2018

Canadian League Against Epilepsy

Book of Abstracts

Scientific Meeting

September 21-23

Oral Presentation: Neuroimaging / EEG

Abstract 1

Investigation of the Alterations in Hippocampal Internal Architecture in Focal Temporal Lobe Epilepsy using 7T MRI

Nickolas Christidis, Jonathan Lau, Jorge Burneo, David Steven, Ali Khan

Western University

Rationale
Since accurate identification of seizure localization is critical for presurgical planning, the search for new markers of seizure onset localization remains important. Alteration of hippocampal internal architecture is an important predictor of seizure onset laterality in patients with focal temporal lobe epilepsy. However, less prominent alterations of hippocampal architecture may be missed due to resolution limits of conventional scanners (1.5 to 3 T). Thus, we assessed the diagnostic utility of ultra-high field (7T) MR in detecting alterations of hippocampal internal architecture as a marker of seizure onset laterality.

Method
Patients undergoing intracranial investigation of refractory epilepsy were recruited and imaged using a 7T MRI protocol in addition to standard of care imaging. Hippocampal architecture was assessed using manual subfield segmentation with subsequent unfolding of the hippocampus for quantitative comparisons of subfield-specific volumetric alterations. Qualitative evaluations of hippocampal architecture abnormalities were compared with post-implantation clinical assessments regarding seizure localization and laterality.

Results
Alterations of hippocampal architecture uncovered at 7T were concordant with intracranial assessment of seizure laterality. Considerable loss of hippocampal digitations was identified in the hippocampus ipsilateral to the clinically determined seizure onset zone. In unilateral temporal lobe epilepsy this alteration was restricted to the ipsilateral hippocampus, sparing the contralateral hippocampal architecture. In bitemporal cases, digitations were lost in both hippocampi.

Conclusions
These preliminary findings suggest alterations of hippocampal architecture in patients with refractory epilepsy can be reliably detected at 7T. This characteristic may be an effective marker of seizure onset laterality that can help improve selection of appropriate candidates for resective neurosurgery.

Acknowledgements: This work was supported by a CIHR Project Grant, the Canada First Research Excellence Fund, Brain Canada, and the Ontario Brain Institute Epilepsy Program (EpLink).

Oral Presentation: Clinical Epilepsy / Antiepileptics

Abstract 2

Short-Term Effects of High Frequency Insular DBS on Epileptic Discharge Rates in Patients with Refractory Epilepsy

Antoine Dionne, Elie Bou Assi, Denahin Toffa, Alain Bouthillier, Dang Khoa Nguyen

University of Montreal Hospital Center (CHUM), University of Montreal

Rationale
Deep brain stimulation (DBS) of several sites such as the thalamus has been proven to reduce seizure frequency and interictal epileptiform activity in patients with refractory epilepsy. Recent findings have demonstrated that the insula is part of the 'rich club' of highly connected brain regions. In this work, we investigate short-term effects of high frequency (HF) insular DBS on interictal epileptiform discharge rates (IEDRs) in patients with refractory epilepsy.

Method
Participants (n=6) received 2 sets of 10-min continuous HF (150 Hz) insular electrical stimulation. A one-hour interval resting-awake was observed between the sets. Epileptiform activity was recorded with intracranial electrodes for a total of 3 hours and 20 minutes, starting one hour prior to Stimulation Set 1 (SS1) and ending one hour after Stimulation Set 2 (SS2). Intracranial electroencephalography recorded spikes were visually labelled by a board-certified electroencephalographist. IEDRs measured during the hour preceding SS1 served as baseline for comparison with post-stimulation IEDRs.

Results
IEDRs diminished by more than 45% after SS1 and by more than 68% after SS2 for 2 of the 6 participants. Increases in IEDRs from baseline were observed for all four remaining patients, ranging from 7% to 56% after SS1 and from 9% to 75% after SS2. Group level statistical analysis showed no significant change between baseline and post-stimulation intervals (t-test; $p<0.05$).

Conclusions
This study reports mitigated results as per the effects of HF insular DBS on IEDRs. Further examination of surgical electrodes' placement, semiology, and stimulation frequency are required to allow for clearer conclusions.

Funding: CIHR, NSERC, FRQS

Oral Presentation: Basic Science/Engineering

Abstract 3

Increasing Glutamate Clearance as a Strategy to Reduce Excessive Excitatory Tone in the Central Nervous System

Crystal Wilkie, Matthew Parsons

Memorial University of Newfoundland

Rationale
Glutamate is the brain's most abundant excitatory neurotransmitter. In excess, it disrupts the excitatory/inhibitory tone in the brain and causes the spread and initiation of seizures. Glutamate transporters, particularly glutamate transporter 1 (GLT-1), are important for decreasing excitatory tone and are possible therapeutic targets to restore the balance and decrease seizures.

Method
Ceftriaxone and LDN/OSU-0212320 are drugs that increase GLT-1 expression. We injected healthy FVB mice with Ceftriaxone or LDN/OSU-0212320 and used a novel optogenetic technique to visualize glutamate clearance in real-time in acute brain slices. We focused on the cortex, hippocampus, and striatum which are important for higher brain function, memory and learning, and motor coordination, respectively. We examined the ability of these drugs to effectively decrease glutamate levels and restore the excitatory/inhibitory tone when faced with a pathological amount of synchronous excitatory activity.

Results
We found that Ceftriaxone significantly lowered the amount of glutamate being released in the cortex and therefore, lowered excitability. However, in the hippocampus and striatum we found that Ceftriaxone did not significantly lower excitability in these regions. For LDN/OSU-0212320, we found that it had no significant effect on excitability in any of the brain regions studied.

