Oral Presentation: Basic Science / Engineering

Abstract #1

The L-Type Calcium Channel Blocker Nicardipine Prevents Sudden Unexpected Death in Epilepsy

Antis George, Alexandra Wall, Jordan Farrell, G. Campbell Teskey

University of Calgary-Hotchkiss Brain Institute

Rationale

Sudden Unexpected Death in Epilepsy (SUDEP) occurs when someone with epilepsy, who is otherwise healthy dies suddenly with no known cause. Our previous work has shown that discrete seizures lead to local vasoconstriction resulting in hypoperfusion, hypoxia and behavioural disturbances which are dependent on the integrity of cyclooxygenase-2. However, L-type calcium channels (LTCC) the final effector in vascular dynamics ultimately mediate this period of severe hypoxia.

Methods

Mice were treated acutely with either (5mg/kg) nicardipine or vehicle, intraperitoneally 30 minutes prior to intra-hippocampal kainic acid administration (1.4μg in 0.4μl). Brainstem and hippocampal EEG and tissue oxygen levels were recorded with chronically implanted probes. Breathing and heart rate were recorded through a chronic bipolar electrode in the diaphragm. Chronically Kv1.1 knockout mice either received nicardipine (2 mg/mL, pumping rate 0.15 uL/hr) or vehicle intracerebroventricularly.

Results

In the acute group, epileptiform activity propagated to the brainstem from the hippocampus, leading to severe hypoxia in brainstem breathing centers. Vehicle mice died during stage 5 seizures with terminal apnea occurring several minutes prior to cardiac arrest in all animals. Acutely, single dose nicardipine significantly extended life. Chronic administration of nicardipine also significantly extended life beyond that of controls.

Conclusion

Our results are in line with previous studies in persons with epilepsy showing that breathing failure is the precipitating cause of SUDEP. The LTCC nicardipine administered both acutely or chronically extended survival time in two different SUDEP mouse models and therefore should be considered as a potential therapeutic to prevent SUDEP.

Oral Presentation: Clinical Epilepsy / EEG / Antiepileptics

Abstract #2

The North American AED Pregnancy Registry: A Subgroup Analysis of Canadian Women

Julien Hébert[1], Susan Conant[2], Lewis Holmes[3], Esther Bui[4]

[1]Columbia University Irving Medical Center, New York Presbyterian Hospital
[2]The North American Antiepileptic Drug Pregnancy Registry, MassGeneral Hospital for Children, Boston, Massachusetts, USA
[3]Medical Genetics and Metabolism Unit, MassGeneral Hospital for Children, Boston, Massachusetts, USA
[4]Toronto Western Hospital, University Health Network, Toronto, Ontario, Canada

Rationale
The North American AED Registry (NAAPR) has been key in providing prospective data aimed at understanding the risks of antiepileptic drug exposure in pregnancy. Clinical data directly applicable to the Canadian context is currently lacking.

Methods
Between 1997 and 2019, Canadian and American pregnant women enrolled to NAAPR completed a questionnaire on their anti-epileptic drug (AED) usage. Enrollment rates to NAARP were compared between the two countries, and between the different Canadian provinces, using population-based enrollment rate ratios (PERR). The AED prescription pattern among Canadian pregnant women was analysed and compared with the USA using chi-squared test for proportions.

Results
During the study period, 10,215 women enrolled into NAAPR: 4.1% (n=419) were Canadian, below expected population-based contribution (PERR=0.42; $p<0.01$).

Within Canada, the three northern territories (PERR=0; $p<0.01$), Prince-Edward Island (PERR=0; $p<0.01$), and Quebec (PERR=0.41; $p<0.01$) had the lowest enrollment rates relative to their population weight within Canada. Lamotrigine was the most prescribed AED in the Canadian cohort. Canadian women were more likely to be taking carbamazepine (24%; $p<0.01$) or valproic acid (21%; $p<0.01$) than their American counterparts.

Conclusion
Although further investigations are needed, Canadian women appeared more likely to be prescribed older AEDs, such as carbamazepine and valproate, than their American counterparts. Greater enrollment of Canadian women to NAAPR, through enhanced clinician referrals, in particular from underrepresented provinces/territories, could lead to more accurate population-specific data and help identify gaps in the care of this vulnerable patient population.

Oral Presentation: Basic Science / Engineering

Abstract #3

MODELLING EPILEPSY IN CEREBRAL ORGANOIDS: OXYGEN-GLUCOSE DEPRIVATION AS A CONVULSANT

Alexandra Santos, Afifa Saleem, Mark Aquilino, Liliana Attisano, Peter Carlen

University of Toronto

Rationale
Epilepsy is a complex neurological condition characterized by recurrent seizures. Human cerebral organoids can be used to model epilepsy and permit personalized drug testing. Oxygen-glucose deprivation (OGD) is a known cause of neonatal seizures in humans; therefore, it was hypothesized that this will induce epileptiform activity in cerebral organoids.

Methods
Cerebral organoids derived from human embryonic stem cells were provided by L. Attisano at 4 and 7 months of age. Organoids underwent electrophysiological recordings with two local field potentials: 5 minutes baseline, 20 minutes OGD, and 30-40 minutes washout. Signals were processed in MATLAB to extract the power spectral density. Raw traces were analyzed in Clampfit 9.0 to identify spontaneous events. T-tests were used to compare means.

Results
The power spectral density area under the curve was significantly greater than baseline in both the OGD ($p<0.02$) and washout ($p<0.05$) conditions, for all signal frequencies in both 7- and 4-month organoids. This effect was strongest at 4 months, and comparable to the known convulsants picrotoxin and pentylenetetrazol. There were significantly more spontaneous events during the post-OGD washout period when compared to baseline, which was strongest at 7 months (0.27 events/minute and 0.09 events/minute respectively, $p=0.01$).

Conclusion
These findings support the presence of epileptiform changes in the cerebral organoid tissue, which to our knowledge is the first induction of seizures in healthy 3D organoids. Further investigation of the exact mechanisms as well as responses to anti-seizure drugs is warranted to develop the organoids as a high-throughput, drug testing platform.

Oral Presentation: Epilepsy Surgery

Abstract #4

Neurostimulation in Drug-Resistant Epilepsy: Systematic Review and Meta-Analysis from the ILAE Evidence-Based Epilepsy Surgery Task Force

Lahoud Touma[1], Bénédicte Dansereau[1], Dario Englot[2], Mark Keezer[1]

[1]*University of Montreal*
[2]*Vanderbilt University Medical Center*

Rationale
Drug-resistant epilepsy (DRE) accounts for up to one third of patients with epilepsy, leading to an important societal burden.

We conducted a systematic review and meta-analysis of vagus nerve stimulation (VNS), responsive neurostimulation (RNS) and deep brain stimulation (DBS) in the treatment of DRE to summarize the current evidence on efficacy and tolerability.

Methods
We searched Ovid Medline, Ovid Embase, and the Cochrane Central Register of Controlled Trials with a pre-specified search strategy. We included all published randomized controlled trials (RCT) and their corresponding open-label extension studies, as well as prospective case series, with samples of at least 20 participants.

Results
Our systematic review identified 30 studies, six of which were RCTs, with the remaining consisting of prospective observational studies. At long term follow-up, five observational studies for VNS reported a pooled mean percentage decrease in seizure frequency at last follow-up of 34.7% (95% CI: -5.1, 74.5). In the open-label extension studies for RNS, the median seizure reduction was 53%, 66% and 75% at two, five and nine years of follow-up, respectively. For DBS, the median reduction was 56%, 65% and 75% at two, five and seven years, respectively. Seizure freedom increased over time in all modalities. The most common complications included hoarseness, cough and throat pain for VNS and implant site pain, headache, and dysesthesia for DBS and RNS.

Conclusion
Neurostimulation modalities are effective for the treatment of DRE, with improving outcomes over time and few major complications. Higher quality long-term data on DBS and RNS suggest larger seizure reduction rates than VNS.

Neuroimaging

Abstract #5

Structural Connectivity Analysis in Operculo-Insular Epilepsy

Sami Obaid[1], François Rheault[2], Manon Edde[2], Guido I. Guberman[2], Etienne St-Onge[2], Alain Bouthillier[1], Dang K. Nguyen[1], Maxime Descoteaux[2]

[1]*University of Montreal Health Center*
[2]*Sherbrooke Connectivity Imaging Lab*

Rationale
Previous studies evaluating structural connectivity patterns in focal epilepsy have revealed increased 'connectivity strength' (CS) within the epileptic network. To our knowledge, no studies have looked at the structural connectivity distribution in patients with operculo-insular epilepsy (OIE).

Methods
The study included 9 patients with OIE, 8 age- and sex-matched patients with temporal lobe epilepsy (TLE) and 22 healthy controls (HC). Diffusion MRI-derived tractograms were built using surface-enhanced tractography. Convex Optimization Modeling for Micro-structure Informed Tractography (COMMIT) was used to compute COMMIT weights, which was used as a marker of CS in structural connectivity matrices. Whole-brain and insular subnetwork connectivity matrices were computed using Brainnetome parcellations.

Results
On whole-brain analyses, significant increases in CS ($p \leq 0.001$, uncorrected) were observed bilaterally in multiple bundles of OIE patients as compared to HCs. A pattern of decreased CS was also observed but was more limited. Similarly, a wider pattern of increased connectivity was detected in OIE patients as compared to TLE patients. Significant increases in CS were noted between the dorsal granular insula and the pregenual cingulate gyrus in OIE patients as compared to HCs when isolating a network linking the insula to all extrainsular regions ($p \leq 0.05$, FDR-corrected). When investigating a subnetwork connecting only insular subregions to each other, an increase in connectivity was seen between the dorsal granular and agranular insula in OIE patients as compared to TLE patients ($p \leq 0.05$, FDR-corrected).

Conclusion
The wide pattern of increased CS in OIE patients suggests a diffuse epileptic network. The differential morphologic pattern of CS could constitute a complementary tool to differentiate OIE from TLE.

Neuroimaging

Abstract #6

Pattern Separation and Hippocampal Integrity in Temporal Lobe Epilepsy

Dora Ladowski, Aathmika Nandan, David Gold, Mary Pat McAndrews

Krembil Brain Institute

Rationale
Determining the functional integrity of the epileptogenic hippocampus is key to predicting postoperative morbidity. Pattern separation (PS) is a fundamental hippocampal process that results in non-overlapping representations of highly similar events. Here, we used recognition tests that conform to behavioral assays of PS to assess its relationship to hippocampal integrity in TLE.

Methods
We obtained a preoperative structural MRI (n = 110) and pre- (n = 110) and postoperative (n = 41) neuropsychological assessments for individuals with unilateral TLE. Automated segmentation of structural MRI was performed to quantify left and right hippocampal volumes, and an asymmetry ratio was computed. Two recognition tests – Names and Doors – were used to capture PS abilities. Each test consists of two conditions: in condition A, lures are more dissimilar to the target (lower PS demands) and in condition B, lures are highly similar (higher PS demands).

Results
Preoperative scores were within normal limits on both tests and equivalent for both right and left TLE groups. Greater hippocampal asymmetry (regardless of the hemisphere affected) was significantly correlated with worse performance on both tests. Hippocampal asymmetry was also correlated with change in Doors B; greater decline postoperatively was associated with lower hippocampal asymmetry preoperatively.

Conclusion
Recognition measures with a high degree of similarity between lures and targets offer a measure of PS that is sensitive to hippocampal integrity in TLE. The lack of a laterality effect is consistent with the hypothesis that PS is an index of hippocampal function unaffected by information specialization in each hemisphere.

Neuroimaging

Abstract #7

EEG and Magnetic Resonance Imaging Abnormalities in Patients with Psychogenic Non Epileptic Seizures

Pouyan Tavakoli Yaraki[1], Joe Yu[2], Mashael Khateeba[1], Miguel Arevalo[1], Samuel Lapalme-Remis[3], Seyed Mirsattari[1]

[1]*Schulich Faculty of Medicine & Dentistry*
[2]*London Health Science Centre*
[3]*Division of Neurology, Centre Hospitalier de l'Université de Montréal*

Rationale
To compare the rate of EEG and MRI abnormalities in a large cohort of PNES patients, with and without suspected epilepsy. Patients were also compared in terms of their demographic and clinical profiles.

Methods
A retrospective analysis of 271 newly diagnosed PNES patients admitted to the Epilepsy Monitoring Unit (EMU) between May 2000 and April 2008, with follow-up clinical data collected until September 2015.

Results
57 of the 77 patients (74.0%) with possible, probable or definite epilepsy exhibited epileptiform activity on EEG, versus only 16 of the 194 patients (8.2%) in whom epilepsy was excluded. Similarly, 24 of these 194 patients (12.4%) had MRI abnormalities. Three of 38 patients (7.9%) with both EEG and MRI changes were confirmed not to have epilepsy. In both PNES patients with EEG or MRI abnormalities vs without, those with abnormalities are more likely to have epilepsy risk factors such as structural abnormalities involving the central nervous system, and less likely to report minor head trauma. The presence of EEG abnormalities in PNES only patients did not influence Anti Seizure Medication (ASM) reduction, whereas those with MRI abnormalities were less likely to have their ASM's reduced.

Conclusion
PNES patients without MRI or EEG abnormalities are much less likely to have associated epilepsy, risk factors for epilepsy, and had different demographic profiles. There is a higher than expected level of EEG and MRI abnormalities in PNES patients without epilepsy. Such patients without MRI abnormalities were more likely to have their ASM's reduced, whereas the presence of EEG abnormalities did not influence ASM reduction.

Neuroimaging

Abstract #8

Pre-Operative Epileptic Network Architecture Constrains Surgery-Induced Connectome Reorganization

Sara Lariviere, Bo-yong Park, Yifei Weng, Jessica Royer, Zhengge Wang, Dewi Schrader, Zhiqiang Zhang, Boris Bernhardt

McGill University

Rationale
Approximately 30% of individuals with temporal lobe epilepsy (TLE) develop chronic pharmacoresistant epilepsy. Resection of the affected temporal lobe remains the most effective treatment to arrest refractory seizures. Here, we investigated the downstream consequences of surgery on the brain's connectome and how this reorganization relates to postoperative seizure outcome.

Methods
Twenty-five adult patients with drug-resistant TLE (13 males, mean age±SD=25.2±7.5 years) underwent T1w and diffusion MRI before and after anterior temporal lobectomy. Postoperative histopathology confirmed hippocampal sclerosis in every patient. Postsurgical seizure outcome was determined according to Engel's modified classification.

Subject-specific structural connectome manifolds, which capture spatial gradients of connectivity variations, were generated and sorted into ipsilateral/contralateral to the focus. Surgical cavities were excluded from all analyses.

Results
Multivariate mixed effects models, performed on the first three structural gradients, assessed pre- to postoperative connectome changes. Following surgery, individuals with TLE showed alterations affecting regions surrounding the resection site ($pFDR<2\times10^{-6}$) as well as contralateral fronto-occipital cortices ($pFDR<4\times10^{-4}$).

To simplify multidimensional gradients, we assessed pre- to postoperative connectome contraction/expansion changes. Postoperative contraction (i.e., increased segregation) was observed in contralateral temporo-limbic cortex, hippocampus, and amygdala ($pFDR<6\times10^{-6}$) while expansion (i.e., increased integration) was observed in ipsilateral fronto-occipital cortices ($pFDR<0.005$).

Lastly, the severity of preoperative ipsilateral hippocampal atrophy was related to greater postoperative contraction in areas of surgery-induced deformations. Favourable surgical outcome was associated with greater postoperative temporo-limbic contraction and fronto-occipital expansion.

Conclusion
Our findings highlight the utility of network neuroscience approaches to contextualize downstream connectome disruptions with clinical and standard neuroimaging parameters.

Neuroimaging

Abstract #9

Personalized Quantitative Analysis of Multimodal Imaging Data in Drug-Resistant Childhood Epilepsy

Sara Lariviere, Kristina Song, Danny Kim, Andrea Bernasconi, Neda Bernasconi, Mary Connolly, Dewi Schrader, Boris Bernhardt

McGill University

Rationale
Magnetic resonance imaging (MRI) has become a powerful tool in the diagnosis and treatment of epilepsy. Despite technical advances, routine clinical visual inspections may lack sensitivity to establish a diagnosis with a sufficient degree of confidence.

Here, we present an analytical pipeline for high-resolution multimodal MRI data of pediatric epilepsy patients. Our approach provides individualized multivariate asymmetry maps to identify subtle cortical pathology that may be initially overlooked by conventional neuroradiological examination.

Methods
Fourteen pediatric patients with drug-resistant epilepsy (five males, mean age±SD=13.21±3.58 years, range=8–18 years) and nine age- and sex-matched healthy children (six males, mean age±SD=11.67±3.39 years, range=6–17 years) underwent 3T MRI scans, including a (i) T1w, (ii) T2-FLAIR, (iii) quantitative T1, and (iv) diffusion MRI.

Patient-specific asymmetry maps comparing left vs. right hemispheres [(L–R)/((L+R)/2)] were derived from cortical thickness, mean diffusivity, as well as quantitative T1 and T2-FLAIR intensities, and were z-scored relative to controls.

Results
We present the cases of two children with drug-resistant epilepsy. Visual inspection of the MRI scans showed a right frontal FCD (case #1) as well as a right parahippocampal ganglioglioma (case #2). Quantitative analyses localized profound changes (i.e., increased atrophy, mean diffusivity, T2-FLAIR signal, qT1 intensity) in areas of high lesion conspicuity. Identified seizure onset zones were confirmed by postsurgical histological findings. Overall, multimodal asymmetry maps alone could identify a putative surgical target in approximately 71% of cases.

Conclusion
The use of multimodal postprocessing methods has shown promise in identifying subtle pathology and may ultimately improve personalized diagnosis and prognosis of patients with drug-resistant epilepsy.

Neuroimaging

Abstract #10

Electrical Source Imaging of the Ictal Onset Zone in the Surgical Evaluation of Children with Epilepsy

Arun Thurairajah[1], Kevin Jones[2], Alexander Freibauer[3], Rajesh Ramachandran Nair[3], Robyn Whitney[4], Puneet Jain[4], Elizabeth Donner[4], Elysa Widjaja[3]

[1]McMaster University
[2]McMaster Medical School
[3]McMaster Children's Hospital
[4]The Hospital for Sick Children

Rationale
To investigate the utility of Electrical Source Imaging generated with low density EEG (LD-ESI) to model the ictal onset zone (IOZ) as part of the surgical work up of children with medically refractory epilepsy.

