Inherited Neuropathy), was developed to better characterize and quantify the population of children affected by pediatric hereditary neuropathies and compare them to adult patients with hereditary neuropathies.
METHODS: Hereditary Neuropathy Foundation created the Global Registry for Inherited Neuropathy (GRIN), to capture detailed Inherited Neuropathy (IN) patient history via an online, IRB approved patient survey from 2013Q1-2020Q1. Natural history data on pediatric patients (n=129) was analyzed in a cross-sectional study to discern trends specific to pediatric patients vs. an adult control group.
RESULTS: 39% of pediatric CMT patients in GRIN are diagnosed with CMT1A, with HNPP (12%) and CMT2 (9%) making up the next two largest disease type cohorts . Diagnosis is overwhelmingly made by a neurologist at 60%. Over 75% of pediatric patients have had a

genetic test for their disease, as compared to 40% of the control adult population. 94% of patients report one or more physical symptoms associated with their disease, which is comparable to the adult cohort. Pediatric patients have experienced less surgery than their adult counterparts, at 19.6% & 39% respectively. Pain is experienced by 44% pediatric patients vs. 62% of adult patients.

CONCLUSIONS: Pediatric patients with hereditary neuropathy present with a range of symptoms early in life. Genetic diagnoses are confirmed more frequently in pediatric as compared to adult patients. Surgery is less common in pediatric patients and is more frequently pursued in adult patients, likely due to the progressive nature of hereditary neuropathies. Pain also becomes a more significant concern in adulthood.

KEYWORDS: ACNN