Conclusions
In contrast to previous studies, we found that increasing GLT-1 expression using Ceftriaxone and LDN/OSU-0212320 did not significantly increase glutamate clearance. Interestingly, we found that Ceftriaxone did lower excitability in only the cortex while LDN/OSU-0212320 had no effect. Therefore, Ceftriaxone may be beneficial in restoring the excitatory/inhibitory tone but it is not a whole brain effect.
Funding from Epilepsy NL.

Oral Presentation: Basic Science / Engineering

Abstract 4

Comparative Analysis of Antiseizure Drugs in Dravet And Episodic Ataxia with Epilepsy Zebrafish and Mice Models

Kingsley Ibhazehiebo

University of Calgary

Rationale
Dravet syndrome is a debilitating childhood epilepsy with unremitting pharmaco-resistant seizures, suggesting novel approaches to drug-screening are needed to uncover drugs with new mechanisms of action. Using zebrafish, we developed a metabolism-based drug screening platform that unbiasedly assays for decreases in metabolic hyperexcitability. Here we compared efficacies of known antiseizure drugs across a Dravet and a more responsive model of epilepsy (e.g., episodic ataxia with epilepsy). We reasoned that if modulating bioenergetics is indeed a reliable readout for efficacious drugs, then fewer antiseizure drugs should be effective in the Dravet zebrafish versus the episodic ataxia with epilepsy model. To test the translation of our approach, positive hits were validated in a Dravet and an episodic ataxia with epilepsy mouse models.

Method
We used CRIPSR/cas9 to introduce mutations into the zebrafish ortholog of SCN1A (e.g., scn1lab) and KV1.1 (e.g., kcna1) epilepsy-associated genes to create Dravet and the generalizable episodic ataxia with epilepsy models, respectively. Extensive metabolic profiles of both scn1lab and kcna1 mutant zebrafish were analyzed with XF24e Seahorse Bioanalyzer. We conducted a shelf screen of twenty-three known antiseizure drugs in both models to test their ability to restore altered metabolic functions. Drugs that restored mitochondrially-mediated bioenergetics to baseline (e.g., wild type) levels were considered efficacious. Furthermore, drugs effective in the zebrafish models were prioritized and validated in Scn1a+/- Dravet mice using a hyperthermia-induced seizure assay and Kv1.1-null mice using video-EEG.

Results
The scn1lab and kcna1 mutant zebrafish exhibited distinct bioenergetics phenotypes for oxidative phosphorylation and glycolysis, including decreases in basal respiration, mitochondrially-mediated respiration, and ATP-linked respiration. On the other hand, the maximum respiratory capacity and non-mitochondria respiration were unchanged. Interestingly, only 8 of 23 antiseizure drugs were effective in the scn1lab mutants, whereas 18 of the 23 drugs were efficacious in the kcna1 mutant zebrafish. Top drugs reduced the frequency of seizures in Kv1.1-null mice and are currently being tested in the Scn1a+/- Dravet model.

Conclusions
The fewer number of compounds efficacious in the scn1lab Dravet syndrome model is consistent with the pharmaco-refractory nature of this disease and suggests that bioenergetics in a robust and reliable readout to identify new antiseizure drugs.

Neuroimaging / EEG

Abstract 5

Withdrawn

Neuroimaging / EEG

Abstract 6

Validation of Two fMRI Paradigms for Pre-Surgical Language Mapping

Antonina Omisade[1], Christopher O'Grady[1], Matthias Schmidt[2], John D. Fisk[1]

[1]Nova Scotia Health Authority
[2]Nova Scotia Health Authority / Dalhousie University

Rationale
Functional MRI (fMRI) is the preferred non-invasive method of determining language dominance before epilepsy surgery but validated, standardized protocols are lacking. We compared a visual pre-surgical language mapping paradigm representing our center's standard of care with a novel auditory-based paradigm designed for individuals with visual impairment or cognitive limitations. We examined whether these paradigms provide results consistent with published proportions of language laterality.

Method
The paradigms included word generation, sentence completion, naming, and passage listening, delivered visually or through headphones. Numbers of voxels with significant activation in left and right temporal and inferior frontal lobes determined individual language laterality indices (LI's) and language dominance (right, left, or bi-lateral). Thirty right-handed and 20 left-handed participants completed both paradigms.

Results
With the visual paradigm, 29/30 (97%) right-handers were classified left hemisphere dominant, one as bilateral. For left-handers, 17/20 (85%) were left-hemisphere dominant, two right-hemisphere, and one bilateral. The auditory paradigm classified 100% of right-handers and 80% of left-handers as left hemisphere dominant. Three left-handers were classified as right-hemisphere dominant, one as bi-lateral. LI's for the two paradigms were highly correlated in the total sample ($r=0.80$, $p<0.0001$), right-handers ($r=0.63$, $p<0.0001$), and left-handers ($r=0.86$, $p<0.0001$). There was 96% agreement in language dominance between the two paradigms.

Conclusions
We demonstrate good agreement between our standard visual and novel auditory fMRI paradigms in determining hemispheric dominance, and proportions of hemispheric dominance for right- and left-handers in a general population sample. Evaluation of both paradigms in patients with epilepsy and healthy individuals with a greater range of IQ is required.