Methods
This was a retrospective review of 12 patients from a district pediatric epilepsy center, from 2014 - 2019. ESI was generated using the Curry 8 software, incorporating T1 Magnetic Resonance Imaging (MRI) scans and EEG recordings. Concordance of the LD-ESI localizations to the epileptogenic zone was assessed by comparing LD-ESI to the anatomical descriptions of the patient's focal resection margins and noting their post-operative outcomes at 1 year. Localizations determined by ictal LD-ESI were also compared to those determined by interictal LD-ESI, positron emission tomography (PET) and magnetoencephalography (MEG).

Results
Ictal ESI correctly localized the ictal onset zone in 4/6 patients, with all four being seizure free at one year. Similarly, interictal ESI localized the irritative zone in 7/9 patients with focal resections, with 6/7 being seizure free at one year. Additionally, we observed ictal ESI to be concordant to interictal ESI in 5/6 patients who had both localizations available. Ictal ESI and interictal ESI were concordant to interictal MEG in 3/6 patients of which two were seizure free. Ictal ESI was concordant with PET in six of seven cases of which 4/6 were seizure free.

Conclusion
LD-ESI is a useful clinical tool to accurately model the IOZ within the pediatric population and has similar accuracy compared to other imaging techniques including MRI, MEG, and interictal ESI.

2. Clinical Epilepsy / EEG / Antiepileptics

Abstract #11

The Phenotypic Spectrum of KCNT1: A New Family with Variable Epilepsy Syndromes and Severity

Juan Pablo Appendino, Christina Cherian, Setareh Ashtiani, Paolo Federico, Christine P. Molnar, Marina Kerr, Aneal Khan, Ping Yee Billie Au, Karl Martin Klein

University of Calgary

Rationale
To show that pathogenic variants in KCNT1 can be associated with milder extra-frontal epilepsies, we report a KCNT1 family with a wide spectrum of phenotypes ranging from developmental and epileptic encephalopathy (DEE) to milder focal epilepsies not consistent with sleep-related hypermotor epilepsy.

Methods
A large Canadian family of Caucasian descent including 10 affected family members was recruited and phenotyped by direct interview and review of medical records. Clinical gene panel analysis was performed in two family members, and research exome was used to investigate the most severely affected family member. Segregation analysis was done by Sanger sequencing in two other affected and one unaffected relatives.

Results
Phenotypic information was available for five family members including two with DEE and three with normal development and focal epilepsy with extra-frontal onset. The latter had predominantly nocturnal seizures without hyperkinetic features and reported clusters of seizures at night with feeling of being unable to breathe associated with gasping for air, choking and/or repetitive swallowing, suggesting possible insular or opercular involvement. Presurgical workup including ictal subtraction SPECT and interictal PET in one individual with focal epilepsy was most consistent with a left temporal onset. Genetic analysis identified a rare heterozygous KCNT1 c.2882G>A, p.(Arg961His) variant that was predicted to be deleterious. Surgery was not recommended.

Conclusion
Our findings indicate that variants in KCNT1 can be associated with milder extra-frontal focal epilepsies. Rare KCNT1 variants should not be excluded during variant interpretation in patients with milder presentations based solely on previously understood gene-disease validity.

Clinical Epilepsy / EEG / Antiepileptics

Abstract #12

Global Pooled Analysis of Perampanel in Epilepsy Patients Treated in Routine Clinical Practice: The PERMIT Study

Vicente Villanueva[1], Wendyl D'Souza[2], Tony Wu[3], Imad Najm[4], Manoj Malhotra[5], Leock Y Ngo[6], Rob McMurray[6], Eugen Trinka[7]

[1]Hospital Universitario y Politécnico La Fe, Valencia, Spain
[2]St Vincent's Hospital Melbourne and The University of Melbourne, Victoria, Australia
[3]Chang Gung Memorial Hospital Linkou Medical Center and Chang Gung University College of Medicine, Taoyuan, Taiwan
[4]Cleveland Clinic, Cleveland, Ohio, USA
[5]Eisai Inc, Woodcliff Lake, New Jersey, USA
[6]Eisai Europe Ltd, Hatfield, Hertfordshire, United Kingdom
[7]Christian-Doppler University Hospital and Paracelsus Medical University, Salzburg, Austria

Rationale
To assess perampanel (PER) when used in everyday clinical practice to treat patients with epilepsy.

Methods
PERMIT is a pooled analysis of real-world data from 44 studies in which patients with focal-onset and generalised-onset epilepsy were treated with PER. Retention was assessed after 3, 6 and 12 months. Effectiveness assessments included 50% responder rate (≥50% seizure frequency reduction) and seizure freedom rate (no seizures since at least prior visit); in those with status epilepticus, effectiveness was assessed as responder rate (seizures under control). Safety/tolerability were assessed by adverse events (AEs).

Results
Full Analysis Set included 5193 patients (50.5% female; mean age, 39.7 years; mean number of previous antiepileptic drugs, 4.9). Baseline seizure types: focal-onset only (81.4%), generalised-onset only (12.6%), focal and generalised onset (4.5%) and status epilepticus (1.5%). Most patients were treated with PER as adjunctive therapy; 5.5% were treated as monotherapy at baseline. Mean PER dosage was 2.4 mg/day at baseline; 6.3 mg/day at last visit. At 3, 6 and 12 months, retention rates were 90.5%, 79.8%, and 64.2%, respectively. Mean time under PER treatment was 10.7 months. At last visit, responder and seizure freedom rates in patients with focal and/or generalised onset seizures were 50.0% and 20.5%, respectively; 52.7% of patients with status epilepticus were responders. AEs were reported for 49.9% of patients; most frequently dizziness/vertigo (15.2%) and somnolence (10.6%). Overall, 17.6% of patients discontinued due to AEs.

Conclusion
PER was effective and generally well tolerated when used to treat patients with epilepsy in everyday clinical practice.

Clinical Epilepsy / EEG / Antiepileptics

Abstract #13

Perampanel as Early Add-on Therapy for Epilepsy Patients with Focal-Onset and Generalised-Onset Seizures Treated in Clinical Practice

Estevo Santamarina[1], Javier Abril-Jaramillo[2], Xiana Rodriguez-Osorio[3], Takamichi Yamamoto[4], Rob McMurray[5], Eugen Trinka[6], Wendyl D'Souza[7], Vicente Villanueva[8]

[1]Vall d'Hebron University Hospital, Barcelona, Spain
[2]Centro de Neurología Avanzada, Sevilla, Spain
[3]Complexo Hospitalario Universitario de Santiago, Santiago, Spain
[4]Comprehensive Epilepsy Center, Seirei Hamamatsu General Hospital, Shizuoka, Japan
[5]Eisai Europe Ltd, Hatfield, Hertfordshire, UK
[6]Christian-Doppler University Hospital and Paracelsus Medical University, Centre for Cognitive Neuroscience, Salzburg, Austria
[7]St Vincent's Hospital Melbourne, The University of Melbourne, Victoria, Australia
[8]Hospital Universitario y Politécnico La Fe, Valencia, Spain

Rationale
To assess perampanel (PER) when used as early add-on therapy in everyday clinical practice.

Methods
Patients treated with PER as early add-on therapy for focal-onset and/or generalised-onset seizures were identified from an interim pooled analysis of data from 18 clinical practice studies. Retention was assessed after 3, 6 and 12 months of PER treatment. Effectiveness assessments comprised seizure freedom rate (no seizures since at least prior visit), responder rate (≥50% seizure frequency reduction). Safety/tolerability were assessed by adverse events (AEs).

Results
Data from 430 patients treated with PER as early add-on therapy were included (52.1% male; mean age, 41.9 years). Baseline seizure types: focal-onset only (85.0%), generalised-onset only (14.3%), and focal and generalised onset (0.7%). Patients had been treated with median of 1 previous antiepileptic drug (AED) and received median of 1 concomitant AED at baseline and at last visit. Mean PER dosage was 3.3 mg/day at baseline and 5.7 mg/day at last visit. At 3, 6 and 12 months, retention rates were 94.4%, 86.1%, and 79.3%, respectively. Mean time under PER treatment was 12.0 months. At last visit, seizure freedom rates in patients with focal-onset and generalised-onset seizures were 34.8% and 56.1%, respectively, and the corresponding responder rates were 80.2% and 80.7%, respectively. AEs were reported for 40.9% of patients; most frequent AEs were: behavioural AEs (aggression/anger/irritability; 15.1%), somnolence (12.9%) and dizziness/vertigo (10.6%). Overall, 13.4% of patients discontinued due to AEs.

Conclusion
PER was effective and generally well tolerated when used as early add-on therapy in clinical practice.

Clinical Epilepsy / EEG / Antiepileptics

Abstract #14

Seizure Freedom in Patients with Focal to Bilateral Tonic-Clonic Seizures (FBTCS) During the Open-Label, Single-Arm FAME Study: A Post Hoc Analysis of Low-Dose Maintenance Perampanel

Sang Kun Lee[1], Manoj Malhotra[2], Dae-Won Seo[3], Sang Ahm Lee[4], Amitabh Dash[5], Ji Woong Lee[6]

[1]Seoul National University Hospital, Seoul, Republic of Korea
[2]Eisai Inc., Woodcliff Lake, NJ, USA
[3]Samsung Medical Center, Sungkyunkwan University School of Medicine, Seoul, Republic of Korea
[4]Asan Medical Center, University of Ulsan College of Medicine, Seoul, Republic of Korea
[5]Eisai Singapore Pte. Ltd., Singapore
[6]Eisai Korea Inc., Seoul, Republic of Korea

Rationale

Perampanel is a once-daily oral anti-seizure medication (ASM) for focal-onset seizures (FOS) and generalized tonic-clonic seizures. Achieving seizure control is important in patients with convulsive seizures, including FBTCS, as these are often refractory and associated with increased mortality rates. This post hoc analysis of FAME (NCT02726074) assessed seizure-freedom rates in patients with FBTCS by perampanel maintenance dose (4–6 mg/day).

Methods

Patients were aged ≥12 years with FOS, with/without FBTCS, and had failed on ASM monotherapy. First adjunctive perampanel was up-titrated to ≤12 mg/day (12 weeks), followed by a 24-week Maintenance Period. Endpoints included 50% responder rates, seizure-freedom rates, and treatment-emergent adverse events (TEAEs). For this analysis, patients with FBTCS were stratified by perampanel maintenance dose.

Results

In the Full Analysis Set, 16/85 (18.8%) patients had FBTCS. Of these, 14/16 (87.5%) patients experienced a ≥50 reduction in seizure frequency at perampanel maintenance doses of 4 or 6 mg/day (n=7 [50.0%] each). Seizure freedom was achieved by 12/16 (75.0%) patients (4 mg/day: n=7/12 [58.3%]; 6 mg/day: n=5/12 [41.7%]). Thirteen patients (81.3%) reported TEAEs (4 mg/day [n=8]; 6 mg/day [n=5]); most common was dizziness (n=8/16; 50.0%). Three patients reported serious TEAEs, one of which led to discontinuation (suicide attempt [perampanel 4 mg/day]; unrelated to treatment).

Conclusion

Most patients with FBTCS achieved seizure freedom with maintenance perampanel 4–6 mg/day, with favorable tolerability. Despite the small sample size, these results suggest convulsive seizure freedom can be achieved with low perampanel doses when administered as an early-line treatment.

Clinical Epilepsy / EEG / Antiepileptics

Abstract #15

Efficacy and Safety of Adjunctive Perampanel for Myoclonic and Absence Seizures: Post Hoc Pooled Analysis of Adult, Adolescent, and Pediatric Patients in Studies 332, 311, and 232

Christian Brandt[1], Manoj Malhotra[3], J Ben Renfroe[2], Leock Y Ngo[3], Anna Patten[4]

[1]Bethel Epilepsy Center, Bielefeld, Germany
[2]Child Neurology Center of Northwest Florida, Gulf Breeze, FL, USA
[3]Eisai Inc., Woodcliff Lake, NJ, USA
[4]Eisai Europe Ltd., Hatfield, Hertfordshire, UK

Rationale
Some anti-seizure medications can exacerbate myoclonic and absence seizures in patients with generalized seizures. This post hoc pooled analysis assessed the efficacy and safety of adjunctive perampanel for myoclonic and absence seizures in adult/adolescent/pediatric patients using data from Phase II/III clinical studies.

Methods
During the randomized, double-blind Study 332 (NCT01393743), patients aged ≥12 years with generalized tonic-clonic seizures (GTCS) received placebo/adjunctive perampanel 8 mg/day. In Study 311 (NCT02849626), patients aged 4–<12 years with focal-onset seizures/GTCS received open-label perampanel ≤16 mg/day. In Study 232 (NCT01527006), patients aged 2–<12 years with epilepsy received open-label perampanel ≤0.18 mg/kg/day. Data from patients with baseline myoclonic and/or absence seizures were pooled. Assessments included: median percent change in seizure frequency/28 days; 50% responder rates; treatment-emergent adverse events (TEAEs).

Results
At baseline, 66/393 patients had myoclonic seizures (placebo, n=23; perampanel, n=43) and 72/393 had absence seizures (placebo, n=33; perampanel, n=39); patients with both seizure types are counted twice. Reductions in seizure frequency/28 days were observed with placebo and perampanel: myoclonic, 52.5% and 24.6%; absence, 7.6% and 25.1%, respectively. Corresponding 50% responder rates were: myoclonic, 60.9% (n=14/23) and 44.2% (n=19/43); absence, 39.4% (n=13/33) and 38.5% (n=15/39), respectively. TEAEs with placebo and perampanel occurred in 18 (78.3%) and 36 (83.7%) patients with myoclonic seizures, and 25 (75.8%) and 34 (87.2%) patients with absence seizures, respectively. With perampanel, the most common TEAEs were dizziness and fatigue.

Conclusion
Despite small patient numbers, these data suggest adjunctive perampanel does not worsen myoclonic/absence seizures in adult/adolescent/pediatric patients.

Clinical Epilepsy / EEG / Antiepileptics

Abstract #16

Long-Term Efficacy and Safety of Adjunctive Perampanel in Elderly Patients with Focal-Onset Seizures (FOS) by Concomitant Anti-Seizure Medication (ASM) Use

Rohit Marawar[1], Manoj Malhotra[5], Ilo E Leppik[2], Robert T Wechsler[3], Anna Patten[4], Leock Y Ngo[5]

[1]Wayne State University, Detroit, MI, USA
[2]University of Minnesota, Minneapolis, MN, USA
[3]Idaho Comprehensive Epilepsy Center, Boise, ID, USA
[4]Eisai Europe Ltd., Hatfield, Hertfordshire, UK
[5]Eisai Inc., Woodcliff Lake, NJ, USA

Rationale
This post hoc analysis evaluated long-term (≤4 years) efficacy/safety of adjunctive perampanel by concomitant baseline ASM use (number/most common) in elderly patients (aged ≥60 years) with FOS during Studies 307 (NCT00735397) and 335 open-label extension (OLEx; NCT01618695).

Methods
Patients completing randomized, double-blind, Phase III studies could enter OLEx Studies 307 (16-week blinded Conversion; 256-week Maintenance) or 335 OLEx (4-week Pre-conversion; 6-week Conversion; ≥46- week Maintenance). Seizure frequency and treatment-emergent adverse events (TEAEs) were monitored throughout.

Results
The Safety Analysis Set included 71 patients (1 ASM, n=8; 2 ASMs, n=33; 3 ASMs, n=30). The most common baseline ASMs were: levetiracetam (n=28 [39.4%]), carbamazepine (n=22 [31.0%]), and lamotrigine (n=20 [28.2%]). During Years 1/2, respectively, median percent reductions in seizure frequency were: 1 ASM, 63.7% (n=8) and 59.1% (n=5); 2 ASMs, 49.0% (n=33) and 45.5% (n=15); and 3 ASMs, 44.1% (n=30) and 51.8% (n=18); for the most common ASMs, reductions were: levetiracetam, 51.6% (n=28) and 51.2% (n=15); carbamazepine, 45.6% (n=22) and 50.9% (n=12); and lamotrigine, 42.8% (n=20) and 53.4% (n=11). Seizure reductions were also observed during Years 3/4 across subgroups. During Years 1/2, 45.8%–100.0% of patients receiving 1–3 concomitant ASMs experienced TEAEs; for the most common ASMs, this was 50.0%–89.3%. Dizziness and fall were the most common TEAEs throughout these OLEx studies.

Conclusion
Despite small patient numbers in some subgroups, these data suggest adjunctive perampanel was well tolerated with sustained seizure reduction for ≤4 years in elderly patients with FOS, regardless of concomitant ASM use.

Clinical Epilepsy / EEG / Antiepileptics

Abstract #17

Cognitive Performance and Retention After 12-Month Adjunctive Brivaracetam in Difficult-To-Treat Patients with Epilepsy in a Real-Life Setting

Bernhard J. Steinhoff[1], Jakob Christensen[2], Colin P. Doherty[3], Marian Majoie[4], Anne-Liv Schulz[5], Fiona Brock[6], Iryna Leunikava[5], John P. Leach[7]

[1]Kork Epilepsy Centre, Kehl-Kork, Germany; Clinic of Neurology and Neurophysiology, University of Freiburg, Freiburg, Germany
[2]Aarhus University Hospital, Aarhus, Denmark
[3]Trinity College Dublin, Dublin, Ireland; FutureNeuro, SFI Research Centre, RCSI, Dublin, Ireland
[4]Academic Center of Epileptology Kempenhaeghe Maastricht University Medical Center, Heeze, The Netherlands
[5]UCB Pharma, Monheim am Rhein, Germany
[6]UCB Pharma, Slough, UK
[7]School of Medicine, University of Glasgow, United Kingdom

Rationale
Evaluate retention and cognitive performance in patients aged ≥16years with focal seizures after 12-month adjunctive brivaracetam treatment in real-world practice.

Methods
Patients received brivaracetam in a prospective, non-interventional post-marketing study in Europe (EP0077/NCT02687711).