Neuroimaging / EEG

Abstract 7

Novel EEG Based Diagnostic Biomarker of Epilepsy

Daniel Moshe Zelig[1], Dan Z Milikovsky[1], Alon Friedman[2]

[1]Departments of Physiology and Cell Biology, Cognitive and Brain Sciences, Zlotowski Center for Neuroscience, Ben-Gurion University of the Negev, Beer-Sheva
[2]Departments of Physiology and Cell Biology, Cognitive and Brain Sciences, Zlotowski Center for Neuroscience, Ben-Gurion University of the Negev, Beer-Sheva / Department of Medical Neuroscience, Dalhousie University

Rationale
Despite the development and availability of clinically applicable technological modalities, diagnosis of epilepsy poses a serious challenge to neurologists throughout the world on a daily basis.
The situation of no observed seizures by medical personnel, and absence of findings in imaging or electroencephalogram (EEG) is not uncommon and strengthen the need of objective diagnostic biomarkers to assist the diagnostician.

Method
To meet this challenge, we investigated interictal EEG or elctrocorticogram (ECOG) signals recorded from patients with epilepsy, as well as from animals of several models (intracerebroventricular (ICV) infusion of albumin/ IL-6 /TGF -β, paraoxon induced Status epilepticus) and tested the potential of the following features to serve as biomarker: Interictal spikes, power band dynamics, prevalence of paroxysmal slow wave events (PSWE).

Results
Consistently with previous works, we found that interictal spikes are sensitive but not sufficiently specific due to physiological phenomena and noise. PSWE however allow unbiased detection of epilepsy in some of the animals' models (paraoxon induced Status epilepticus but not in ICV infusion) as well as in human patients.

Conclusions
Our findings suggest that PSWE may serve as a diagnostic biomarker, and further research in greater scale is essential to establish these results and integrate them in the clinical practice.

Neuroimaging / EEG

Abstract 8

Seizure Detection in the Intensive Care Unit Using Automated Seizure Detection Algorithms

Farah Din, Suptharishi Lalgudi Ganesan, Tom Akiyama, Craig Stewart, Ayako Ochi, Hiroshi Otsubo, Christina Go, Cecil Hahn

The Hospital for Sick Children

Rationale
To compare the performance of commercially-available computerized seizure detection algorithms with that of QEEG-based seizure identification by EEG experts.

Method
Nineteen continuous EEG recordings from critically ill children were reviewed by a board-certified neurophysiologist and EEG technologists who marked the individual seizures (comparison standard). The raw EEG recordings were processed using four computerized seizure detection algorithms: ICTA-S, NB, Persyst11 (P11) and Persyst13 (P13). These nineteen recordings were transformed to aEEG and CDSA trends and, neurophysiologists and EEG technologists then marked 'suspected' seizures on these trends without access to raw EEG. We calculated sensitivity for seizure identification and false-positive rate for each modality.

Results
The automated detectors, median sensitivity was 33.3% with ICTA-S, 100% with NB, 74.1% with P11, and 91.2% with P13. Sensitivity was greater for bilateral or long seizures in all modalities. Median 24-hour false-positive rates were 1.00 with ICTA-S, 115.10 with NB, 0 with RR, 1.54 with P13, 0.78 with CDSA, and 0.58 with aEEG. The neurophysiologists and EEG technologists had a median sensitivity of 84.6% with CDSA and 82.4% with aEEG. However, there was wide variability among individual recordings.

Conclusions
Sensitivity of newer automated seizure detectors is approaching that of EEG experts using aEEG and CDSA; however false positive rates are higher. This suggests that newer automated seizure detection algorithms could complement the use of QEEG and facilitate more timely seizure detection in critically ill patients.

Neuroimaging / EEG

Abstract 9

Practical Considerations for Scanning Patients at 7 Tesla: Experience in a Prospective Cohort Scanned at the Western CFMM

Jonathan Lau[1], Trevor Szekeres[2], Joseph Gati[2], Andrew Parrent[1], Jorge Burneo[1], David Steven[1], Terry Peters[2], Ali Khan[2]

[1]Department of Clinical Neurological Sciences, Western University
[2]Centre for Functional and Metabolic Mapping, Robarts Research Institute, Western University

Rationale
Seven Tesla (7T) magnetic resonance imaging (MRI) has recently been approved by the United States Food and Drug Administration for clinical use, and may play a valuable role in the investigation of patients with epilepsy. We report our experiences with scanning participants on the head-only 7T MRI scanner at the Western University Centre for Functional and Metabolic Mapping (CFMM).

Method
Scan-related details and participant experiences were logged in a prospective series of participants scanned at 7T (1 hour research protocol).

Results
We report findings in 62 consecutive participants (N= 34 controls, N=28 patients). Eleven participants were being investigated for medically refractory epilepsy. Out of a total of 65 scheduled scan sessions, 59 scans were successfully completed (90.8%). Of the 6 incomplete studies, 4 were the result of scanner issues (e.g. software reboot) and 2 due to patient-related factors (claustrophobia, in-scanner seizures in a patient with epilepsy). Of 5 participants with documented claustrophobia, 4 out of 5 (80%) completed scanning successfully. The individual who was unable to complete scanning due to claustrophobia required sedation for their clinical 1.5T MRI scan. Five participants (8.1%) reported dizziness either at the beginning or end of the scan session, which resolved within seconds to minutes. No participants aborted the procedure because of dizziness. One participant experienced a sore shoulder and another experienced low-back pain mid-protocol but both completed scanning.

Conclusions
Overall, these findings suggest that scanning in both the general population and patient groups is as well-tolerated on the Western CFMM 7T scanner as on standard clinical scanners. Prospective recruitment is ongoing.

Neuroimaging / EEG

Abstract 10

"Spectre Spike-Wave": A Pathological Variant of Benign Phantom Spike-and-Wave in Patients with Neurologic Disease

Graham McLeod, Michelle-Lee Jones, Marcus C Ng

University of Manitoba

Rationale
Phantom spike-and-waves (PSWs) on EEG are understood as a benign epileptiform variant (BEV) which occur regularly in a small number of healthy persons. PSWs, like other BEVs, have no decisive link to pathology. The EEG literature warns against over-interpreting these signals on the EEGs of healthy patients. However, in ill patients with neurologic complications, PSWs may not be as benign.

Method
We present a case series of three patients for whom PSWs were associated with pathology: de novo non-convulsive status epilepticus (NCSE), left temporal lobe epilepsy secondary to glioma, and multiple small ischemic strokes due to septic emboli.

Results
Patient 1 presented with two generalized tonic-clonic seizures (GTCs) in 24 hours and bizarre behaviour. EEG demonstrated near-continuous generalized PSW complexes. NCSE was diagnosed after Phenytoin therapy normalized the EEG and completely resolved abnormal behaviour. Patient 2 presented with medically refractory left temporal lobe epilepsy secondary to a presumed low-grade glioma on magnetic resonance imaging, causing semiologically bizarre focal to bilateral tonic-clonic seizures. EEG demonstrated left temporal PSW as the first unequivocal ictal electrographic change. Patient 3 presented with multiple small ischemic strokes due to septic emboli secondary to MRSA-infective endocarditis. EEG demonstrated frequent bilateral parietal-sagittal PSW.

Conclusions
While PSWs are well recognized as BEVs in healthy patients, these cases indicate that neurologic disease may be associated with pathologic EEG signals that are morphologically similar or identical to PSWs, which we term the "spectre spike-wave". Caution should be taken in interpreting PSW-appearing waveforms of ill patients with neurologic disease.

Neuroimaging / EEG

Abstract 11

Imaging Blood-Brain Barrier Dysfunction in Epileptic Patients

Jonathan Ofer

Ben-Gurion University

Rationale
Blood-brain barrier disruption (BBBD) was shown to underlie epileptogenesis in multiple animal models and was suggested as a therapeutic target for prevention of epilepsy. However, its role during the chronic period of epilepsy is not clear yet, and it has been proposed that it may aggravate the disease. Therefore, clinically-applicable methods for quantifying BBBD are necessary for investigating new novel therapeutic approaches, as well as a diagnostic and pharmacodynamic biomarker of epilepsy.

Method
DCE-MRI was used for quantification of blood-brain barrier dysfunction (BBBD) in 17 patients with epilepsy and 50 healthy controls.
We generate two types of BBB permeability maps using two different post processing methods. The first method is the Tofts two compartment model. The second is the Veksler method which calculates a linear fit for each voxel on the later stages of the scan (6-17 min). Positive slopes reflect contrast agent accumulation due to BBBD.
Comparison of patients was done by counting pathological voxels. Pathological voxels are defined as permeability exceeding the 95th percentile of the corresponding cumulative distribution function (CDF) of healthy young controls.

Results
Quantification of the percentage of pathological brain voxels revealed significant differences in both Tofts ($P=0.013$) and Veksler ($P<0.01$) methods between epileptic patients and healthy controls.

Conclusions
By showing a significant difference in BBB permeability between epileptic patients and healthy controls we further strengthen the assumption that BBB permeability imaging may be used as a biomarker for epileptogenesis and pose it as a possible therapeutic approach.

Neuroimaging / EEG

Abstract 12

Cerebral Hemodynamics Improve Seizure Prediction in Multimodal Electroencephalographic Functional Near Infrared Spectroscopic Recordings

Parikshat Sirpal[1], Ali Kassab[2], DK Nguyen[2], Frederic Lesage[1]

[1]*École Polytechnique de Montréal, Université de Montréal*
[2]*Université de Montréal*

Rationale
In recent years, multi-modal approaches have emerged integrating functional near-infrared spectroscopy (fNIRS) with electroencephalography (EEG) to offer dual hemodynamic and electro-potential characterization of a seizure event. Herein, we employ deep learning methods to multimodal time series data to propose a novel means of seizure prediction.

Method
We designed a multilayered recurrent neural network (RNN) and used as input multi-modal data from 40 patients between the ages of 22–70 years of age suffering from recalcitrant bilateral temporal lobe epilepsy. For each recording, distinct pre-ictal and ictal states were partitioned. Initially, for validation purposes, standalone EEG data was used as input, followed by standalone NIRS data and finally multi-modal data.

Results
Extensive hyper-parameter optimization and data regularization techniques, help to show that multi-modal EEG-fNIRS data provide superior performance metrics in a seizure prediction task with low generalization error and loss, with sensitivity and specificity of 90%, 96% respectively. Either EEG or fNIRS alone led to lower sensitivity and specificity of 82% and 90% and 85% and 92% respectively. False prediction rates were generally low, with 11.84% and 5.61% corresponding to EEG and multimodal data respectively.

Conclusions
These results exemplify the enhanced prediction value of multi-modal neuroimaging, particularly fNIRS, in epileptic patients. Furthermore, the neural network models proposed and characterized herein offer a promising framework for future multi-modal EEG-fNIRS investigations in precocious seizure prediction. Furthermore, the value of multimodal recordings will help to confirm seizure prediction and focus localization capabilities of EEG-fNIRS in epileptic patients.