Results
544/548 patients received ≥1 brivaracetam dose (=safety set [SS]; mean age: 43.6years; 52.8% female; mean time since epilepsy diagnosis: 22.7years; median baseline focal seizures/28days: 3.7; mean lifetime antiseizure medications [ASMs] [=historical ASMs+ASMs taken at entry]: 7.3; 77.9% had ≥2 concomitant ASMs at entry). Median brivaracetam exposure duration: 355.0days (SS). Twelve-month brivaracetam retention was 57.7% in full analysis set (FAS; SS patients not receiving prior brivaracetam; n=541), 60.3% in modified FAS (SmPC brivaracetam use; n=310). In FAS, the proportion of patients reporting mildly or significantly impaired cognitive performance (EpiTrack) was lower at 12months (4.9%, 36.1%; n=61) versus baseline (14.8%, 49.3%; n=142); that with excellent or average cognitive performance was higher (6.6%, 52.5%) versus baseline (2.8%, 33.1%). Modified FAS trends were similar. 23.0% of patients reported significant total EpiTrack score improvement (≥4 increase) from baseline to 12months (n=61); 67.2% remained unchanged (change of −2 to 3); 9.8% reported worsening (≥3 decrease) (FAS). 41.2% of SS patients experienced ≥1 treatment-emergent adverse events (TEAE); 25.9% discontinued due to TEAEs; 36.0% experienced TEAEs considered drug-related by investigator (≥5%: drug ineffective [11.4%], seizure [6.3%]). Two deaths (0.4%) were reported (relationship to brivaracetam: one unavailable, one unrelated).

Conclusion

In difficult-to-treat patients with epilepsy, >50% remained on brivaracetam for 12months. Two-thirds reported no significant change in cognitive function; one-quarter improved. Brivaracetam introduction was well-tolerated.

Clinical Epilepsy / EEG / Antiepileptics

Abstract #18

The Treatment of Epilepsy in Older Adults: A National Survey

Nafisa Husein[1], Mark Keezer[1], Timothé Langlois Terrien[1], Nathalie Jetté[2], Colin Josephson[3]

[1]*Université de Montréal*
[2]*Icahn School of Medicine*
[3]*University of Calgary*

Rationale
The optimal treatment of epilepsy in older adults remains understudied and uncertain. Comorbidities, polypharmacy and frailty are all factors that add to the complexity of treating older adults with epilepsy.

Methods
We surveyed geriatricians, neurologists and epileptologists from across Canada. Our survey included 15 questions on medical and surgical opinions and medical practices. We transmitted a link to our online survey by facsimile to all geriatricians, neurologists and epileptologists listed in the Scott's Medical Directory. After 3 facsimile attempts, an additional invitation was mailed to the initial non-respondents. We used descriptive statistics to map these responses.

Results
182 geriatricians, neurologists and epileptologists responded to our survey (response rate of 15%). Levetiracetam and lamotrigine were the preferred antiseizure medication (ASM) to prescribe in 75% or more of older adult patients among surveyed geriatricians. These two medications and lacosamide were the preferred prescribed ASM among surveyed neurologists without epilepsy training. Compared to the other two physician groups, more epileptologists prescribed lacosamide. Most neurologists, epileptologists and geriatricians ranked control of seizure as the highest priority when prescribing an ASM to an older adult with new focal-onset. ASM tolerability was generally ranked third by the respondents. 30.8% and 31.8% of epileptologists and geriatricians, respectively, are "likely" to propose surgery to treat someone with bilateral tonic-clonic seizures at least once per month if they are aged 60-69 years old. This number went up to 38.8% among neurologists without epilepsy training. All 3 physician groups were more likely to propose surgery to patients aged 40-49 years as compared to individuals aged 60 years and above.

Conclusion
Our study establishes that there are important differences in opinion and treatment practices between physician groups. Our surveyed geriatricians, neurologists and epileptologists differed in their approach to ASM choice as well as surgical treatments. This may relate to the lack of clear and accepted clinical practice guidelines. This may also point to the need for more robust evidence.

Clinical Epilepsy / EEG / Antiepileptics

Abstract #19

Investigating Physiological and Interictal Epileptiform Discharges Using Intracranial Recordings in Human

Nasim Mortazavi[1], Milad Khaki, Greydon Gilmore, Jorge Burneo[2], David Steven[2], Lyle Muller[3], Julio Martinez-Trujillo[1], Ana Suller Marti[2]

[1]*Robarts, Schulich, University Of Western Ontario*
[2]*Lawson Health Research*
[3]*Brain And Mind*

Rationale
Interictal epileptiform discharges (IEDs) and Sharp Wave ripples (SWR) are pathological and physiological events in patients with temporal lobe epilepsy. IEDs demonstrate a state of hypersynchronous depolarization of neuronal activity. SWRs are the most synchronous neuronal activity evoked by the hippocampus. Although these two events display similar temporal patterns, they carry different energy in frequency bands. We developed an algorithm to detect and classify them utilizing their spectro-temporal characteristics.

Methods
We analyzed the SEEG recordings obtained from patients with medically resistant epilepsy at the Epilepsy Unit in Western University Hospital. After preprocessing and removing sleep and ictals, the power of signal waveforms in sleep and non-sleep intervals were extracted symmetrically in non-overlapping intervals of 500 ms, and their energy distributions were calculated. Then the spectro-temporal features for each contact of each electrode were extracted.

Results
The recordings included 14 sessions of 24 hours of recordings from two patients with 336 hours extracted from four hippocampus electrodes, including anterior and posterior. Our results indicate that SWRs energy distribution is significantly more stationary than IEDs in non-sleep periods. IEDs carrying the most energy in the bands [30-45] Hz, SWR, on the other hand, are distributed between and [25-40] Hz and [90-110] Hz. Our algorithm successfully distinguished IEDs from SWRs during non-sleep with an accuracy of 76.43%.

Conclusion
Our automated algorithm successfully distinguished IEDs from SWRs in the hippocampus electrodes using extracellular SEEG recordings in epilepsy patients. The finding shows that the waveforms' energy is more significant in sleep than awake periods.

Clinical Epilepsy / EEG / Antiepileptics

Abstract #20

Identifying Priorities for Epilepsy Research in Canada

Rebecca Woelfle[1], Amaya Singh[1], Rachel Chepesiuk[2], Carla Southward[2], Jordan Antflick[2], Katherine Cowan[3], Kathryn Hum[4], Ana Suller-Marti[5]

[1]*EpLink - The Epilepsy Research Program of the Ontario Brain Institute*
[2]*Ontario Brain Institute*
[3]*James Lind Alliance*
[4]*The Centre for Addiction and Mental Health*
[5] *Western University, Departments of Clinical Neurological Sciences and Paediatrics*

Rationale
Health research agendas are often set by researchers or by industry and may not reflect the needs of people who live and work with epilepsy. The James Lind Alliance (JLA) provides a process for gathering unanswered questions or evidence uncertainties from patients, caregivers and health care providers. This JLA priority-setting partnership, the first such initiative for epilepsy in Canada, was undertaken to identify and prioritize unanswered questions relating to epilepsy and seizures.

Methods
In a survey conducted from October 2019–Feb 2020, stakeholders across Canada were asked to submit their questions about epilepsy and seizures. Under the guidance of a national steering committee, and led by a team of information specialists, submissions were formed into summary questions and checked against existing evidence. A list of 43 unanswered questions was sent out in an interim survey where respondents selected up to 10 priority questions. In April 2021, a final workshop was held with representatives of all stakeholder groups where a top 10 list was reached by consensus.

Results
A total of 516 Canadians submitted over 1000 questions for review. Submissions were refined, summarized and categorized into 198 unique research questions. Results from the interim survey were used to generate a shortlist of 16 questions from which the top 10 priorities were selected and ranked at the final workshop.

Conclusion
These priorities will help guide researchers and funding organizations toward areas of focus that meet the needs of people with epilepsy and/or seizures, their care providers and health care providers.

Clinical Epilepsy / EEG / Antiepileptics

Abstract #21

Withdrawn

Clinical Epilepsy / EEG / Antiepileptics

Abstract #22

Development and Implementation of a Mnemonic Testing Tool to Improve Periictal Assessments of Patients in the Epilepsy Monitoring Unit (EMU)

Grissel Crasto

University Health Network

Rationale
Nurses provide care to Epilepsy Monitoring Unit (EMU) patients within a mixed neurology and neurosurgery inpatient unit setting at Toronto Western Hospital (TWH). The unit currently does not have an efficient standardized testing tool to comprehensively test patients periictally (during seizures). A complex and lengthy chart is currently available for testing patients during seizures at the bedside. This chart is not being adequately utilized by nurses to test for seizures in a complex and mixed medical surgical unit according to physician and nursing input. Accurate and detailed assessments are critical to establish a diagnosis, to localize and classify seizures in this patient population. The EMU at TWH has also had a high turnover among its novice nursing staff over the last three years. This turnover and the absence of a standardized testing method may have contributed to inconsistencies in practice. Although a European consensus (Beniczky et al., 2016) on testing patients post-ictally exists, there is still no international consensus on the comprehensive periictal testing of patients in the EMU. This quality improvement initiative proposes the development and use of a mnemonic-based assessment tool called the "ICTAL" tool to improve the practice and efficacy of assessing patients in the EMU at Toronto Western Hospital, University Health Network. By assessing the criteria of cognitive, sensory, behavioural and motor functions in patients post-ictally, this nursing assessment tool aims to help epileptologists and healthcare providers with diagnostic lateralization (identifying the hemisphere) and localization (identifying the cerebral lobe) of seizures to improve and enhance patient care outcomes in the EMU. The ICTAL tool will also assist epileptologists and healthcare providers with the classification of seizures for diagnostic purposes.

Methods
An assessment audit tool was developed in collaboration with EMU nurses, physicians, clinical nurse educators and nursing professional practice. Assessment audits for five seizure dimensions safety, level of consciousness (LOC), speech, mobility and aura were conducted over a four-week period in the EMU. The audits were completed by EMU staff physicians who already review weekly event recordings in the EMU to ensure confidentiality and prevent observer bias. The ICTAL tool was introduced to nurses along with education on how to use the tool and how to document their findings through workshops. Post introduction of the tool and nursing documentation workshops, Audits were completed again over a four-week period.

Results
Safety assessments were completed 100% of the time for all types of seizures. For simple partial seizures, LOC assessments improved from 75% to 100% and speech assessments improved from 25% to 75% . For complex partial seizures, both LOC and mobility assessments improved from 80% to 100%. For

generalized seizures, speech assessments improved from 25% to 60%, while LOC and safety remained consistent at 100%. No psychogenic events were noted during the data collection period.

Conclusion

Improvements in bedside assessments were noted in simple partial, complex partial and generalized seizures for the dimensions of speech and LOC. While safety was assessed at 100% for all types of seizures, assessment for other dimensions were lacking. A second educational workshop will be delivered along with annual refreshers to reinforce the importance of assessing all types of seizures for all five dimensions. Due to COVID-19 related closures of the EMU, these educational workshops will be delivered after EMU are reopened in full capacity.

Clinical Epilepsy / EEG / Antiepileptics

Abstract #23

A Case Study of Lacosamide Monotherapy Overdose in a Paediatric Patient.

Ahmed Elmardenly, Randa Sultan, Manal Bajammal, Hebah Qashqari, Osama Muthaffer

King Faisal Specialist Hospital & Research Center

Rationale

Lacosamide is one of the new-generation antiseizure drug approved by the FDA as adjunctive therapy for partial-onset seizures. Studies suggest that Lacosamide acts as sodium channel modulator.

Methods

We are presenting a 5-year-old Saudi boy with global developmental delay and drug resistance epilepsy. He was commenced on lacosamide with clear instruction and documentation to build up the dose gradually. Unfortunately, his care giver administered 10 times the recommended initial dose for 7 days (100mg twice daily instead of 10mg twice daily).

He was brought to the emergency department with somnolence, chocking, respiratory distress and fever. He was admitted to the hospital for aspiration pneumonia management. The medication reconciliation, revealed a clear history of incorrect lacosamide dose that does not fit the documentation nor the recommended dose for weight.

Results

During his admission, lacosamide was held and the toxicology team were informed. Supportive care was provided, he was placed on cardiac monitor with close neuro-vitals observation. EEG confirmed absence of non-convulsive status. Serial EKGs were normal (PR, QT & QRS duration). After 72 hours, he regains his baseline activity and he was discharged in stable condition.

Conclusion

To our knowledge, this is the first case report of lacosamide monotherapy overdose in a paediatric patient. Additionally, this child received frequent high doses instead of a single event of lacosamide overdose. Our case supports the overall safety profile of lacosamide in paediatric population. However, further studies by an expert panel are highly recommended to examine this theory.

Clinical Epilepsy / EEG / Antiepileptics

Abstract #24

'Optimal' EEG Montage (24 Channels) to Perform Accurate and Simple Source Localization in Daily Clinical Setting.

Giovanni Pellegrino, Eliane Kobayashi

Montreal Neurological Institute and Hospital

Rationale
Magnetoencephalography (MEG) and high-density electroencephalography (hd-EEG) are useful in presurgical evaluation of patients with drug-refractory epilepsy, as they improve the localization of the epileptic focus, surgical decision and, potentially, post-surgical outcome. Nonetheless, these two techniques are underused as they are costly, time-demanding and difficult to handle in everyday clinical practice. In this study we evaluated the localization performance of an 'optimal' EEG montage consisting in adding to standard 10-20 positions a few electrodes around the region where interictal epileptiform discharges show maximal amplitude. This would be a reasonable strategy under the assumption that the topographical distribution of the electric field in the vicinity of the focus is more relevant to source localization.

Methods
We retrospectively analyzed data of patients who underwent simultaneous EEG-MEG recordings (24 patients) and for whom the epileptic focus could be localized thanks to invasive EEG or epilepsy surgery(gold-standard). We compared the following strategies for source localization of interictal activity: a) MEGsource localization, b) EEG-MEG fusion source localization, c) low-resolution EEG source localization (21channels), d)'optimal' EEG source localization (10-20 + n channels around the peak of the spike), e) same number of electrodes as (d) but randomly drawn from a 64 10-10 layout. The primary endpoint was thedistance of the peak of the source from the epileptic focus.

Results
Best localization performance was achieved by MEG and EEG-MEG fusion (localization error 7.4mm and7.5 mm). Low-resolution EEG had the worst performance (16mm localization error), but adding a few channels optimally located quickly improved localization performance (22ch = 14mm, 23 channels = 13mm, 24 channels = 8 mm). Adding more channels did not further improve the performance. Drawing additional channels randomly did not improve the localization error.

Conclusion
Source localization from optimal EEG montage with just 24 channels achieves a localization error roughlycomparable to MEG and EEG-MEG fusion, while being cheaper, easier, time-saving. Optimal EEG source localization could be explored in clinical setting whenever hd-EEG and MEG are not readily available.

Clinical Epilepsy / EEG / Antiepileptics

Abstract #25

Marijuana Use Habits in the Epilepsy Population in Canada Post-Legalization

Caroline Esmonde-White[1], Jayme Arts[2], Ana Suller-Marti[3]

[1]*Schulich School of Medicine & Dentistry*
[2]*London Health Sciences Centre*
[3]*Western University, Departments of Clinical Neurological Sciences and Paediatrics*

Rationale

Patients with epilepsy may turn to alternative treatments such as marijuana to manage both their epilepsy and medication side-effects. The legalization of recreational marijuana by the Canadian government in 2018 increased accessibility and awareness, despite a lack of evidence that it is beneficial for epilepsy patients. The goal of our study is to review Marijuana use in patients with epilepsy in Canada.

Methods

A Canadian cross-sectional survey was launched to investigate if marijuana is used, usage habits, and perceptions of marijuana, in patients with epilepsy.

Results

99 surveys were analysed. 75.8%(n=75) were female and 83.8%(n=83) were completed by participants. The mean age of participants was 32.2 years(IQR=24-40). The duration of epilepsy was over 10 years in 56.1%(n=55) and the most common seizure frequency is once per month 50.5%(n=49). From the total participants, 76.8%(n=76) have used marijuana. 33.9%(n=21) of users report using marijuana because of their epilepsy. Buying marijuana at a dispensary without a prescription was the most common way of obtaining it (60.7%;n=37). 30%(n=18) of users smoked marijuana and 7.6 grams(IQR=2-7) is the mean weekly dose. 63.2% of users feel more comfortable using marijuana because it is "natural", though 61.4% have felt the need to hide marijuana usage. 51.1%(IQR=15-73) reported a beneficial effect after using marijuana. Stigma against people using marijuana was found in 89.7% of users and 68.2% of non-users.

Conclusion

Marijuana is a common concern in caregivers and patients with epilepsy. These results suggest that more data is required on the use of marijuana in the Canadian population suffering from epilepsy.

Clinical Epilepsy / EEG / Antiepileptics

Abstract #26

Toward an Explicit Neuroethics Approach to Epilepsy Monitoring Unit Triage

Jason Randhawa, Chantelle Hrazdil, Patrick McDonald, Judy Illes

University of British Columbia

Rationale
Epileptologists generally triage patients to epilepsy monitoring units (EMUs) via unwritten protocols that vary by institution. In the absence of explicit guidance, decisions can be ethically taxing and easily challenged. We sought to formalize an approach to address the challenges of EMU triage guided by ethics literature.

Methods
We performed a scoping review of the triage literature available from neurology and other areas of medicine including critical care, transplant medicine, infectious disease, and psychiatry to inform ethical principles that could guide a model for the EMU setting.

Results
A model with two components emerges from our findings. The first component addresses three strategic targets for waitlist management infrastructure at the institutional level: (1) accountability to the patient and the public; (2) engagement of clinicians and hospital administrators; and (3) empowerment of dedicated wait list managers. The second component applies a combination of three ethics principles prioritarianism, utilitarianism, and justice to triage at the patient level.

Conclusion
Implementation and testing of the model will reveal its strengths and weaknesses in different settings, both for those that are well-resourced and others to which access to EMUs is scarce. Nonetheless, consolidation of these strategic and principled components may help to navigate the pressures of complex decisions involved in EMU triage, even in the face of diverse practice patterns, patient populations, and constraints on resource distribution.

Clinical Epilepsy / EEG / Antiepileptics

Abstract #27

Epilepsy and Pregnancy: An Audit of Specialized Care

Jimmy Li[1], Dènahin Hinnoutondji Toffa[2], Dang Khoa Nguyen[2]

[1]Centre de Recherche du Centre Hospitalier de l'Université de Montréal
[2]Centre Hospitalier de l'Université de Montréal

Rationale
Caring for women with epilepsy (WWE) during pregnancy poses unique challenges. We conducted an audit of the care our epilepsy clinic provided to pregnant WWE.

Methods
We performed a retrospective study on all pregnancies followed at a Canadian tertiary care centre's epilepsy clinic between January 2003 and March 2021. Among 81 pregnancies in 53 patients, 72 pregnancies in 50 patients were analyzed to determine patient-related, follow-up-related, antiseizure-medication-related, and child-related pregnancy characteristics. Univariate analyses were performed to explore if these characteristics were associated with disabling seizure occurrence during pregnancy. Qualitative data were gathered by interviewing six randomly chosen patients.