Neuroimaging / EEG

Abstract 13

T1/T2 Ratio MRI and Diffusion Imaging of Oligodendrocyte Hyperplasia and Focal Cortical Dysplasia in Children with Drug-Resistant Epilepsy

Jeremy Moreau[1], Roohi Vinaik[2], Elisabeth Simard-Tremblay[3], Bernard Rosenblatt[3], Christine Saint-Martin[3], Steffen Albrecht[3], Sylvain Baillet[4], Roy Dudley[3]

[1]Montreal Neurological Institute / Montreal Children's Hospital, McGill University
[2]McGill University
[3]Montreal Children's Hospital
[4]Montreal Neurological Institute

Rationale
Malformations of cortical development are the most frequent cause of drug-resistant childhood epilepsy, but newly characterised histopathological entities such as oligodendrocyte hyperplasia (OH) may explain some of the previously described negative pathology cases. The imaging characteristics of OH are however poorly characterised. Here we propose novel post-processing methods for enhancing visualisation of standard clinical MRI sequences.

Method
We obtained 3T T1, T2, and diffusion MRI pre- and post-operatively in 3 patients with OH, 3 patients with FCD, and 13 age-matched healthy controls. Surgical specimens were stained with OLIG2, an immunohistochemical marker of oligodendrocytes. Quantitative cell density measurements of OLIG2-positive cells were performed. MRI volumes were co-registered, normalised, segmented, and T1/T2 ratios computed. Mean T1/T2 ratio and apparent diffusion coefficient (ADC) values were extracted from lesion and surgical cavity masks.

Results
Patients with OH showed greater OLIG2-positive cell densities (3026±389 cells/mm2) than FCD patients (1010±217 cells/mm2) or literature-reported autopsy values (~950±200 cells/mm2). T1/T2 ratio imaging enhanced lesion contrast beyond what was visible in either T1 or T2 images independently and correlated with ADC values. Contrasts between individual patients and healthy controls helped highlight areas of abnormality. 3/3 FCD patients and 2/3 OH patients were seizure free at last follow-up.

Conclusions
T1/T2 ratio and ADC imaging are a useful addition to the presurgical evaluation, especially in cases of subtle poorly defined lesions. Quantification of normalised image intensities and contrasting against healthy controls can further help outline lesions. Our work demonstrates that post-processing of routine clinical MRI could improve diagnostic yields in patients with OH.

Neuroimaging / EEG

Abstract 14

Seizure Forecasting by Means of Bispectrum Analysis in Naturally Occurring Canine Epilepsy

Laura Gagliano[1], Elie Bou Assi[1], Dang K. Nguyen[2], Sandy Rihana[3], Mohamad Sawan[1]

[1]Polystim Neurotech Lab, Institute of Biomedical Engineering, Polytechnique Montreal
[2]University of Montreal Hospital Center (CHUM),Univeristy of Montreal
[3]Biomedical Engineering Department, Holy Spirit University of Kaslik (USEK), Jounieh, Lebanon

Rationale
Seizure forecasting would improve the quality of life of patients with refractory epilepsy. Seizure prediction relies on the adequate identification of seizure activity precursors from electroencephalography (EEG), however, no single feature is currently capable of characterizing brain dynamics prior to seizures. This work evaluates the suitability of the bispectrum, a measure of non-linear interactions based on the higher order spectra (HOS), for seizure prediction in canine epilepsy.

Method
Continuous intracranial EEG recordings, from 16 bilateral contacts, acquired in 3 dogs with naturally occurring epilepsy, were obtained from the international IEEG.org portal (https://www.ieeg.org/). Quantitative features were extracted from the bispectrum of 30-sec segments and 2 statistical tests assessed the existence of significant differences between preictal and interictal HOS features. Extracted features were used as input to train a 5-layer perceptron neural network classifier which aimed to classify preictal and interictal recordings.

Results
Analysis of variance tests (ANOVA) comparing interictal and preictal features displayed statistically significant differences between interictal and preictal bispectral features ($p < 0.01$) for all 3 dogs. A non-parametric seizure specific analysis (Mann Whitney test) showed that for each dog, there exists a significant preictal bispectral change in at least 3 contacts for 100% of seizures. Feature inputs to the multi-layer perceptron classifier, normalized and squared bispectral entropy, and mean magnitude achieved respective held-out test accuracies of 78.11%, 72.64%, and 73.26%.

Conclusions
This work demonstrates the existence of a preictal phase characterized by a statistically significant change in bispectrum which highlights the feasibility of seizure forecasting based on HOS features.

Authors acknowledge financial support from the Natural Sciences and Engineering Research Council of Canada (NSERC), and the Institute for Data Valorization (IVADO).

Neuroimaging / EEG

Abstract 15

Assessing the Added Value of Diffusion Kurtosis Imaging in Detecting Brain Microstructural Changes in Patients with Temporal Lobe Epilepsy

Loxlan Kasa, Ali R. Khan, Terry Peters, Seyed M. Mirsattari

University of Western Ontario

Rationale
A challenge during diagnostic process in temporal lobe epilepsy (TLE) is when patients exhibit no structural abnormalities in their MRI scans. Diffusion tensor imaging (DTI) have demonstrated the ability to detect abnormalities in diffusion measurements in areas proximal to epileptogenic temporal lobe but assumes free water diffusion in the brain microstructure. The aim of this work was to assess the added value of diffusion kurtosis imaging (DKI), an extension to DTI in identifying anomalies in the white-matter (WM) using supervised machine learning.

Method
All subjects underwent diffusion MRI scan on a 3 Tesla scanner. The data were pre-processed and registered to a WM atlas. Mean values from WM regions were extracted from respective DKI and DTI maps. We performed multi-class (control, left-TLE, and right-TLE) classification by training multiple binary classifiers, which were combined together using an error-correcting code approach. Features selected using support vector machine were used for training each of the binary classifiers, which were cross-validated and tested using leave-one-out cross validation strategy.

Results
The classifier trained with mean diffusivity plus mean kurtosis (MD+MK) scored higher overall accuracy of 87.1%. On the other hand, when the classifier was trained with mean diffusivity alone, the overall accuracy was 80.6%. MD+MK outperformed MD in identifying the right TLE patients, this could be due to subtle changes that MD alone was not able to detect.

Conclusions
Diffusion kurtosis imaging has potential to increase the ability of traditional DTI in accurately detecting brain microstructural changes in TLE patients and could improve the diagnosis of TLE.

This work was supported by CIHR Foundation, NSERC Discovery, the Canada First Research Excellence Fund, Brain Canada, and the Ontario Brain Institute Epilepsy Program (EpLink)

Neuroimaging / EEG

Abstract 16

Intraoperative Hyperspectral Imaging of Brain Hemodynamics During Epileptiform Activity

Audrey Laurence[1], Leticia Angulo-Rodriguez[1], Alain Bouthillier[2], Dang K. Nguyen[2], Frederic Leblond[1]

[1]*Polytechnique Montreal*
[2]*Centre hospitalier de l'Université de Montréal*

Rationale
Resective brain surgery is usually considered in patients with refractory epilepsy associated with a localized epileptogenic zone. Despite available imaging techniques used in pre-operative planning (MRI, PET, SPECT, EEG), full extent of lesions and epileptogenic zone are in some cases ill-defined. Those cases are usually associated with low seizure-free rates because lesions cannot be fully detected neither visually nor using state-of-the-art imaging technologies. Attaining complete resection of the epileptic focus while minimizing the impact on brain function (cognitive, motor) is then challenging.

Method
An optical imaging technique using a hyperspectral camera is used to detect temporal changes associated with oxygenated hemoglobin (HbO) and deoxygenated hemoglobin (HbR) concentration variations. The intraoperative imaging system integrates a 16-band snapshot hyperspectral camera in the visible range (from 475 to 650 nm), directly connected to a neurosurgical microscope, reconstructing the hemodynamic response at 20 frames per second. Electrocorticography (ECoG) recordings are performed simultaneously.

Results
We achieve reconstruction of real-time videos showing the hemodynamic response to epileptic spikes acquired in 13 patients undergoing epilepsy surgery. Average hemodynamic response to interictal discharges shows an increase in HbO concentration after the events, with maximum occurring 3-4 seconds after discharges. Localization of changes correlates with the position of the epileptic focus as identified by ECoG.

Conclusions
We show that the low-frequency hemodynamic response to interictal discharges detected with our hyperspectral imaging system correlates with the position of the epileptic focus. The system shows great potential for mapping epileptic activity during surgery and possibly improving resection accuracy.

Clinical Epilepsy / Antiepileptics

Abstract 17

Integrated Commercial-Academic Partnership Approach for Delivery of Hereditary Epilepsy NGS Panel to High-Throughput Clinical Diagnostic Genetic Services

Jaime Jessen[1], Jennifer Kerkhof[2], Alan Stuart[2], Hilary Racher[1], Franny Jewett[1], Bekim Sadikovic[3]

[1]Dynacare, Bowmanville
[2]Molecular Genetics Laboratory, London Health Sciences London
[3]Department of Pathology and Laboratory Medicine, Western University Molecular Genetics Laboratory, London Health Sciences London

Rationale
Genetic healthcare depends upon accessible, cost effective and high quality genetic testing. Large-scale commercial laboratories enable access and throughput for effective service delivery. Academic medical centers are well positioned to enable specific test development which often requires combined clinical, technological and research expertise. Industry-academic partnerships can optimize diagnostic genetics services by integrating commercial with specialized clinical and research expertise.

Method
London Health Sciences Center (LHSC) Molecular Genetics Laboratory is a Canadian referral genetic laboratory. As part of a collaborative effort involving clinical, scientific and laboratory expertise custom NGS gene panel-based technology was developed that enables simultaneous sequencing and copy number assessment that outperforms the classic gold standard of Sanger sequencing and MLPA. As the provincial clinical center of excellence for neurology genetics, LHSC applied this technology to develop NGS-based gene panels for epilepsy, Charcot-Marie-Tooth and mitochondrial genome sequencing. Using 1,000's of clinical specimens tested in the LHSC clinical laboratory, we demonstrate sensitivity and specificity that is superior to Sanger sequencing and MLPA testing combined, as part of a cost-effective clinical pipeline.

Results
LabCorp and Dynacare (owned by LabCorp), two of the largest laboratories in the USA and Canada respectively, commercialize these tests providing market access, billing and insurance support and high throughput and quality clinical testing. Analytics, informatics and clinical reporting are provided by LHSC's experts. LabCorp's tele-genetic counsellors are available to support non-genetics ordering physicians with comprehensive pre- and post-test genetic counselling.

Conclusions
This industry-academic partnership demonstrates effective, scalable, and industry-leading quality for delivery of genetic testing services.