Results
Most pregnancies were intended (71.6%) and occurred in women who used folic acid pre-pregnancy (75.8%) and who followed recommended blood tests for antiseizure medication levels (70.5%). Most often used antiseizure medications were lamotrigine (43.1%), followed by carbamazepine (31.9%) and levetiracetam (13.0%). One child was born with a thyroglossal duct cyst; our congenital malformation rate was thus 1.9%. Disabling seizures occurred in 23.6% of pregnancies. Exploratory analyses suggested that disabling seizure occurrence during pregnancy was associated with younger patient age (p=0.018), higher number of antiseizure medications used during pregnancy (p=0.048), lamotrigine usage in polytherapy (p=0.008), and disabling seizure occurrence pre-pregnancy (p=0.027). All respondents to the qualitative aspect of our study expressed overall satisfaction with our services.

Conclusion
This Canadian audit provides an in-depth description of pregnancies benefiting from specialized epilepsy care. Our results suggest an association between disabling seizure occurrence during pregnancy and lamotrigine usage in polytherapy that warrants further evaluation.

Clinical Epilepsy / EEG / Antiepileptics

Abstract #28

Classification of Ictal and Inter-Ictal States Using Breathing and Heart Rates Obtained with the Hexoskin Wearable Device

Yassine Lamrani[1], Jérôme St-Jean[1], Manon Robert[1], Dehanin Toffa[1], Yen Phuoc Tran[1], Dang Khoa Nguyen[2], Elie Bou Assi[2]

[1]University of Montreal Hospital Research Center (CRCHUM)
[2]University of Montreal Hospital Research Center (CRCHUM), Department of Neuroscience, University of Montreal

Rationale
While recent studies have explored seizure detection based on smartwatches or bracelets, little attention has been given to connected shirts. In this work, we analyzed respiration and electrocardiography signals recorded with the Hexoskin smartwear between interictal and ictal epochs. A support vector machine (SVM) classifier was then trained and tested.

Methods
Patients admitted to the CHUM epilepsy monitoring unit were asked to wear the Hexoskin smartwear. Breathing rate (BR) and heart rate (HR) were extracted from respiratory and electrocardiography signals respectively (1-sec window). The Wilcoxon signed-rank test was used to evaluate the existence of a statistically significant difference in terms of BR and HR respectively between inter-ictal and ictal epochs. A SVM classifier was then trained to classify epochs based on HR and BR. K-fold validation was performed to determine optimal hyperparameters using a GridSearch

Results
67 seizures from 13 patients were analyzed. A significant difference was observed in BR (p < 0.01) and in HR (p < 0.01) between the ictal and inter-ictal epochs. Performances on the held-out test set (20%) reached an accuracy of 78,69% when combining BR and HR features (accuracy of 66,29% and 65,63% for HR and BR alone respectively).

Conclusion
We suggest that the combination of cardiac and respiratory signals improves the classification of interictal and ictal epochs. Results show promise regarding the use of the Hexoskin smart wear for seizure detection. Further analyses implementing a seizure detection algorithm using data from a larger cohort of patients are required to confirm our suggestions.

Clinical Epilepsy / EEG / Antiepileptics

Abstract #29

An Evaluation of Gait, Parkinsonian Features,and Adaptive Behaviours in Adults with Dravet Syndrome

Arunan Selvarajah, Carolina Gorodetsky, Paula Marques, Quratulain Zulfiqar Ali, Alfonso Fasano, Danielle Andrade

University Health Network

Rationale
Gait abnormalities, which are sometimes different than those reported in childhood, have also been reported in a few adults. In 2014, DS adults with SCN1A pathogenic variants were reported to develop signs of parkinsonism in their early 20's. Our primary objective was to examine clinical gait analysis and modified Unified Parkinson's Rating Disease Scale (mUPDRS) scores in DS adults. Our secondary objective was to evaluate whether there a loss of adaptive behaviours occurred over a 5-year period.

Methods
Gait analysis data was extracted from a gait mat built with sensors and the ProtoKinetics software. Clinical mUPDRS scores were assigned to resting tremors, facial expression, arising from a chair, gait, posture, and body bradykinesia. Regression analyses were performed for the gait and mUPDRS data. We also performed a longitudinal observational study, examining the Vineland Adaptive Behaviour Scales 2nd edition (VABS-II) in 2014 and again in 2019.

Results
Gait analysis showed young DS adults performed worse than an average healthy 62-year old control group in most gait parameters. We also show a parkinsonian-like gait in these adults. Parkinsonian features got worse with age. Initially, we observed improvements in expressive and socialization skills, and decreases in gross motor and communication skills.

Conclusion
So far, these patients are seen and treated as having a neurodevelopmental epileptic encephalopathy. However, understanding how their adult brains age is of utmost importance to proper patient care. The study findings suggest performing similar assessments as early as possible, to allow for a holistic approach to care and use of support services.

Clinical Epilepsy / EEG / Antiepileptics

Abstract #30

Epilepsy and Sleep: A Preliminary Study on the Use of a Smart Shirt for Sleep Assessment in Patients with Epilepsy

Laurence Beauregard[1], Manon Robert[1], Denahin Toffa[1], Dang Khoa Nguyen[2], Elie Bou Assi[2]

[1]University of Montreal Hospital Research Center (CRCHUM)
[2]University of Montreal Hospital Research Center (CRCHUM), Department of Neuroscience, University of Montreal

Rationale

Epilepsy is commonly associated with sleep disturbances. Bad sleep quality reduces seizure control while seizures disrupt sleep, causing a vicious cycle. Diagnosis and management of sleep disturbances should be addressed to improve the quality of life of patients with epilepsy (PWE). Polysomnography (PSG) is the gold standard for sleep assessment, but access to this exam is limited. Wearable technology becomes interesting for long-term sleep monitoring. The aim of this study was to assess sleep efficiency (SE) of PWE using the Hexoskin smart shirt (SS).

Methods

Forty-four PWE hospitalized at the CHUM Epilepsy Monitoring Unit (EMU) were recruited. Based on cardiac, respiratory and movement data, the Hexoskin algorithm calculated SE. A total of 365 nights, corresponding to 2428.9 hours of sleep monitoring, were recorded and categorized depending on epileptic seizure occurrence. A statistical analysis was performed using the Mann-Whitney-U test.

Results

Nocturnal seizures impacted SE in comparison with nights without seizures. Average SE decreased from 92,88% to 89,33% when nocturnal seizures occurred ($p<0.05$). No significant differences in SE were obtained between pre-seizure and post-seizure nights. Nights preceded and followed by seizures had an average decrease of 3,44% in SE when compared to reference nights ($p<0.05$). Average SE acquired with the shirt were higher than normative SE obtained previously with PSG ($p<0.05$) (Boulos et al., 2019).

Conclusion

Hexoskin-based sleep monitoring suggests that SE decreases when nights are preceded and followed by seizures or when nocturnal seizures occur. Further studies with a higher number of PWE, ideally with simultaneous PS and SS recordings, are needed. Authors acknowledge financial support from CIHR, NSERC, and IVADO.

Clinical Epilepsy / EEG / Antiepileptics

Abstract #31

Spectral Shifts Across Distributed Networks in Cortex Predict Seizure Onset

Maryam Hasanzadeh Mofrad, Greydon Gilmore, Ali Khan, David A. Steven, Jorge G. Burneo, Julio Martinez-Trujillo, Lyle Muller, Ana Suller-Marti

Western University

Rationale
Research has generally focused on the balance between excitation and inhibition at the seizure focus. However, epilepsy is increasingly recognized as a network disorder. With this in mind, we hypothesized that the most predictive pre-seizure changes in activity may be distributed across cortical networks.

Methods
We studied intracranial electroencephalogram (iEEG) recordings in 5 patients (London Health Sciences Centre) with therapy resistant epilepsy. We seek to understand patterns of narrow- and broad-band spectral shifts prior to seizure onset in these patients. We quantified changes in carefully normalized δ, α and β frequency bands with respect to the wideband spectrum (1-100 Hz). We then developed a regularized classification model to identify spectral shifts that are predictive of seizure onset.

Results
Patients were 22-63 years old with the onset age of 0.75-24 years when hospitalized and tried 3-9 anti-seizure medications. They were recorded for 154-315 hours with 18-100 seizures detected during recordings. We find predictions of seizure occurrence with high accuracy 15-25 minutes prior to seizure onset, with AUC metrics comparable to or surpassing previous approaches. Moreover, applying the classification model over the stream of iEEG signals reveals the abnormal brain activity, opening the possibility to provide advanced warning.

Conclusion
By taking subtle spectral shifts across distributed brain networks into account, we can predict seizure occurrence with high accuracy. In future work, we will investigate how these distributed patterns underlie shifts in the balance of excitation and inhibition at the seizure focus through further computational analyses. [L.M. and A.S. contributed equally to this work]

Clinical Epilepsy / EEG / Antiepileptics

Abstract #32

Exploring the Source Cloud: the Spatial Extent of Sleep-Wake Epileptic Source Localizations over a Thousand Thresholds

Darion Toutant[1], Graham McLeod[2], Parandoush Abbasian[1], Amirhossein Ghassemi[1], Maziar Darbandi[1], Marcus Ng[1]

[1]*University of Manitoba*
[2]*University of Calgary*

Rationale
Thresholding constraints can greatly affect the spatial extent of calculated source localization solutions. In standardized low resolution brain electromagnetic tomography (sLORETA), convention uses a 50% threshold. We assessed whether the spatial sum of source localizations (the "source cloud") derived from spikes in the same person across five sleep-wake states (SWS: N1, N2, N3, awake, REM) can remain different over 1000 spatial thresholds.

Methods
We used Curry 8 (Compumedics, Australia) to perform sLORETA on EEG co-localized to MRI from epilepsy monitoring unit patients recorded using 10-20 electrodes and a subtemporal chain. With MATLAB (MathWorks, USA), we plotted the percentage of brain voxels containing a source generator when spatially thresholded 1000 times over 0.1% increments from 0-100%. After calculating areas under the curve (AUC) for each SWS, we compared SWS within the same person by taking the absolute value between AUC. We used ANOVA to test 10 SWS-AUC comparisons.

Results
From 1132 spikes in 49 epilepsy patients, we found the greatest intra-individual AUC differences between REM and other SWS over 1000 spatial thresholds (delta-AUC range 8.1-12.6, n=27-34, p=0.0016). N2 and N3 differed least from other SWS (delta-AUC range 7-11.4, n=25-34).

Conclusion
We demonstrate that the spatial extent of "source clouds" from 5 SWS can remain different within the same person over 1000 spatial thresholds. Future directions include finding new ways of calculating the optimal threshold to best estimate the spatial extent of source clouds between SWS, and clarifying the highly variable source cloud of REM sleep when compared to wakefulness, N3, and N2.

Clinical Epilepsy / EEG / Antiepileptics

Abstract #33

Discrimination of Normal Brain Tissue From Dysplastic Tissue in Focal Cortical Dysplasia Using Raman Spectroscopy

Trang Tran[1], Frederick Dallaire[2], Romain Cayrol[3], Steffen Albrecht[4], Roy Dudley[5]

[1]Université de Montréal and Centre Hospitalier de l'Université de Montréal
[2]Polytechnique
[3]Centre Hospitalier de l'Université de Montréal
[4]McGill University Health Center
[5]Division of Neurosurgery, McGill University Health Center

Rationale
Focal cortical dysplasias, characterized by abnormal cortical architecture, are the most common cause of refractory focal epilepsy in the pediatric population. Only surgery can remove FCD lesions to cure focal epilepsy, but surgical success depends on the ability to resect the lesion completely while minimizing damage to perilesional normal tissues. Therefore, it remains extremely challenging to remove FCD lesions completely. Thus, better methods of delineating FCD lesions and their borders are needed to improve post-surgical seizure outcomes. Raman spectroscopy induces vibrations in the molecules of a sample and the scattered radiation is used to characterize it. The goal of this in vitro study is to use Raman spectroscopy to discriminate between normal brain tissue and dysplastic tissue using specimens of focal cortical dysplasia patients.

Methods
Stained sections of biopsy specimens from 20 patients with focal epilepsy were acquired and assessed by a pediatric neuropathologist. Raman map points were recorded from targeted abnormal regions with structures characterizing FCD: dysmorphic neurons and balloon cells.

Results
Significant spectral differences were observed between the dysplastic tissue regions and normal regions in the cortex. Indeed, FCD tissues exhibit increased spectral at 1302 cm-[1], 1660 cm-[1] and 1156 cm-[1] peaks, indicating a higher intensity of protein components and abnormal stretching mode of protein, lower quantity of lipids and most interestingly, a higher intensity of glycogen in the dysplastic tissues, respectively. In addition, the fingerprint region contains bands from nucleic acids and other biomolecules.

Conclusion
These findings suggest the potential spectral fingerprint of dysplastic tissues as an aid to delineating FCD borders.

Clinical Epilepsy / EEG / Antiepileptics

Abstract #34

Stiripentol Naïve Adults with Dravet Syndrome: Watch for Ammonia and Carnitine

Quratulain Zulfiqar Ali, Paula Marques, Arunan Selvarajah, Tara Sadoway, Sepideh Tabarestani, Danielle Andrade

Toronto Western Hospital

Rationale
Dravet Syndrome (DS) is a rare cause of severe and pharmacoresistant epileptic encephalopathy. Stiripentol (STP) has a significant therapeutic benefit in the pediatric DS population. However, STP effects on adult patients have not been well studied. In our adult-STP-naïve DS patient population, STP initiation was associated with encephalopathy, despite decreases in valproate and clobazam dosages. Here we explored the cause and treatment of encephalopathic manifestations associated with STP in adults.

Methods
28 patients with a confirmed clinical and genetic diagnosis of DS who attended the Adult Epilepsy Genetics Clinic were identified retrospectively. Patients who declined or discontinued STP after less than three months of use, patients who were deceased before starting STP or seizure-free when the genetic diagnosis was confirmed, and those who started STP before leaving the pediatric system (<18 years) were excluded (Figure 1). Levels of ammonia, carnitine and other anti-epileptic drugs (AEDs) were observed for patients receiving STP. Patients with high ammonia levels who received carnitine supplementation were reevaluated. They were also offered an increased dosage of STP if treatment with carnitine improved the encephalopathy.

Interestingly, several patients who were diagnosed with DS in adulthood did not start STP immediately after the diagnosis. In 30% of the patients, STP administration happened five or more years after the diagnosis (Figure 2). Often families declined STP as they thought adult seizure control was "better than childhood" and their adult child was "already on too much medication". However, after some years of living with the new diagnosis and parents doing their own research on DS, they started to accept using STP to further improve seizure control.

Results
We observed hyperammonemic encephalopathy in 77% of patients treated with STP (Figure 3). These patients were treated with carnitine. In seven out of nine patients, we observed a rate of improvement in ammonia levels of 35% (95% CI: 21-49%) at a mean carnitine dose of 991+/-286mg/day (Range: 660-1320mg/day). Five patients whose ammonia levels normalized were also offered an increase in STP dose and they were able to tolerate higher doses with improvement in side effects. Despite such adjustments, the mean maximum Stiripentol dose reached was 14.89+/-8.72mg/kg/day, which is lower than what is typically recommended in children (50mg/kg/day).

Conclusion

We report hyperammonemia in adult-STP-naïve patients who were on valproate and clobazam, despite dose reduction of the latter drugs. It is still unclear if STP has a role in ammonia metabolism or if the hyperammonemia is simply a result of increases in the other antiepileptic drug levels. We also report that treatment with carnitine improved hyperammonemia, allowing the continuation of STP.

Clinical Epilepsy / EEG / Antiepileptics

Abstract #35

Withdrawn

Clinical Epilepsy / EEG / Antiepileptics

Abstract #36

Withdrawn

Clinical Epilepsy / EEG / Antiepileptics

Abstract #37

Interictal Entropy of Alpha Band as a Predictor of Seizure Recurrence in Ambulatory EEG

Jean-Daniel Tessier[1], Emile Lemoine[2], Geneviève Pelletier-McDuff[3], Manon Robert[3], Denahin Toffa[3], Dang Khoa Nguyen[4], Elie Bou-Assi[4]

[1]Centre de Recherche du CHUM (CRCHUM)
[2]CRCHUM & Polytechnique Montreal (Institute of Biomedical Engineering)
[3]CRCHUM
[4]CRCHUM & University of Montreal (Department of Neuroscience)

Rationale
The development of new quantitative interictal markers of epilepsy could increase the diagnostic performance of ambulatory electroencephalography (EEG). Sample Entropy (SampEn) of EEG signals is a potential marker for seizure risk. However, the frequency range for which SampEn is most associated with seizure risk remains unknown.

Methods
We screened patients who underwent a routine EEG recording at the CHUM between December 2017 and July 2018. Medical charts were reviewed to assess seizure recurrence during the entire follow-up duration after the EEG. EEG signals were band-pass filtered in the theta (4-8 Hz), alpha (8-13 Hz) and beta (13-40 Hz) frequency ranges in which SampEn was calculated. We used Student's t-test to check the frequency ranges that showed the greatest difference in SampEn between patients with and without seizure recurrence, stratifying by age group (<40, 40-60, >60).

Results
A total of 335 EEGs from 271 patients were included. Median follow-up period was 84 weeks (IQR 32.5–116.5). Out of these EEGs, 129 (38.5%) were from patients diagnosed with epilepsy. For 106 EEGs (31.6%), the patient had a seizure during the follow-up period after the EEG. In patients <40 y.o. (129 EEGs), SampEn values of the alpha range were significantly lower for patients with seizure recurrence (0.720 vs. 0.773, p = 0.012). In other age groups, no individual frequency range demonstrated a significant difference.

Conclusion
SampEn of the alpha frequency range is associated with seizure recurrence risk in young patients undergoing routine EEG. These findings could guide the development of more efficient interictal markers of epilepsy.

Pediatric Epilepsy

Abstract #38

Comparison of School Performance in Children with New-Onset Seizures to Children with Psychiatric Disorders

Anita Datta, Peter Wong

University of British Columbia

Rationale

Children with seizures and children with psychiatric disorders experience more challenges with school-performance (SP) than healthy children. The study objective was to determine if differences exist in the incidence and severity of SP difficulties in children with seizures, compared to children without seizures, and specifically children with psychiatric disorders.

Methods

All school-aged children with an initial EEG in 2016 were included in this single-center retrospective study. Children were divided into the following groups based on the presence or absence of: 1) seizure, 2) no-seizure, and 3) psychiatric disorder (subset of 2nd group). SP difficulties were defined as the requirement of additional school-assistance, with graded severity level. The incidence and severity of SP difficulties of the seizure group was compared to the no-seizure and psychiatric groups at baseline and at 2 to 4 years follow-up.