Clinical Epilepsy / Antiepileptics

Abstract 18

Prevalence of Marijuana Use Among Epilepsy Monitoring Unit Patients and its Effect on Their Quality of Life

Ahmad Attar[1], Youssef Althobaiti[1], Nirmeen Zagzoog[1], Ginette Moores[1], Brindan Sivanandan[2], Luis Morillo[1]

[1]McMaster University, Hamilton Health Sciences Centers
[2]McMaster University

Rationale
Background: Despite recent medical advances, many people with epilepsy continue to suffer from seizures. Furthermore, anti-epileptic medications often come with unpleasant side effects. This has led many patients and families to seek alternative treatment options. The use of marijuana among epilepsy patients has increased over the past several years, especially in patients with medically-refractory seizures who require an admission to an epilepsy monitoring unit. Accordingly, multiple studies have shown increased prevalence of marijuana use among those patients in comparison to patients with mild and well-controlled epilepsy in outpatient clinics. Nevertheless, marijuana itself could have negative consequences on a patient's daily activities, quality of life, and intellectual functions, which subsequently might worsen their pre-existing neuropsychological morbidity.

Objectives: This study will estimate the proportion of individuals using marijuana among patients who have been admitted to our centre epilepsy monitoring unit. In addition, it will evaluate the impact of marijuana on their overall health, quality of life, and intellectual and motor capabilities. Patients' awareness regarding the efficacy and the potential medical and psychological consequences of marijuana use will also be investigated.

Method
Methods: We plan to estimate the prevalence of marijuana use among patients who have been admitted to our regional epilepsy monitoring unit at Hamilton Health Sciences Centre-Hamilton general hospital from January 2014 to June 2018. Data will be collected through a research questionnaire and a brief marijuana consequences questionnaire (B-MACQ), which will be sent through Canada Post Xpresspost in secured prepaid envelopes along with the consent forms. Subsequently, data extraction and statistical analysis will be performed using Microsoft Excel and Stata software. This research is funded by a fellow grant through the postgraduate studies at McMaster University.

Results
Results: The study is ongoing and we will be collecting data until June of this year, with analysis to follow.

Conclusions
Currently, with the information obtained to date, we estimate that the percentage of marijuana users is higher among epilepsy patients who required an admission to epilepsy monitoring unit in comparison to epilepsy patients in the outpatient clinics, based on data from another recent study at the same medical center. This study documented that 30.6% of epilepsy outpatients either currently use or have used marijuana previously.1

Clinical Epilepsy / Antiepileptics

Abstract 19

Assessment of the Long-Term Efficacy and Safety of Adjunctive Perampanel in Adolescent Patients: Post-Hoc Analysis of Open-Label Extension (OLEx) Studies

J Eric Piña-Garza[1], Vicente Villanueva[2], William Rosenfeld[3], Harumi Yoshinaga[4], Francesco Bibbiani[5], Anna Patten[6], Betsy Williams[7], Antonio Laurenza[5]

[1]*The Children's Hospital at TriStar Centennial, Nashville*
[2]*Hospital Universitario y Politécnico La Fe*
[3]*Comprehensive Epilepsy Care Center for Children and Adults*
[4]*National Hospital Organization, Minami-Okayama Medical Center*
[5]*Formerly: Eisai Inc.*
[6]*Eisai Ltd.*
[7]*Eisai Inc.*

Rationale
Perampanel is a once-daily oral antiepileptic drug for partial-onset seizures and primary generalized tonic-clonic seizures (PGTCS). Patients completing Phase II/III randomized, double-blind, placebo-controlled adjunctive perampanel studies could enter OLEx studies: 307 (NCT00735397), 335 OLEx (NCT01618695), 235 OLEx (NCT01161524), and 332 OLEx (NCT02307578). Here, we report long-term efficacy and safety outcomes of adjunctive perampanel in adolescent patients (aged ≥12–≤17 years) with secondarily generalized seizures (SGS) or PGTCS from these OLEx studies.

Method
All OLEx studies comprised a blinded Conversion Period (6–16 weeks) and a Maintenance Phase (27–256 weeks; perampanel ≤12 mg/day). Efficacy and safety assessments (for ≤4 years) included median percent change in seizure frequency/28 days, 50% and 75% responder and seizure-free status rates, and monitoring of treatment-emergent adverse events (TEAEs).

Results
The Safety Analysis Set included 129 adolescent patients (SGS, n=110; PGTCS, n=19). Median percent reductions in seizure frequency/28 days were 62.8% and 84.0% (Year 1), and 71.8% and 97.4% (Year 3) for SGS and PGTCS, respectively. 50% and 75% responder and seizure-free status rates were: 56.9%, 39.5%, and 22.9% (Year 1), and 66.7%, 44.4%, and 30.6% (Year 3) for SGS; and 63.2%, 52.6%, and 21.1% (Year 1), and 83.3%, 83.3%, and 50.0% (Year 3) for PGTCS. For each seizure type, TEAE incidence was highest during Year 1; the most common TEAE was dizziness.

Conclusions
: Long-term (≤4 years) adjunctive perampanel (≤12 mg/day) was efficacious and well tolerated in adolescent patients with SGS or PGTCS. These results are encouraging, given the refractory nature of these seizure types.

Funding: Eisai Inc.

Clinical Epilepsy / Antiepileptics

Abstract 20

Retrospective, Phase IV Study of Perampanel in Real-World Clinical Care of Patients With Epilepsy: An Interim Analysis

Robert Wechsler[1], James Wheless[2], Katherine Moretz[3], Betsy Williams[4], Antonio Laurenza[5], Anna Patten[6], Manoj Malhotra[4]

[1]*Idaho Comprehensive Epilepsy Center*
[2]*University of Tennessee, Le Bonheur Children's Hospital*
[3]*Meridian Clinical Research LLC*
[4]*Eisai Inc.*
[5]*Formerly: Eisai Inc.*
[6]*Eisai Ltd.*

Rationale
There is limited information regarding real-world use of perampanel, a once-daily oral antiepileptic drug (AED) for partial-onset seizures and primary generalized tonic-clonic seizures. Study 506 is being conducted to assess retention rate, dosing experience, and safety with perampanel administered to epilepsy patients during routine clinical care.