Results

At baseline, SP difficulties were similar between the seizure (n=146) and no-seizure (n=332) groups respectively [38/146 (26%) vs. 91/332 (27%)]. At follow-up the seizure group (n=119) had significantly higher incidence of SP difficulties than the non-seizure (n=215) group (54% vs. 47%), and greater severity of difficulties (both $p<0.005$). In the seizure group, more anti-seizure medications ($p<0.01$), > 30 total seizures ($p<0.03$) and epileptiform discharges on initial EEG ($p<0.04$) were predictive of SP difficulties. Notably, no difference was observed in SP, including severity, between the seizure (n=119) and psychiatric (n=69) groups at baseline (31% vs. 43%) or at follow-up (54% vs. 55%).

Conclusion

Over time, children with new-onset seizures experience more SP difficulties than children without seizures, but similar SP difficulties to children with psychiatric disorders. These findings confirm the importance of regular SP assessments in these vulnerable populations.

Pediatric Epilepsy

Abstract #39

Impact Of COVID-19 in Pediatric Patients with Self-Limited and Genetic-Generalized Epilepsy via Telemedicine Evaluation

Stephanie Kwok, Anita Datta

University of British Columbia

Rationale
The objective of this prospective observational study was to determine the impact of COVID-19 pandemic on mood and anxiety in children with self-limited (SLE) and genetic-generalized epilepsy (GGE).

Methods
Patients performed the Children's Depression Inventory-2 (CDI2) and Multidimensional Anxiety Scale for Children-2 (MASC2) questionnaires prior (June 2019 - February 2020) and during (June 2020 - May 2021) the pandemic via phone visits; retaking these questionnaires and answering a pandemic-related lifestyle survey and the COVID-19 obsession scale (COS).

Results
50 subjects were included (median 9.33 years of education and median 4.85 years of epilepsy). Phone survey: Sixteen (32%) had worse sleep, 24 (48%) less exercise, 19 (38%) worse mood, 21 (42%) more anxiety and 34 (68%) increased screen time (with median of 1 hour/day on COVID-19 updates). Fourteen (28%) believed epilepsy increased COVID-risk, 13 (26%) that epilepsy limited activities during COVID-19 compared to peers and 46 (92%) that hospital visits increased COVID-19-risk.

There was no significant difference in pre and pandemic MASC2/CDI2 scores. Of twenty-six patients with worse CDI2 scores, risk factors included increased screen time $P<0.031$), worry hospital visits increase COVID-19-risk ($P<0.05$) and worse sleep ($P<0.018$). Of twenty patients with worse MASC2 scores, risk factors included lower maternal education ($P<0.027$), worry epilepsy increased COVID-19-risk ($P< 0.05$), financial concerns ($P<0.038$) and pandemic-related job changes ($P<0.038$).

Conclusion
Patients with SLE and GGE, with few pre-existing co-morbidities, still require routine screening of epilepsy-related co-morbidities, as a subset experienced significant subjective lifestyle and emotional changes, and subclinical worsening of test scores during the pandemic.

Pediatric Epilepsy

Abstract #40

Telehealth for Children with Epilepsy is Effective and Reduces Anxiety Independent of Healthcare Setting

Kerstin Klotz[1], Felippe Borlot[2], Morris Scantlebury[3], Eric Payne[3], Juan P Appendino[3], Jan Schönberger[1], Julia Jacobs[3]

[1]*Department of Neuropediatrics and Muscle Disorders, Medical Center-University of Freiburg, Faculty of Medicine, University of Freiburg, Freiburg, Germany*
[2]*Alberta Children's Hospital Research Institute, Cumming School of Medicine, University of Calgary, AB, Canada*
[3]*University of Calgary*

Rationale
Telemedicine use has grown exponentially as an alternative to providing care to epilepsy patients during the current pandemic. We investigated the impact of the COVID19 pandemic among children with epilepsy from two distinct epilepsy centers and compared perceptions among parents who received telemedicine against those who did not.

Methods
We developed a 32-question survey with ten stratified questions according to telemedicine exposure. Families followed in Freiburg and Calgary were invited to participate.

Results
126 families (80 in Freiburg, 46 in Calgary) participated, and 40.3% received telemedicine care. Most children had chronic epilepsy but not well-controlled seizures. Negative impacts were reported by 36% and 65% of families who had to re-schedule visits and diagnostics, respectively. Nearly 2/3 of families reported no seizure frequency change, while 18.2% reported either worsening or improvement of seizures. Behaviour worsening was reported by 28.2%. Families who received telemedicine care had a statistically significant reduction of parental self-reported anxiety after virtual visits compared to those who did not. Families with telemedicine consultations were more likely to consider future virtual care (84% vs. 65.2%), even after the pandemic. Patient data safety, easy access to specialists, and consistency with the same provider were graded as important in both centers, while a shorter waiting time was most relevant in Calgary.

Conclusion
In our cohort, some children with epilepsy experienced increased seizures and worsening behaviour during the first nine months of the pandemic. Telemedicine might reduce parental anxiety symptoms, and families who experienced telehealth were more open to similar appointments in the future.

Pediatric Epilepsy

Abstract #41

Proposed Pathway for the Utilization of Pediatric Ambulatory EEG

Felippe Borlot[1], Silvia Kozlik[2], Leanne Alfaro[2], Alice Ho[3], Juan P Appendino[3], Eric Payne[3], Morris Scantlebury[3], Julia Jacobs[3]

[1]Alberta Children's Hospital Research Institute, Cumming School of Medicine, University of Calgary
[2]Alberta Children's Hospital, University of Calgary
[3]University of Calgary

Rationale
The clinical utility of pediatric ambulatory-EEG (A-EEG) has been studied for decades, but limited information exists regarding which variables influence its utility. We aimed to evaluate clinical/EEG variables that may influence A-EEG yields and to develop a pathway for A-EEG utilization in children.

Methods
Single-center retrospective review of A-EEGs performed from July 2019 to January 2021 in a tertiary referral center. The primary outcome was whether the A-EEG test successfully answered the referring physician's clinical question or influenced therapy. When it did, the A-EEG test was deemed useful. Clinical and EEG variables were assessed for their ability to predict utility. Further, our literature review generated ten relevant prior studies whose details were used to generate a pathway for A-EEG utilization in children.

Results
142 A-EEG studies were included (mean age 8.8 years, 48% males, mean A-EEG duration 33.5 hours). Overall, A-EEG was considered useful in 106 (75%) children but heavily influenced by A-EEG indication. Specifically, it was deemed useful for 94% of patients evaluated for electrical status epilepticus in slow-wave sleep (ESES), 92% of those evaluated for interictal/ictal burden, and 63% of those undergoing spell classification. The test indication (P < .001), a diagnosis of epilepsy (P = .02), and an abnormal routine EEG (P = .04) were associated with A-EEG test utility.

Conclusion
Pediatric A-EEG is extremely useful for evaluating ESES and ictal/interictal burden and is often helpful for spell classification. A prior epilepsy diagnosis and abnormal routine EEG are associated with better A-EEG test utility.

Pediatric Epilepsy

Abstract #42

SCN2A-Related Epilepsy of Infancy with Migrating Focal Seizures: Report of a Variant with an Apparent Loss of Function Effect

Juan Pablo Appendino[1], Xiao-Ru Yang[1], Vamsi Krishna Ginjupalli[2], Olivier Theriault[2], Hugo Poulin[2], Mohamed Chahine[2], Ping Yee Billie Au[1]

[1]Alberta Children's Hospital, University of Calgary
[2]CERVO Brain Research Center, Université Laval

Rationale
SCN2A encodes a voltage-gated sodium channel (NaV1.2) expressed throughout the central nervous system in predominantly excitatory neurons. Pathogenic variants in SCN2A are associated with epilepsy and neurodevelopmental disorders. Genotype-phenotype correlations have been described, with loss of function variants typically being associated with neurodevelopmental delay and later onset seizures, while gain of function variants more often result in early infantile-onset epilepsy. However, the true electrophysiological effects of most disease-causing SCN2A variants have yet to be characterized.

Methods
We report an infant who presented with migrating focal seizures in the neonatal period.

Results
She was found to have a mosaic c.2635G>A, p.Gly879Arg variant in SCN2A. Voltage-clamp studies of the variant expressed on adult and neonatal NaV1.2 isoforms demonstrated a mixed gain and loss of function, with predominantly a loss of function effect with reduced cell surface current density. Additional small electrophysiological alterations included a decrease in the voltage dependence of activation and an increase in the voltage dependence of inactivation.

Conclusion
This finding of a predominantly loss of function effect was unexpected, as the infant's early epilepsy onset would have suggested a predominantly gain of function effect. This case illustrates that our understanding of genotype phenotype correlations is still limited, and highlights the complexity of the underlying electrophysiological effects of SCN2A variants. Further studies are warranted to elucidate the predominate biophysical phenotype associated with disease manifestation for patient carrying G879R mutation.

Pediatric Epilepsy

Abstract #43

Treatment of Children with Infantile Spasms: Systematic Review and Network Meta-Analyses

Puneet Jain[1], Ravindra Arya[2], Jitendra Sahu[3], Vann Chau[1]

[1]The Hospital for Sick Children
[2]Cincinnati Children's Hospital Medical Center
[3]Postgraduate Institute of Medical Education & Research (PGIMER)

Rationale
Multiple randomized controlled trials (RCTs) for infantile spasms (IS) have been published exploring different treatments, doses, and combinations. We aimed to perform a systematic review and network meta-analysis (NMA) to obtain comparative efficacy and rankings

Methods
Structured literature searches were run in Medline, Embase and Cochrane Central Register of Controlled Trials (OVID). All randomized controlled trials (RCTs) studying children aged 2 months to 3 years of age with IS (with hypsarrhythmia or hypsarrhythmia variant on EEG) receiving appropriate first-line medical treatment were included. The review was registered with the PROSPERO International prospective register of systematic reviews (CRD42020198183).

Results
This review included 21 RCTs comparing first-line treatments for children with IS; of which 15 studies were included in the NMA. Both frequentist and Bayesian network rankings for electroclinical remission showed that ACTH/ MgSO4 combination, methylprednisolone, prednisolone high dose (HD)/pyridoxine combination and prednisolone HD were most likely to be the "best" interventions, although these were not significantly different from each other. For clinical remission, prednisolone HD, ACTH low-dose, prednisolone HD/pyridoxine combination and ACTH HD were the best. Studies with higher proportion of children with symptomatic etiology and longer lead time to treatment were found to have lower electro-clinical remission rates. This review was limited by poorly connected network, small and single studies for most head-to-head comparisons, and inconsistencies between direct and indirect evidence.

Conclusion
Treatments involving ACTH and prednisolone HD are more effective in achieving clinical and electroclinical remission in children with infantile spasms.

Pediatric Epilepsy

Abstract #44

Sex Differences in Mental Health Impact on Transition Variables in Adolescents with Epilepsy

Sarah Healy[1], Sharon Whiting[2]

[1]CHEO
[2]CHEO and The University of Ottawa

Rationale
Research has consistently shown that adolescents with epilepsy have more mental health issues than typically developing adolescents. These mental health issues are particularly problematic when adolescents are preparing to transition to adult care, as mental health issues are associated with lower quality of life (QoL) and lower transition readiness. To date, little research has looked to see whether the impact of mental health differs between males and females in this population.

Methods
Baseline data were analyzed in 93 adolescents with epilepsy (M= 16.02 years, 48 females) enrolled in a transition clinic.

Results
When accounting for mental health severity, there were no significant sex differences in total QoL. However, there were significant sex differences when looking at some of the individual QoL subscales and transition scores. Specifically, females scored significantly lower on memory ($p=.047$) and stigma ($p=.045$) subscales, while males with mental health concerns scored significantly lower on the social support ($p=.014$) subscale and on the transition readiness scale ($p=.033$).

Conclusion
Analyses suggest that transition-aged males and females may be impacted differently by mental health symptoms; especially in the areas of memory, stigma, social support, and transition readiness. These differences should continue to be monitored as patients progress through the transition clinic.

Pediatric Epilepsy

Abstract #45

Investigating Risk Factors for SUDEP in Dravet Syndrome

Amir Aschner[1], Anne Keller[1], Ingrid Scheffer[2], Jay Jeschke[3], Chloe Verducci[3], Orrin Devinksy[3], Daniel Friedman[3], Elizabeth Donner[1]

[1]*The Hospital for Sick Children*
[2]*University of Melbourne, Austin Health and Royal Children's Hospital*
[3]*New York University Langone Comprehensive Epilepsy Center*

Rationale

Dravet Syndrome (DS) has greatly increased mortality rates compared to other epilepsy populations, including higher rates of Sudden Unexpected Death in Epilepsy (SUDEP). General risk factors for SUDEP have been identified but their importance may vary among epilepsy syndromes.

Methods

Cases of SUDEP in DS were collected from The Canadian Pediatric SUDEP Registry, North American SUDEP Registry, and University of Melbourne Epilepsy Genetics Database.

Results

26 cases (12F, 46%) were identified. Median age at death was 8.53 years (IQR=12.65); 17 (65%) occurred before age 13. 18 (69%) deaths occurred in bed, 21 (81%) were unwitnessed. SCN1A pathogenic variants confirmed in 22 (85%) cases, 22 reported seizure onset within the first year of life, and 22 had multiple seizure types. 9 (35%) reported declining seizure frequency over the 6 months before death, and 9 reported no generalized tonic-clonic seizures (GTCs) in the month before death. 11/22 (50%) reported no evidence of a seizure immediately preceding death. 14 (54%) reported a recent illness.

Conclusion

Years living with epilepsy and frequent GTCs are common risk factors for SUDEP, however, this DS cohort tended toward early age of death, stable or improved seizure control, and few recent GTCs. Further, 50% of cases showed no evidence for a seizure immediately preceding death and a recent mild illness was noted in half the subjects. Thus, SUDEP in DS may involve unique risk factors, while common SUDEP risk factors may be less significant. Expansion of this cohort may further elucidate the hypothesis that SUDEP in DS involves unique factors.

Pediatric Epilepsy

Abstract #46

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

Anup D. Patel[1], Teresa Gasalla[2], Xavier Nondonfaz[3], Sami Elmoufti[2], Jan-Peer Elshoff[4]

[1]Nationwide Children's Hospital and The Ohio State University College of Medicine, Columbus, OH, USA
[2]UCB Pharma, Raleigh, NC, USA
[3]UCB Pharma, Brussels, Belgium
[4]UCB Pharma, Monheim am Rhein, Germany

Rationale

Assess tolerability and retention-rate (effectiveness) of adjunctive brivaracetam in children with primary generalized seizures (PGS) or mixed seizure types. In US, EU, and Canada, brivaracetam is indicated for treatment of focal seizures (FOS) in patients aged ≥4years.

Methods

Pooled interim analysis (cut-off March-15-2017) of PGS or mixed seizure type patients enrolled in N01263 (NCT00422422), an open-label trial of adjunctive brivaracetam in children aged ≥1month to <16years uncontrolled by 1–3 concomitant antiseizure medications (ASMs), with up-titration of brivaracetam dose over 3weeks (0.8–4mg/kg/day), and open-label extension N01266 (NCT01364597) of flexible-dose brivaracetam (1–5mg/kg/day, maximum 200mg/day; equivalent to 50–200mg/day for patients weighing ≥50kg).

Results

Fifty-one children with PGS/mixed seizure types were enrolled (mean age 5.6years; 54.9% female; mean epilepsy duration 3.4years; median of 3.0 prior and 2.0 concomitant ASMs). Median brivaracetam exposure duration: 541days; median modal dose: 4.0mg/kg/day (equivalent to 200mg/day for patients ≥50kg). At cut-off, 20 (39.2%) were ongoing, 29 (56.9%) had discontinued (adverse event [21.6%], lack of efficacy [17.6%], caregiver choice [11.8%]). Forty-eight (94.1%) patients experienced ≥1 treatment-emergent adverse event (TEAE), mostly nasopharyngitis (31.4%), pyrexia (29.4%), and upper respiratory tract infection/diarrhea/convulsion/vomiting (23.5% each). Nineteen (37.3%) experienced drug-related TEAEs, mostly somnolence (9.8%), decreased appetite (7.8%), fatigue (5.9%). Eleven (21.6%) discontinued due to TEAEs. Two (3.9%) died (pneumonia/septic shock and circulatory collapse), not brivaracetam-related. Kaplan-Meier-estimated 12- and 24-month retention-rates: 56.9% and 47.1%.

Conclusion

Long-term adjunctive brivaracetam was generally well-tolerated in children with PGS or mixed seizure types. Two-year retention-rate (~50%) suggests potential treatment benefit in this pediatric population.

Author disclosures

Pediatric Epilepsy

Abstract #47

The Comorbidity of Headaches in Pediatric Epilepsy Patients: How Common and what Types?

Hanin AlGethami[2], Muhammad Talal Alrifai[2], Ahmed Al-Rumayyan[2], Waleed Al-Tuwaijri [2], Duaa Ba-armah[2]

[1]*King Salman Hospital, Riyadh, Kingdom of Saudi Arabia*
[2]*King Abdullah Children Specialist Hospital, King Abdulaziz Medical City, Riyadh, Kingdom of Saudi Arabia*

Rationale
To estimate the prevalence and characteristics of headache in pediatric epileptic patients.

Methods
This cross-sectional study was performed over 6 months period from January 2018 to June 2018 at King Abdullah Specialist Children Hospital, King Abdulaziz Medical City, Riyadh, Kingdom

of Saudi Arabia using a structured questionnaire in pediatric patients with epilepsy.

Results
There were 142 patients enrolled (males, 57.7%; average age, 10.7±3.1 years) with idiopathic epilepsy (n=115, 81%) or symptomatic epilepsy (n=27, 19%). Additionally, patients had focal epilepsy (n=102, 72%) or generalized epilepsy (n=40, 28%), and among them, 11 had absence epilepsy. Overall, 65 (45.7%) patients had headaches compared with 3/153 (2%) in the control group (p<0.0001). Among the 65 patients with headaches, 29 (44.6%) had migraine-type, 12 (18.4%) had tension-type, and 24 (36.9%) had unclassified headache. There was no significant difference in age, gender, type of epilepsy syndrome, and antiepileptic used except in patients with or without headache. For migraine patients, there was a lower headache prevalence in the subgroup treated with valproic acid compared with other treatments.

Conclusion
Headache, predominantly migraine, is a common problem in pediatric epileptic patients and choosing valproic acid when possible, can be important in preventing migraine in these patients.

Pediatric Epilepsy

Abstract #48

Treatment with High Dose Oral Prednisolone (8 Mg/Kg/Day) in Children with Infantile Spasms who Failed Vigabatrin: A Retrospective Study

Wafaa Ali Ahmed Al Shehhi[1], Puneet Jain[2], Van Chau[2], Carter Snead[2], Elizabith Donner[2], Cristina Go[2], Jennifer Boyd[2], Rohit Sharma[2]

[1]The Royal Hospital
[2]The Hospital for Sick Children

Rationale
This study aimed to study the short-term seizure outcomes following treatment with 8 mg/kg/day prednisolone in children with infantile spasms refractory to vigabatrin. We hypothesized that high-dose prednisolone may result in similar rates of electroclinical remission as compared to published ACTH rates.

Methods
All consecutive children with hypsarrhythmia, hypsarrhythmia variant, or multiple independent spike foci (MISF) on EEG with/without infantile spasms, who had been treated with vigabatrin as first-line anti-seizure medication (ASM) followed by high dose oral prednisolone (8 mg/kg/day) in cases who did not respond to vigabatrin, were included. Clinical and electroclinical remission at 2 weeks following initiation of treatment and adverse effects were assessed.

Results
Sixty-five children were included. A genetic etiology was seen in 38.5% of cases. The median estimated delay from onset of spasms to treatment was 11 days. Preceding normal development was seen in 33.8% of cases. Complete ECR was seen in 30.8% (20/65) of the patients two weeks after vigabatrin. Complete ECR was noted in 77.8% (35/45) of the patients, two weeks after prednisolone initiation in children who failed vigabatrin, and this was sustained at 6 weeks in 66.7% (30/45) patients. Prednisolone was generally well-tolerated.

Conclusion
High dose (8 mg/kg/day) of oral prednisolone resulted in complete electroclinical response (at 2 weeks) in more than three-fourth of children with hypsarrhythmia or hypsarrhythmia variant on EEG with/without parentally reported infantile spasms who had failed vigabatrin. This was sustained at 6 weeks in two-thirds of the children. It was generally well-tolerated and found to be safe. It may be a reasonable and more feasible alternative to ACTH for the treatment of infantile spasms. Further trials exploring the comparative effectiveness of 8 mg/kg/day prednisolone with ACTH, dose-response relationship with prednisolone, and exploring various drug combination therapies to improve efficacy are warranted.

Pediatric Epilepsy

Abstract #49

Ketogenic Diet or Vagal Nerve Stimulation in Children with Tuberous Sclerosis Complex (TSC) with Drug-Refractory Epilepsy

Ahmed Abushama

The Hospital for Sick Children

Rationale
Ketogenic diet (KD) and VNS are commonly used in patients with TSC with drug refractory epilepsy (DRE) who are not candidates for resective surgery. The aim of this study was to determine the effectiveness of KD and VNS in DRE in TSC.

Methods
Retrospective chart review was conducted. Seizure outcomes and adverse effects were assessed in children with TSC and DRE who received dietary therapies or VNS at two centers in Ontario from 2010 to 2020.

Results
Twenty children included, median age at seizure onset was 5 months. All children had daily seizures at initiation of KD and VNS implantation. 73% had TSC2 pathogenic variants. All children had ≥ 1 TSC associated neuropsychiatric disorder (TAND) features. Fifteen children (75%) were treated with KD (10 classic, 4 MCT and 1 modified Atkins) with median age at initiation 4.2 years. Seven children (47%) had >50% reduction in seizure frequency after a median follow-up duration of 23 months. Eleven discontinued the diet after a median of 17 months. The common adverse effects on diet were constipation [47%] and vomiting [33%]. Five of the 9 children who had VNS, were referred for VNS after failed or discontinued KD. Median age at implantation was 12 years; 6/9 (67%) had >50% reduction in seizures after a median follow up of 37 months; 7/9 (78%) had some response to the magnet.

Conclusion
Nearly half of the children with TSC/DRE had >50% seizure reduction on KD; nearly two-thirds of the children had >50% seizure reduction after VNS implantation.

Pediatric Epilepsy

Abstract #50

Adrenal Insufficiency Among Children Treated with Hormonal Therapy for Infantile Spasms

Gabrielle Doré-Brabant[1], Geneviève Laflamme[1], Maude Millette[1], Bradley Osterman[2], Nicolas Chrestian[1]

[1]Centre Hospitalier de l'Université Laval

[2]Children's Hospital & CHU Ste-Justine

Rationale
Hormonal therapy is a standard treatment for children with infantile spasms. The high doses given and long treatment duration expose patients to the risk of adrenal insufficiency (AI). This study aims to quantify the incidence of AI among children with infantile spasms treated with high-dose corticosteroids and/or adrenocorticotropic hormone (ACTH).

Methods
A retrospective chart review of patients treated for infantile spasms was performed between January 2009 to March 2020 in one pediatric specialized hospital. Variables collected included patient and treatment characteristics, risk factors of AI and adrenal function testing. Analysis included descriptive statistics such as incidence and bivariate analysis.

Results
Thirty-one patients met the inclusion criteria and received a total of 33 separated courses of treatment (17 corticosteroids [prednisone/prednisolone], 12 ACTH et 4 both). Adrenal function following each course of treatment was evaluated in all patients. Hydrocortisone replacement therapy was received by 32/33 (97%) children. AI occurred in 25/33 (76% [95CI 58-89]) children. There was no predictive factor of AI. No drug regimen was deemed safe. Two patients (6%) presented an acute adrenal crisis the days following weaning off of hormonal treatment. They were the youngest of the cohort.

Conclusion
Adrenal suppression is frequent after standard hormonal therapy regimen for infantile spasms. This can lead to serious complications, such as adrenal crisis, if not supplemented. A routine laboratory assessment of adrenal function should be done after hormonal therapy for all patients. Hydrocortisone replacement therapy should be given at the end of hormonal therapy and until testing results are obtained, particularly for younger infants.

Pediatric Epilepsy

Abstract #51

An Assessment of Next-Generation Panel Testing in Epilepsy

Heather Leduc-Pessah, Taila Hartley, Daniela Pohl, David Dyment

Children's Hospital of Eastern Ontario

Rationale

With the routine use of microarrays and next-generation sequencing (NGS) in clinical genetics and pediatric neurology it is important to know the baseline outcomes experienced by children with epilepsy as they relate to clinical care in Ontario. We sought to assess the diagnostic yield of genetic epilepsy testing, and whether enhanced testing impacts patient care. Furthermore, we assessed the performance of the provincial criteria for epilepsy multigene testing.

Methods

We conducted a retrospective chart review of patients with epilepsy seen at CHEO between 2012-2020 for whom genetic testing was pursued. 699 patients were identified and screened for inclusion. Eligible patient charts were then reviewed for presenting clinical concerns, genetic testing results, and resulting changes to management.

Results

Diagnostic yield was approximately 14% for multi-gene epilepsy testing. Variants of unknown significance (VUS) were reported in 60% of patients tested. A direct impact on patient care as a result of the molecular diagnosis was evident for a small portion of patients (<10%). The majority of patients diagnosed met the provincial testing criteria. Additional variables that increased the likelihood of a diagnostic result included younger age (<3 years) and clinical co-morbidities such as intellectual disability or a syndromic presentation.

Conclusion

The diagnostic yield of genetic epilepsy testing conducted at CHEO is comparable to other reported rates. VUS resulted in additional segregation studies and re-analyses on follow-up. Genetic testing did result in clinical benefits of recurrence risk counselling, prognosis and surveillance though a direct change in management was seen in only a minority of individuals.

Pediatric Epilepsy

Abstract #52

Do Patients with Epilepsy Develop Complex Febrile Convulsions at the Onset of their Syndrome?

Kerensa Newark, Christopher Woolley

Aneurin Bevan University Health Board

Rationale
Complex febrile convulsion is a focal or generalized seizure lasting longer than 15 minutes and occurs more than once in 24 hours. To identify if the patients diagnosed with complex febrile convulsions were treated with buccal midazolam, recurrence of seizures and ultimately, whether a diagnosis of epilepsy was subsequently made.

Methods
The electronic notes for all patients with seizures, who were admitted to the paediatric wards of the Royal Gwent and Nevill Hall Hospitals from the 1st March 2018 - 28th February 2019, were reviewed. Data was retrospectively collected looking at the description of the seizures, use of buccal midazolam, referral to epilepsy specialist nurse, readmission, and the progression to a diagnosis of epilepsy.

Results
Eleven patients were identified as having complex febrile convulsions. Buccal midazolam was given to 8 patients upon discharge and 6 (75%) of this cohort were followed up in clinic. The recurrence rate of seizures in the study group was 55% (6) and all were previously treated with buccal midazolam. 3 patients were referred to the epilepsy specialist nurse, of which 2 (18%) were subsequently diagnosed with epilepsy and commenced on anti-epileptic drugs.

Conclusion
Children with complex febrile convulsions should be offered buccal midazolam and this was supported by the audit which revealed that parents felt able to give buccal midazolam. Patients not treated with buccal midazolam were not subsequently readmitted. We were able to identify the children who will go on to develop epilepsy or who have had complex febrile convulsions at the onset of their epilepsy syndrome.

Pediatric Epilepsy

Abstract #53

The Spectrum of Epilepsy in Children with 15q13.3 Microdeletion

Arjun Nair, Elizabeth McCready, Anne Keller, Brandon F. Meaney, Kevin Jones, Rajesh RamachandranNair, Robyn Whitney

McMaster University

Rationale
We sought to further define the epilepsy phenotype in a cohort of children with 15q13.3 microdeletion syndrome.

Methods
We retrospectively reviewed the phenotypic spectrum of children < 18 years with epilepsy and confirmed pathogenic or likely pathogenic 15q13.3 microdeletions.

Results
Thirteen children were included, 69% were female. Median age at seizure onset was 4 years. Eighty-five percent had intellectual disability. Nine children (69%) had a history of typical/atypical absence seizures with median onset at 5 years. One child had early-onset absences. Three children (23%) had status epilepticus (2 absence, 1 focal). Four children (31%) had focal seizures. Eleven children (85%) had an epilepsy syndrome and in half, an unspecified genetic generalized epilepsy with overlap clinical features was identified. Seizures were medically refractory in a third. Electroencephalography showed generalized (85%) and focal epileptiform discharges (62%) and background slowing (33%). One child had electrical status epilepticus of sleep. Neuroimaging was performed in 5 children (38%) and was abnormal in 3. Out of the 12 children with a history of anti-seizure medication treatment, valproate most commonly resulted in seizure freedom as mono or combination therapy in 5 (42%). Two children tried cannabidiol and one tried the ketogenic diet; neither was effective.

Conclusion
The epilepsy phenotype in children with 15q13.3 microdeletion syndrome is defined by childhood onset absence seizures, which may persist into adolescence, with or without status epilepticus, and intellectual disability. Additional features include focal seizures and refractory epilepsy. Valproate seemed to be most effective, however future studies should explore other therapies.

Pediatric Epilepsy

Abstract #54

Febrile Seizure Incidence and Age at First Occurrence are Associated with Changes in Placental Normalized Gene Expression: The '3D' Pregnancy Cohort Study

Delphine Aubin[1], Fanny Thébault-Dagher[1], Morgane Robles[2], Catherine M. Herba[3], Jean R. Séguin[1], William D. Fraser[4], Cathy Vaillancourt[2], Sarah Lippé[1]

[1]Université de Montréal
[2]Institut national de la recherche scientifique (INRS)
[3]Université du Québec à Montréal
[4]Centre hospitalier universitaire de Sherbrooke

Rationale
Self-reported maternal prenatal stress (MPS) has been associated with earlier febrile seizure (FS) age of onset in offspring. The aim of this study was to investigate whether placental markers of MPS are linked to FS incidence and age at first occurrence.

Methods
A subsample of children with FS (n = 28) and matched controls (n = 84), were drawn from our longitudinal 3D pregnancy cohort (N = 2366 mother-child dyads). Expression of placental genes associated with glucocorticoids, serotonin, and fetal/placental growth were analysed from placental tissues, compared between groups and associated with age at first FS.

Results
Overall placental normalized gene expression was statistically different (p<0.001). Children with FS showed overexpression of the serotonin transporter (mean difference (MD)=0.61, 95%CI=0.9-1.13), connexin 43 (MD 0.69, 95%CI=0.30-1.09), zonula occludens-1 (MD 0.84, 95%CI=0.42-1.26), and underexpression of glucocorticoid receptor β (MD 0.84, 95%CI=-1.49--0.19) and serotonin receptor 2B (MD 1.57, 95%CI=-2.35- -0.78) compared to controls. Increased expression of the serotonin transporter predicted 37.2% of variation in age at first FS. Pregnancy-specific anxiety during the 2nd trimester was moderately correlated with age at first FS (R=-0.38) but was not a significant predictor in the regression model.

Conclusion
Changes in placental gene biomarkers was associated with MPS in children with FS. Our results suggest that placental genes associated with the glucocorticoid, serotonergic and fetal/placental growth systems may be candidate mechanisms underpinning the associations between MPS and offspring FS. The mechanisms causing changes in placental genes and their association with seizure disorders remain to be further investigated.

Pediatric Epilepsy

Abstract #55

Long-Term Efficacy of the Ketogenic Diet (KD) in Pediatric Epilepsy: A Single Center Study

Hassan Kiani, Rajesh RamachandranNair

McMaster University

Rationale
We analyzed the long-term seizure outcomes of patients with epilepsy initiated on KD.

Methods
In children aged <13 years initiated on the KD over 15.5 years (>1 seizure per month), good seizure outcome was defined as >50% and excellent as >90% seizure reduction.

Results
In the 65 patients (M:F 34:31,2 mo - 12 yrs 4 mo), median seizure frequency reduced from baseline (M = 616.9) to 2 years (M = 295.0); $p < 0.05$. At 2 years, 56.7% had good seizure control (median ratio 2.66), including 26 (43.3%) with excellent seizure outcomes (median ratio 2.49) and 17 (28.3%) with no seizures (median ratio 2.41). 39 patients continued the diet past 2 years. At 5 years, seizure frequency reduced significantly from baseline to 5 years (M = 36.3,); $p < 0.05$. 31/39 (79.5%) patients had good seizure control (median ratio = 2.65), including 23 (59.0%) with excellent seizure outcomes (median ratio = 2.09) and 15 (38.5%) with no seizures (median ratio = 2.00). Of the 19 patients still on the diet at 5 years, 16 (84.2%) had good seizure control, 12 (63.2%) with excellent seizure outcomes and 6 (31.6%) with no seizures). 3/19 (15.8%) patients had poor seizure control with 2 (10.5%) experiencing an increase in seizures. The most common reasons for discontinuation were ineffectiveness (27) and therapy complete (8).

Conclusion
Our results demonstrate that the KD is both an effective and safe treatment option for children with medically refractory epilepsy, and good results can be achieved at lower ratios.

Pediatric Epilepsy

Abstract #56

Dissemination of Education Resources to Optimize School Success for Children with Epilepsy

Tamara Tavares[1], Elizabeth Kerr[1], Mary Secco[2], Karen Bax[3], Mary Lou Smith[1]

[1]*The Hospital for Sick Children*
[2]*Epilepsy Southwestern Ontario*
[3]*Western University*

Rationale
Teachers have limited knowledge about epilepsy and thus may use poor strategies to support children with epilepsy (CWE) at school. Epilepsy and School Success (EPASS) is a Canadian toolkit that provides appropriate classroom strategies to address the cognitive, psychological and social consequences, and has been shown to significantly improve teachers' knowledge about epilepsy (Tavares et al, 2021 Epilepsy Behav). After developing and evaluating EPASS, our team identified a KT Plan of Action to disseminate the toolkit.

Methods
The EPASS toolkit is available at www.epilepsyforeducators.ca. Information about the toolkit is being distributed to the Ontario Ministry of Education, Ontario School Boards, Private and Independent Schools, Teacher's Colleges, and the Ontario Teacher Federations. To target health care practitioners who are involved in providing recommendations to families, patients and teachers, the toolkit is being sent to the Canadian Epilepsy Alliance, EpLink (Ontario Brain Institute), Canadian Psychological Association, CPEN, epilepsy.com, and personal networks.

Results
We will describe the implementation and uptake of the toolkit. Early reactions from teachers, psychologists and pediatric epileptologists have been positive: "amazing initiative", "you have my full support", "wonderful", "super resource", "important materials", "you are doing great things for kids with epilepsy".

Conclusion
Teachers have access to a huge repository of information on the internet and may not know which resources are relevant and authoritative. Our KT plan will provide teachers, psychologists and parents with the right tools to support CWE in the classroom.

Pediatric Epilepsy

Abstract #57

Emotion Recognition and Empathic Responding in Adolescents with Epilepsy: A Canada-Wide Investigation

Tamara Tavares[1], Lindsay Oliver[2], Mary Lou Smith[1]

[1]*The Hospital for Sick Children*
[2]*Centre for Addiction and Mental Health*

Rationale

Adolescents with epilepsy (AWE) experience greater peer and social difficulties compared to healthy youth. Social cognition includes the ability to recognize emotions, understand others' mental states (cognitive empathy), and experience the affective states of others (emotional empathy). Deficits in social cognition interfere with appropriate social behaviours and forming meaningful relationships, which may impact quality of life. Although AWE demonstrate social difficulties, few studies have examined their social cognitive abilities. The objective of this study is to delineate emotion recognition, cognitive and emotional empathy in AWE and the mechanisms underlying these potential deficits.

Methods

This newly launched study will recruit AWE, their parents and controls from SickKids and Canadian Epilepsy Support Centers. Youth will complete a facial emotion recognition task and an adolescent-adapted Multifaceted Empathy Task to index cognitive and emotional empathic responding. Additionally, participants and their parents will complete validated questionnaires assessing the adolescents' empathic abilities and social behaviour. All study measures will be completed online with a research assistant.

Results

Preliminary data will include task and questionnaire responses, and an examination of relationships between these two data sources. Potential group differences will be evaluated using T-Tests and repeated measures ANOVA.

Conclusion

Evaluating the specific social cognitive deficits in AWE is the first step to inform future interventions. The results of this study can be used to prepare caregivers and educators for the specific social cognitive challenges in AWE. With this knowledge, specific interventions and educational plans can be created to better accommodate and strengthen these areas of dysfunction.

Status Epileptics / Critical Care

Abstract #58

Withdrawn

Status Epileptics / Critical Care

Abstract #59

Refractory Status Epilepticus did not solely lead to Cerebrospinal Fluid Pleocytosis within first 24 hours of onset.

Sargun Bajaj, Donald Griesdale, Yahya Agha-Khani, Farzad Moien Afshari

University of British Columbia

Rationale
Status epilepticus (SE) has traditionally been thought to cause cerebrospinal fluid (CSF) pleocytosis. However, attributing CSF pleocytosis solely to SE without addressing the underlying etiology may lead to poor outcomes. Leukocyte recruitment to CSF has been shown to peak around 24 hours after prolonged seizures in animal studies, suggesting that CSF pleocytosis within the first 24 hours of SE onset may be due to underlying causes. The goal of this study is to assess if SE per se is associated with CSF pleocytosis within the first 24 hours of onset.

Methods
We completed a historical cohort study of adult patients with SE admitted to the intensive care unit of Vancouver General Hospital between March 2010 and May 2019.

Results
Of the 441 patients admitted with SE during the study period, 107 met our inclusion criteria leading to 111 lumbar punctures (LPs), with 4 patients receiving two LPs. CSF pleocytosis was seen in 12 of 72 patients who underwent an LP within the first 24 hours of SE onset. In all 12 patients, a secondary etiology for the pleocytosis was observed aside from SE. Of the 6 CSF samples collected after 24 hours of onset that demonstrated pleocytosis, 4 had no cause for pleocytosis other than SE.

Conclusion
In all 12 patients with CSF pleocytosis in the first 24 hours of onset of SE, an underlying etiology was identified. Therefore, any pleocytosis noticed within the first 24 hours of onset of refractory SE should not be attributed solely to SE.

Status Epileptics / Critical Care

Abstract #60

Effectiveness of the Ketogenic Diet for Super Refractory Status Epilepticus: A Canadian Experience.

Vanessa Giuliano[1], Lysa Boissé Lomax[2], Garima Shukla[2], Gavin Winston[2]

[1]Queen's University
[2]Queen's University/ Kingston General Hospital

Rationale
The objective of this study was to assess the effectiveness of using the ketogenic diet (KD) to treat patients with super refractory status epilepticus (SRSE).

Methods
A single-center, retrospective, chart review was completed on consecutive critically ill patients in SRSE, admitted to the intensive care unit of this tertiary care center, treated with the KD between 2018 and 2020. Demographic data and details pertaining to antiseizure therapy, serum beta-hydroxybutyrate (BOHB) concentrations, duration of SRSE and KD treatment, and adverse events, were collected. EEG or clinical resolution of SRSE was the primary outcome measure whereas secondary outcome measures included survival post-hospital discharge and serum BOHB concentrations. Other parameters analysed were duration of SRSE prior to initiation of KD, and number of anti-seizure drugs (ASD) trialed before KD initiation.

Results
Seven patients (3/4 M:F, median age 38y, IQR 25.5) fulfilled the inclusion criteria. The median number of days patients were in SE prior to initiation of the KD was 3 (IQR 3.5) and the median number of ASD trialed before the start of the KD was 5 (IQR 1.5). EEG or clinically diagnosed SRSE resolved in 5 patients. All patients who achieved ketosis (serum BOHB > 2mmol/L) survived (4/7 patients). Of the patients that did not achieve ketosis (3/7 patients), one survived. Recorded adverse effects related to the KD included constipation, nausea, and vomiting.

Conclusion
The KD is an effective treatment for critically ill patients with SRSE. Future randomized controlled trials comparing the KD to other therapies for SRSE are warranted.

Basic Science / Engineering

Abstract #61

Early Seizure-Induced Dysfunction of Hippocampal Fast-Spiking Interneuron is Rescued By Activation of Trkb Receptors

Ting Ting Wang

Carleton University

Rationale
Early life seizures (ELS) are often refractory to conventional anticonvulsant treatments and can result in later life epilepsy and severe cognitive deficits. Our recent study demonstrated that ELS acutely reduced the excitatory synaptic inputs onto hippocampal fast-spiking (FS) interneurons through affecting presynaptic neurotransmitter release, which plays a crucial role in ELS pathophysiology. Thus, enhancing excitatory synaptic afferents onto FS interneurons will represent a logical approach to normalize the function of FS interneurons in ELS.

Methods
Acute hippocampal slices were prepared from control and ELS, P10-12 mice and incubated in 500 nM of partial TrkB agonist, LM22A-4 for 1 hour at room temperature before whole-cell patch electrophysiology recording. The effects of partial TrkB agonist were abolished by adding TrkB antagonist, ANA-12.

Results
We found that activation of TrkB receptors using a partial TrkB receptor agonist, LM22A-4, significantly increased the frequency of AMPA receptor mediated sEPSCs, but not sEPSC amplitude in CA1 FS interneurons in slices from 1 hour post-ELS mice, through increasing the probability of neurotransmitter release as evidenced by increased paired pulse ratio of evoked AMPAR EPSCs. Furthermore, LM22A-4's effects were abolished by co-administration of the TrkB receptor antagonist, ANA-12.

Conclusion
These data strongly support a critical role of TrkB receptors in mediating ELS-induced dysregulation of hippocampal fast-spiking interneurons and provide a potential therapeutic option for early life epilepsy.

Basic Science / Engineering

Abstract #62

Resilience Through Diversity: Loss of Neuronal Heterogeneity in Epileptogenic Human Tissue Renders Neural Networks More Susceptible to Sudden Changes in Synchrony

Taufik Valiante[1], Scott Rich[2], Homeira Moradi Chameh[2], Jeremie Lefebvre[3]

[1]*University Health Network*
[2]*Kembil Brain Insitute*
[3]*University of Ottawa*

Rationale
Rationale: Many pathological changes associated with epilepsy, including the loss of individual cell types, the misexpression of ion channels, and synaptic sprouting, can be recast as decreases in cell and circuit heterogeneity. We hypothesize that epileptogenesis can be recontextualized as a process where reduced neuronal heterogeneity renders neural circuits less resilient to seizure onset.

Methods
Methods: Patch clamp recordings were performed on human cortical pyramidal neurons from live epileptogenic and non-epileptogenic tissue obtained during surgical resection. Experimentally observed heterogeneous levels of neural excitability were implemented in computational excitatory-inhibitory (E-I) neural networks in which the tendency for a sudden transition into a synchronous, hyperactive state (paralleling ictogenesis) was quantified. These networks were further analyzed mathematically to uncover differences in their dynamical structure manifesting due to changes in neural heterogeneity.

Results
Results: We experimentally determined that heterogeneity in intrinsic neuronal excitability was significantly decreased in epileptogenic human cortical tissue. This decreased heterogeneity rendered model neural circuits more vulnerable to ictogenesis-like transitions. Decreased heterogeneity also explained a significant decrease in single-cell excitability, quantified by experimentally obtained activation functions, in epileptogenic tissue. Mathematical analyses revealed a unique structure in networks with low heterogeneity, providing a fundamental principle explaining their predisposition to seizure-like transitions.

Conclusion
Conclusions: This interdisciplinary study highlights that neuronal heterogeneity is lost in human epilepsy, describes the ictogenic consequences of this loss, and proposes a theoretical mechanism for these effects. This strongly supports the hypothesis that biophysical heterogeneity serves a fundamental role in the brain by imparting resiliency to seizure onset.

Basic Science / Engineering

Abstract #63

Dual Effect of Mitochondrial Uncoupler 2,4-Dinitrophenol on Brain Oxygen Levels and Postictal Hypoxia

Bianca R. Villa[1], Antis G. George[1], Renaud C. Gom[1], Dhyey Bhatt[1], Timothy E. Shutt[1], Patrick G. Sullivan[2], Jong M. Rho[3], G. Campbell Teskey[1]

[1]University of Calgary
[2]University of Kentucky
[3]University of California San Diego

Rationale
After a seizure, brain tissue oxygen levels drop below the severe hypoxic threshold (pO2 < 10 mmHg) for over an hour. Mitochondria thrive on oxygen, which is critical for cellular homeostasis. The pharmacological agent 2,4-dinitrophenol (DNP) – a mitochondrial uncoupler – has recently demonstrated therapeutic potential in a broad spectrum of neurological diseases. This study investigated the effects of DNP on tissue oxygenation in the hippocampus - a brain region that is highly seizure-prone – before and during postictal hypoxia, associated cognitive deficits, and mitochondrial dysfunction.

Methods
The electrical kindling model of seizures and epilepsy was used in rats. Hippocampal oxygen profiles were recorded using a chronically implanted oxygen-sensing probe, before, during, and after an evoked electrographic seizure. Rats were either acutely injected with DNP or continuously treated with the uncoupler added to the drinking water for 24 days. Postictal cognitive impairment was tested in rats using the novel object recognition task. Isolated mitochondria from both hippocampi were used for in vitro bioenergetics assays.

Results
Acute administration of a high dose of DNP caused a significant drop in hippocampal oxygen levels and worsened postictal hypoxia. However, continuous very low doses of the uncoupling agent raised tissue oxygenation and ameliorated postictal hypoxia. Mild mitochondrial uncoupling also rescued postictal hypoxia-induced cognitive deficits and prevented mitochondrial dysfunction.

Conclusion
Collectively, these findings provide evidence for a link between mitochondria and tissue oxygenation and establish low doses of DNP as a potential therapeutic strategy to attenuate the postictal state and prevent the associated pathological outcomes.

Basic Science / Engineering

Abstract #64

The Influence of Sex on Gene X Environment Interactions in Epileptogenesis in a Mouse Model of Dravet Syndrome

Cristie Noschang, Arthur Omorogiuwa, Natasha Klenin, Deborah Kurrasch

University of Calgary

Rationale
Dravet syndrome is one of the more common epileptic encephalopathies that usually appears in the first year of life and is characterized by normal development before seizure onset. Although over 80% of children with Dravet have a disruption in Scn1a gene, environmental factors also contribute to disease onset. Here, we tested the interplay of gene x environment factors and sex in the Dravet disease.

Methods
Genetically, we used mice that harbour a mutation in Scn1a and environmentally, we used heat since a warm bath or fever can trigger seizures in Dravet children. Three groups were generated for both sexes: control animals without the genetic disruption; animals with the Scn1a genetic mutation; animals with genetic disruption and exposed to heat. The electrical activity in the brain was recorded and analyzed for the frequency and amplitude of seizures.

Results
We observed sex differences in the number of spontaneous seizures between groups, with males showing an interplay between genetic and environmental factors to initiate disease onset ($P<0.01$), while in females the genetic component alone was sufficient to display seizures ($P=0.05$).

Conclusion
This work demonstrates that environmental factors, heat in this case, can sex-specifically influence the induction of seizures in a genetic model of Dravet. Our data suggest extra care perhaps should be taken to avoid over-heating specifically in boys who harbour a SCN1A mutation. Over the long-term it is important to gain a better understanding of the gene x environment x sex interactions in Dravet to help identify measures that can prevent disease onset and/or progression.

Basic Science / Engineering

Abstract #65

Amygdala Kindling Alters Pain Sensitivity and Pain-Related Emotional Behaviours in Rats

Kerri Mozessohn, Neil M. Fournier, Evana Xiao, Kaylea MacDonald

Trent University

Rationale

A surprising number of pain conditions have been reported to occur alongside epilepsy, including chronic headache disorders, migraines, neuropathic pain, and fibromyalgia. These pain conditions may occur at a much higher rate than the general population. However, few studies have directly examined the issue of pain sensitivity in epilepsy and as a result important information regarding prevalence, diagnosis and treatment remains largely unknown.

Kindling is the process by which daily administration of electrical stimulations to a particular brain region results in the gradual development and intensification of motor seizures. We found that amygdala kindling produces long-lasting increases in fear and anxiety-related behaviour in rats. Interestingly, there is evidence that many of the same neural circuits impacted amygdala kindling are also involved in processing nociceptive or pain information. This has led us to hypothesize that recurrent kindled seizures might sensitize brain regions that regulate pain responses, which in turn could lead to impairments in the processing of sensory and affective features of pain.

Methods

In the present study, Long-Evans rats underwent short-term (30 stim) and extended (99 stim) amygdala kindling. At various time points (pre-kindling, 24 hrs, 48 hrs, and 1 week post-kindling), we conducted sensory/reflexive nociceptive measurements, including von Frey hair stimulation, Hargreaves test for noxious stimulation. In addition, we also examined the affective component of pain by training animals in the formalin-induced conditioned place aversion task. Briefly, this task involves repeated pairing of two conditioning compartments (A or B) with an aversive stimulus (formalin) or control treatment (saline). Following conditioning, rats are allowed to freely access either compartment (A or B) with no aversive stimulus present, and the time spent in each compartment (i.e. avoidance of aversive paired context) is used as an inference of pain-related affect.

Results

Our preliminary results found evidence that initial nociceptive thresholds are elevated for both kindled groups 24-hr after the last kindling stimulation. However, rats that underwent 99 kindled stimulations showed a reduction in nociceptive thresholds and evidence of hyperalgesia when examined 1-week post-kindling. Importantly, while all rats showed aversion to the formalin-paired chamber when a high concentration of formalin was used, long-term kindled rats showed higher levels of aversion to this chamber even when a suboptimal formalin concentration was given—suggesting that kindling may sensitize affective processing of painful stimuli. Additional experiments are being performed to examine the neurobiological mechanisms that may underlie this enhanced responsiveness to nociceptive stimulation during epilepsy.

Conclusion

A significant proportion of people with epilepsy suffer from comorbid pain conditions. While pain thresholds are elevated immediately following a seizure event, during interictal periods pain thresholds may be significantly decreased resulting in pain hypersensitivity and chronic pain.

Basic Science / Engineering

Abstract #66

Investigating the Role of Rac1 in Mediating Accelerated Long-Term Forgetting in an Animal Model of Epilepsy

Emily E. Gordon, Neil M. Fournier, Morgan Bujokas, Lianne Bradnt, Linda E. El-Ayday, Hugo Lehmann

Trent University

Rationale

Memory difficulties are common among people with epilepsy, particularly temporal lobe epilepsy. One type of memory deficit that is particularly common among these patients is accelerated long-term forgetting (ALF), which is characterized by an initially normal acquisition and retention of memories over short periods of up to 30 minutes, but abnormally fast forgetting over periods of days or weeks after the event. Despite the prevalence of memory deficits among epileptic patients, the neurobiological mechanisms contributing to these problems remain obscure.

Recent evidence supports a role for the removal of postsynaptic AMPA receptors in mediating normal long-term forgetting. The small GTPase Rac1 regulates AMPAR trafficking and increased expression in Rac1 is known to promote active forgetting. Interestingly, several studies have also found that pharmacological inhibition of Rac1 reduces the rate of normal forgetting in mice. Given these observations, the purpose of this study was to examine if Rac1 inhibition could prevents memory loss associated with repeated seizure activity

Methods

In the present study, male Sprague Dawley rats were trained using a strong contextual fear learning procedure (5 foot shocks delivered at 1.2 mA each, 3 training sessions). Following acquisition, rats underwent 2 weeks of chemical kindling with PTZ or received saline injections (non-kindled controls). Follow up, memory retention tests were conducted 72 hrs after the last PTZ or saline treatment by placing the rats into the conditioning chambers and measuring for freezing behaviour.

Results

We found that rats that underwent strong fear conditioning form a particularly robust memory of this event that remains intact with repeated testing. Importantly, rats that were trained with the same protocol but underwent 2-weeks of PTZ kindling 48 hrs after learning, showed evidence of a rapid decay or loss of this previously acquired fear memory upon re-testing. Interestingly, repeated seizures also caused a reduction in hippocampal GluA2 expression along with higher levels of Rac1 suggesting that repeated seizures might promote the retraction of AMPA postsynaptic receptors and serve as a potential mechanism accounting for memory loss. To address this possibility, a subset of rats received treatment with a Rac1 inhibitor (NSC23766) 24 hrs after the last PTZ seizure and for each day before assessment of the context fear memory. Our preliminary data suggests that Rac1 inhibition might abrogate seizure-induced memory loss after PTZ kindling.

Conclusion

Our findings highlight a potential role hippocampal Rac1 signalling in contributing to memory dysfunction associated with epilepsy and suggests that targeting Rac1 could be a novel strategy for the treatment of epilepsy-related cognitive impairments.

Basic Science / Engineering

Abstract #67

Pre-Trained Wavelet Transformer for Seizure Detection Using Scalp EEG

Yi Cheng Zhu[1], Qi Xu[2]

[1]University of Toronto
[2]University of Manitoba

Rationale
Deep machine learning has been shown to achieve outstanding performance on processing high volume complex non-linear data in other fields and has recently been applied to EEG seizure detection. One significant limitation of the application of machine learning in the medical field is the lack of high-quality data.

Methods
We introduced a novel transformer based neural network architecture for seizure detection. Our model can be pretrained on a large, unlabeled dataset before being fine-tuned on a small, labeled dataset. We pretrain our model on the TUH EEG Corpus then fine tune on the TUH EEG Seizure Corpus.

We preprocess the raw, standard 10-20 system 21 channels EEG data by normalizing the per channel data to a Z-score. Our model consists of a learnable wavelet transformer layer, a convolutional down sampling layer, a transformer encoder decoder, and a convolutional up sampling layer. The model is trained to perform the masked reconstruction task. In the fine-tuning step, the transformer decoder is replaced with 2 fully connected linear layers.

Results
We evaluated the model's performance on the dev-test subset of the TUH EEG Seizure Corpus. We used the Time-Aligned Event score (TAES). The pilot model achieved 1.26% sensitivity and a False Alarm Rate of 857.01 per 24 hours.

Conclusion
Our model has shown promising initial results on the TUH EEG dataset. Further training is expected to yield improvements upon these results. The adaptability of the pretrained model allows it to be easily fine-tuned to work on other EEG tasks.

Basic Science / Engineering

Abstract #68

Prevention Of Trauma-Induced Epileptogenesis Using Transcranial Direct Current Stimulation

Rachel Barr

Universite Laval

Rationale

Traumatic brain injury triggers epileptogenesis. We postulate that the decrease of activity in traumatized areas triggers homeostatic plasticity (HSP) processes that up-regulate neuronal excitability.

We propose to use transcranial direct current stimulation (tDCS) to increase neuronal activity following trauma. The intervention would prevent silence of deafferented areas thereby preventing HSP. This would require a localized, depolarizing influence of tDCS.

Methods

To investigate the extent by which DCS (60 uA, 5 min) depolarizes/hyperpolarizes neurons, intracellular recordings were performed in anesthetised mice. To determine whether the effects of DCS are localized, LFP was recorded at varying distances from the stimulation electrode.

To investigate the effects of DCS and tDCS on cellular, LFP and EEG measures of slow wave sleep (SWS), we applied stimulation (60-100 uA, 5-20 min) over the suprasylvain gyrus of naturally sleeping cats.

Results

During DCS in mice, the amplitude and frequency of LFP located within 1 mm of stimulating electrode was increased. This effect was not detected at distances above 2 mm. In single neurons, DCS modified the membrane potential in a polarity-dependent manner.

In cats, the amplitude and duration of slow waves was increased following tDCS up to 10 mm from the stimulating electrode, with some less pronounced effects up to 20-30 mm away. DCS only produced effects 2 mm from the stimulating electrode.

Conclusion

The effects of DCS are strong and local. tDCS has measurable regional effects with small effects extending to the whole hemisphere.

Basic Science / Engineering

Abstract #69

The Influence of Seizure-Induced Stress on Fear and Anxiety Behavior

Renaud Gom

University of Calgary

Rationale
Up to half of people with epilepsy suffer from emotional comorbidities, including depression and anxiety disorders, which can severely impair quality of life. Alterations in emotionality following repeated seizures have previously been linked to endocannabinoid system dysfunction. The aim of this study was to determine whether activation of the hypothalamic-pituitary-adrenal (HPA) axis following seizures mediates the changes in endocannabinoid levels and fear and anxiety behavior.

Methods
Young adult Long-Evans rats were stereotaxically implanted with bipolar stimulating electrodes in the right basolateral amygdala (BLA). Seizures were elicited at a suprathreshold current on a fixed schedule and either metyrapone, a corticosterone synthesis inhibitor, or vehicle was administered prior to each seizure. In addition to measuring fear behavior and CORT concentration, we also measured seizure thresholds, seizure severity, seizure duration, and endocannabinoid levels were collected.

Results
Plasma corticosterone levels were highly elevated after seizures, however no long-term changes in baseline corticosterone were observed during the 2-week kindling process. Pre-seizure metyrapone administration completely prevented seizure-induced corticosterone increases. Rats administered vehicle and had seizures showed impaired fear memory retention at 24 and 48 hours after auditory fear conditioning relative to non-seizure controls. Impaired memory retention did not occur in rats administered metyrapone prior to each seizure.

Conclusion
These experiments illustrate that an increase in HPA axis activation following seizures result in changes in fear processing and memory and could be targeted in future treatments of comorbid psychiatric conditions in people with epilepsy.

Basic Science / Engineering

Abstract #70

A Novel Mouse Model of FASN-Associated Neurodevelopmental Disorders

Samuel Boris Tene Tadoum[1], Alexandros Hadjinicolaou[2], Smrithi Raghuram[1], Praveen Kumar Raju[1], Mathieu Lachance[1], Philippe Campeau[3], Elsa Rossignol[4]

[1]*Neuroscience Department, Université de Montréal / CHU Ste Justine Research Center*
[2]*CHU Ste Justine Research Center*
[3]*Pediatric Department, Université de Montréal / CHU Ste Justine Research Center*
[4]*Neuroscience Department, Université de Montréal / Pediatric Departement, Université de Montréal / CHU Ste Justine Research Center*

Rationale
Developmental epileptic encephalopathies are clinically and genetically heterogeneous disorders. Recent studies revealed mutations in the FASN gene in two unrelated children with early-onset epilepsy. We have now identified a cohort of 12 children carrying recessive or de novo FASN mutations and presenting a spectrum of neurodevelopmental disorders, ranging from global developmental delay and intellectual deficiency to severe developmental epileptic encephalopathy.

The FASN gene encodes Fatty acid synthase, a multifunctional protein responsible for de novo lipogenesis from acetyl-Coa and malonyl-Coa in the presence of NADPH. FASN is ubiquitously expressed in the embryo and its loss results in prenatal lethality. However, its roles in brain development are unclear.

Methods
In this study, we expand the phenotypic description of patients with de novo FASN mutations while generating by CRISPR/Cas 9 gene-editing, a novel mouse model carrying a patient-derived FASN mutation. We also characterized our FasnS154N mouse model using various behavioural tests and Video-EEG recording.

Results
The homozygous FasnS154N knock-in mice are not viable. However, heterozygous FasnS154N mice display a clinical phenotype reminiscent of the patients' phenotypes, with anxiety-like behavior, altered spatial learning, spontaneous interictal spikes on electroencephalograms (EEG), and a tendency to a reduced PTZ-induced seizure threshold.

Conclusion
Our work thus reveals the phenotypic spectrum of FASN-associated neurodevelopmental disorders, while providing unique animal model to advance mechanistic studies that will ultimately drive therapeutic innovation for this disorder.

Basic Science / Engineering

Abstract #71

Withdrawn

Basic Science / Engineering

Abstract #72

Electrophysiological Studies of Medical Cannabis in Epileptic Mouse Cerebral Cortex

Yasaman Javadzadeh[1], Shanthini Mylvaganam[2], Peter Carlen[1]

[1]*University of Toronto*
[2]*University Health Network*

Rationale
30% of patients with epilepsy exhibit drug-resistance, elucidating the need for novel anticonvulsant drugs. Cannabidiol (CBD) and Delta-9 Tetrahydrocannabinol (Δ9-THC), phytocannabinoids from the cannabis plant, have been shown to have great potential in epilepsy treatment. However, we lack knowledge as to which compound(s) to use and their pharmacological targets. We examined the anticonvulsant effect of CBD alone and in combination with Δ9-THC and explored the role that the 5-HT1α receptor plays in CBD's effect.

Methods
4-aminopyridine was used to induce seizure activity in mouse cortical brain slices, after which CBD alone and in combination with Δ9-THC was applied. To examine CBD's mechanism of action, slices were pre-treated with a 5-HT1α receptor antagonist. Extracellular field recordings were measured in layer 2/3 of the cortex.

Results
30µM and 100µM CBD application significantly reduced seizure duration, amplitude, and coastline length, a measure of seizure intensity. 10µM CBD application displayed a non-significant anticonvulsant trend. Adding low dose Δ9-THC to 10µM CBD potentiated the effects of CBD, displaying a significant anticonvulsant effect that was larger than either cannabinoid alone. Lastly, blocking the 5-HT1α receptors prior to CBD application significantly abolished the effects of CBD.

Conclusion
CBD, especially at higher concentrations, displays anticonvulsant effects in the cortex. Cannabinoids combined at lower concentrations display anticonvulsant effects similar to higher concentrations alone. CBD exerts its effects, at least in part, through the 5-HT1α receptors. These results could address the barrier of drug-resistance while providing insight into CBD's mechanism of action, laying the groundwork for further testing of cannabinoids as anticonvulsants.

Epilepsy Surgery

Abstract #73

Efficacy of VNS for Drug-Resistant Epilepsy in Structural Brain Lesions.

Hanin AlGethami[1], Ashwaq Alshahrani[2], Mubarak Aldosari[2], Majed Alhameed[2]

[1]King Salman Hospital, Riyadh, Kingdom of Saudi Arabia
[2]Epilepsy Monitoring Unit, Neuro-Science Center, King Fahad Medical City, Riyadh, Saudi Arabia

Rationale
Vagus nerve stimulation (VNS) has been used for the treatment of drug-resistant epilepsy, especially in patients who are not candidates for surgical intervention. In fact, it was approved by the US FDA in 1997 as an adjunctive treatment for medically intractable epilepsy.

Methods
We retrospectively analyzed the effect of VNS on 25 patients diagnosed with intractable epilepsy-associated SBL, and compared the results to 19 patients with intractable epilepsy and normal neuroimaging. All patients underwent VNS insertion at the National Neurosciences Institute, King Fahad Medical City (Riyadh, Saudi Arabia) between 2008 and 2018.

Results
The response rate (RR) for patients with drug-resistant epilepsy-associated SBL was 24% after 3 months, 36% after 6 months, and 48% after 1 year, reaching 76% over time. The mean follow-up period was 63.3 months. For non-SBL patients, the RR was 10.5% after 3 months, 36.8% after 6 months, and 47.4% after 1 year, reaching 73.7% over time. The mean follow-up period was 59.2 months. There was no statistically significant difference between the two groups regarding RR, VNS settings, and other parameters, including anti-epileptic drug use and demographics data.

Conclusion
VNS is strongly considered for intractable epilepsy in SBL patients, especially if they are not candidates for surgical intervention. Over time, those patients will receive increased benefits from VNS therapy.

Epilepsy Surgery

Abstract #74

Comparison of the Real-World Effectiveness of Vertical Versus Lateral Functional Hemispherotomy Techniques for Pediatric Drug-Resistant Epilepsy

Alexander Weil[1], Aria Fallah[2], George Ibrahim[3], Olivia Kola[2], Jia-Shu Chen[4], Tristan Brunette-Clément[1], HOPS Research Group

[1]*Centre Hospitalier Universitaire Sainte-Justine, Montreal*
[2]*David Geffen School of Medicine at University of California Los Angeles*
[3]*The Hospital for Sick Children*
[4]*Warren Alpert Medical School of Brown University, Providence, Rhode Island, USA*

Rationale

For pediatric epilepsy patients with multi-lobar or hemispheric epileptogenic lesions, hemispherotomy is generally favored over anatomic hemispherectomy due to lower risk for complications and possibly better seizure outcomes. However, no high-quality studies comparing the lateral and vertical hemispherotomy techniques exist.

The Hemispherectomy Outcome Prediction Scale (HOPS) identified predictors of seizure freedom following hemispheric surgeries. We performed a post-hoc analysis of HOPS comparing the vertical parasagittal and lateral peri-insular/peri-Sylvian hemispherotomy techniques with respect to long-term seizure freedom.

Methods

Using participants from the HOPS dataset undergoing vertical parasagittal, lateral peri-insular, or lateral peri-Sylvian hemispherotomy, we assessed and calculated differences in seizure freedom rates using the time-to-event and Kaplan-Meier survival methods.

Results

Data was collected for 672 participants across 23 centers. Of these, 72 (10.7%) underwent vertical parasagittal hemispherotomy and 600 (89.3%) underwent lateral peri-insular/peri-Sylvian hemispherotomy. At 10-year follow-up, 62.4% (95% CI=53.5-70.2%) of the entire cohort attained seizure freedom. Seizure freedom was 88.8% (95% CI=78.9-94.3%) at 1-year follow-up and persisted at 85.5% (95% CI=74.7-92.0%) across 5- and 10-year follow-up in the vertical subgroup, but decreased from 89.2% (95% CI=86.3-91.5%) to 72.1% (95% CI=66.9-76.7%) and then 57.2% (95% CI=46.6-66.4%) at 1-, 5-, and 10-year follow-up, respectively, in the lateral subgroup. Vertical hemispherotomy was also associated with more durable seizure-free progression (p=0.01) and patients undergoing a lateral hemispherotomy had shorter time-to-seizure recurrence (HR=2.56; 95% CI=1.08-6.04; p=0.03) and increased seizure recurrence odds (OR=3.67; 95% CI=1.05-12.86; p=0.04).

Conclusion

This study demonstrated greater durability of seizure freedom from the vertical hemispherotomy technique compared to lateral peri-insular/peri-Sylvian techniques.

Epilepsy Surgery

Abstract #75

Stereoelectroencephalography Versus Subdural Electrode Implantations for Drug Resistant Epilepsy: Comparisons of Surgical and Non-Surgical Candidates After Invasive Investigations.

Paule Lessard Bonaventure, Alan Chalil, Jorge G. Burneo, David A. Steven

London Health Science Center

Rationale
A shift from subdural electrodes (SDE) toward stereoencephalography (SEEG) is trending in epilepsy centers worldwide. Some epilepsy centers have noticed a decrease in the proportion of resective surgery offered to patients since the adoption of SEEG. We aimed to perform a comparative analysis of non-surgical candidates following SEEG vs SDE.

Methods
Single center retrospective cohort study from 2006-2021 of adult cases undergoing intracranial investigations at the London Health Science Centre, Ontario. We performed descriptive statistics. The probability of surgical candidacy was assessed using univariate and multivariate logistic regression models.

Results
A total of 363 patients underwent 397 intracranial evaluations. The SDE (n=182) and SEEG (n=213) groups had similar demographic and radiological characteristics. Resective surgery was offered to 57.7% of SDE cases vs 64.8% of SEEG cases. The characteristics of non-surgical candidates were similar in both groups. A higher proportion of SDE non-surgical cases required additional electrodes (13% vs 0%, p=0.001). Reasons precluding resective surgery differed between the groups. More SDE cases had multifocal seizures (48.0 vs 26.0%, p=0.005) and incomplete/unprecise investigations (19.8 vs 13.7%). SEEG cases had more bitemporal seizures (39.7 vs 22.7%,) and non-epileptic seizures (5.5% vs 0, p=0.05). A bilateral implantation (OR 2.6, p= <0.001), a non-lesional MRI (OR 2.0, p=0.004) and length of monitoring (OR 1.4, p=0.005) were associated with a higher likelihood of non-surgical outcome.

Conclusion
In this cohort study, SDE and SEEG cases were overall similar. Resective surgery was offered in similar proportions between the two groups, but reasons precluding surgery varied. SEEG is a more precise method with fewer patients needing additional electrodes and led to less frequent imprecise or unsuccessful recordings. Length of monitoring, non-lesional MRI and having a bilateral implantation was associated with non-surgical outcome, suggesting more complex cases

6. Epilepsy Surgery

Abstract #76

Barriers to Pediatric Epilepsy Surgery: A Scoping Review

Rami Hatoum[1], Nabil Nathoo-Khedri[1], Nathan A. Shlobin[2], Andrew Wang[3], Alexander G. Weil[4], Aria Fallah[3]

[1]University of Montréal School of Medicine
[2]Department of Neurological Surgery, Northwestern University Feinberg School of Medicine, Chicago
[3]Department of Neurosurgery, David Geffen School of Medicine at UCLA
[4]Division of Neurosurgery, Ste. Justine Hospital, University of Montréal

Rationale
Up to 40% of pediatric epilepsy cases are drug-resistant and associated with neurocognitive, psychosocial, developmental comorbidities, and higher mortality. Epilepsy surgery (ES) must be considered after the failure of two anti-epileptic drugs as it was shown to be safe and effective, yielding 50 to 90% seizure reduction. However, only a minor proportion of children receive surgical care, likely due to difficulties throughout the decision-making process. This scoping review aims to elucidate barriers to pediatric ES to understand the reasons for its underutilization.

Methods
Embase, PubMed, and Scopus were searched from inception through July 2020 for the following PICO terms: "pediatric", "parents", "epilepsy", "surgery", and "decision-making". Studies exploring barriers to ES were included and qualitatively synthesized. Primary outcomes were barriers hindering ES and were assigned to thematic categories. PRISMA Sc-R guidelines were followed.

Results
From 1929 screened studies, 11 were included. Barriers to ES were classified into four categories. 82% of studies reported parental barriers originating from misperception, lack of knowledge regarding surgery's outcomes, and emotional vulnerability. 55% of articles outlined physician-based barriers, including lack of clinical expertise, trust, and communication, leading to inadequate informed consent and referral to surgical evaluation. Patient-based barriers were reported in 36% of studies and included clinical characteristics modulating acceptance of ES. 18% of studies pointed out healthcare system-based barriers, including intricate insurance policies not adapted to sociodemographic disparities.

Conclusion
This study highlights the complexity of barriers to pediatric ES, contributing to significant impediments to surgical treatment. Our findings emphasize the need for multileveled strategies to address these obstacles.

Epilepsy Surgery

Abstract #77

The Effect of Vagus Nerve Stimulation on the Quality of Sleep in Medically Refractory Epileptic Patients

Jayant Seth, Ana Suller-Marti

London Health Sciences Center

Rationale
The quality of sleep is frequently impacted in patients with epilepsy. Vagus Nerve Stimulation is a relatively common treatment used in patients with medically resistant epilepsy. Some studies show an improvement in quality of life, however, there is limited data on the impact on sleep quality.

Methods
A database analysis was conducted on Medline, Embase, and Cochrane to find studies that examined the VNS's effect on quality of sleep in medically resistant epilepsy. These studies included randomized clinical trails, case studies or reports, cohort studies, and systematic reviews.

Results
75 papers were reviewed and 16 studies from eight countries were included in the analysis. A total of 93 patients with ages ranged from 10 – 49 were included. Analyzing the change in the quality of sleep after VNS was evaluated using Multiple Sleep Latency Test. The literature showed that at low stimulus intensities, VNS treatment improves daytime sleepiness in patients. However, VNS setting titration has a dose-dependent effect on obstructive sleep apnea where higher VNS frequencies are related to higher apnea events.

Conclusion
Limited data is available on the impact of VNS on the quality of sleep. Further studies are required to evaluate the improvement of sleep in patients with VNS.

Epilepsy Surgery

Abstract #78

Machine Learning for Prediction of Seizure Outcome After Pediatric Epilepsy Surgery

Omar Yossofzai[1], Aria Fallah[2], Cassia Maniquis[2], Alexander Weil[3], Tristan Brunette-Clement[3], Andrea Andrade[4], George Ibrahim[5], Nicholas Mitsakakis[1], Elysa Widjaja[5]

[1]University of Toronto
[2]University of California Los Angeles
[3]Centre Hospitalier Universitaire Sainte-Justine, Montreal
[4]University of Western Ontario
[5]The Hospital for Sick Children, University of Toronto

Rationale
Seizure outcome following pediatric epilepsy surgery is variable. This study aimed to use machine learning (ML) to develop a prognostic tool for predicting seizure outcome after pediatric epilepsy surgery.

Methods
This multicenter retrospective cohort study recruited children ≤18 years of age who had undergone resective epilepsy surgery from four pediatric centers between 2000-2019, with follow-up of at least one year. Exclusion criteria included corpus callosotomy, vagal nerve or deep brain stimulation. We extracted 20 pre-surgical features from medical records for ML classifier development including clinical data, diagnostic tests (MRI, video-EEG, PET, magnetoencephalography), and surgical variables. Data was split into 80% training set and 20% testing set. We evaluated 35 combinations of 5 feature sets with 7 machine learning classifiers (logistic regression, random forest, decision tree, XGBoost, naïve bayes, neural network, support vector machine) using 5-fold cross-validation on the training set. The best performing combination was then evaluated on the testing set. Seizure outcome was categorized as seizure-free or not seizure-free.

Results
Of the 685 children who were included, 440 (64.2%) achieved seizure freedom at one-year. Our best ML classifier on the training cohort (n=548) was a random forest model using the full feature set. On the testing set (n=137), this classifier achieved an area under the curve of 0.74 (sensitivity=0.90, specificity=0.51, at optimal operating point using Youden's index). Feature selection identified MRI findings, followed by resective surgery type as the most important features for prediction of seizure-free outcome.

Conclusion
ML could improve prognostication of seizure outcome following epilepsy surgery, thereby improving pre-surgical counselling.