Method
Study 506 (NCT03208660) is an ongoing, Phase IV, retrospective, non-interventional study of epilepsy patients initiating perampanel after January 1, 2014. Medical record data included: AED history; seizure frequency; perampanel titration/dosage; treatment-emergent adverse events (TEAEs). Based on the Safety Analysis Set (SAS), primary and secondary endpoints included retention rate (proportion of patients remaining on perampanel at 3, 6, 12, 18, and 24 months), dosing experience, and safety.

Results
The SAS included 187 patients (mean age: 26.7 years; female: 51.3%; mean time since diagnosis: 17.5 years; ILAE seizure classification: partial, 49.2%; idiopathic generalized epilepsy, 23.0%). At Baseline, the majority of patients received 1–3 concomitant AEDs (82.4%; enzyme-inducing AEDs 17.1%). The mean (range) maximum perampanel dose was 7.1 (1.5–20.0) mg, and mean cumulative duration of exposure to perampanel was 15.4 months. Retention rate ranged from 84.9% (3 months) to 58.5% (24 months). 75 (40.1%) patients discontinued treatment (primary reasons for study discontinuation: AEs 25.1%; inadequate therapeutic effect 10.2%; other reasons 3.2%; unknown reasons 1.1%; patient choice 0.5%). Dizziness (9.1%) was the most commonly reported TEAE.

Conclusions
An interim analysis of Study 506 found that over half of epilepsy patients (58.5%) receiving perampanel as part of routine clinical care remained on treatment at 24 months.

Funding: Eisai Inc.

Clinical Epilepsy / Antiepileptics

Abstract 21

Clinical Factors Associated with a Major Response (≥75% Reduction in Seizure Frequency/28 Days) in Phase III Trials of Adjunctive Perampanel in Patients with Partial Seizures: Post-Hoc Multivariate Analysis

Elinor Ben-Menachem[1], Gregory Krauss[2], Robert Wechsler[3], Anna Patten[4], Betsy Williams[5], Antonio Laurenza[6]

[1]*Sahlgrenska Academy, University of Gothenburg*
[2]*Johns Hopkins Hospital*
[3]*Idaho Comprehensive Epilepsy Center*
[4]*Eisai Ltd.*
[5]*Eisai Inc.*
[6]*Formerly: Eisai Inc.*

Rationale
Perampanel is a once-daily oral antiepileptic drug for partial-onset seizures (POS) and primary generalized tonic-clonic seizures. Approval for POS was based on three randomized, double-blind, placebo-controlled, phase III studies of adjunctive perampanel (Studies 304 [NCT00699972], 305 [NCT00699582], and 306 [NCT00700310]). A post-hoc multivariate analysis was performed to identify predictive factors for achieving a major response (≥75% reduction in seizure frequency/28 days) with adjunctive perampanel during these studies.

Method
Patients (aged ≥12 years) with refractory POS, with/without secondarily generalized seizures (SGS), received placebo or adjunctive perampanel 2–12 mg/day across a 19-week, double-blind phase. Univariate analysis (logistic regression) identified factors associated with a major response during maintenance. Significant predictors were subsequently included in a multivariate model.

Results
Across studies, 175/1374 (12.7%) patients had a major response to perampanel (mean age, 35.5 years; 50.3% female). At the univariate level, significant predictors of a major response were: decreasing number of baseline antiepileptic drugs (AEDs), absence of baseline enzyme-inducing AEDs, absence of structural etiology, presence of SGS at baseline, increasing age at diagnosis, decreasing time since diagnosis, and increasing perampanel plasma concentration. Baseline seizure frequency, simple/complex POS at baseline, and genetic/idiopathic etiology were not significantly associated with a major response. The best predictors of a major response in the multivariate model were presence of SGS at baseline, increasing age at diagnosis, and perampanel plasma concentration.

Conclusions
These findings may help guide clinicians when prescribing perampanel for patients with POS. Perampanel was particularly effective in controlling SGS, one of the most serious seizure types.

Funding: Eisai Inc.

Clinical Epilepsy / Antiepileptics

Abstract 22

The Risk of New-Onset Epilepsy and Pharmacologically Refractory Epilepsy in Older Adult Stroke Survivors

Jorge Burneo[1], Tresah Antaya[1], Britney Allen[2], Andrea Belisle[2], Salimah Shariff[2], Gustavo Saposnik[3]

[1]*Western University*
[2]*Institute for Clinical Evaluative Sciences Western*
[3]*University of Toronto*

Rationale
Despite stroke being a common cause of new-onset epilepsy in older adults, stroke-related epilepsy has rarely been studied in this population.

Method
We conducted a population-based, retrospective cohort study using linked, administrative healthcare databases. The Ontario Stroke Registry was used to identify patients 67 years and older who were hospitalized for a stroke at a designated stroke centre in Ontario, Canada between April 1, 2003 and March 31, 2009. Multivariable Fine-Gray hazard models were used to examine risk factors of new-onset epilepsy and refractory epilepsy, accounting for the competing risk of death. Five-year mortality and the receipt of diagnostic care were evaluated for those who developed epilepsy.

Results
Among 19,138 older adults hospitalized for a stroke, 210 (1·1%) developed epilepsy and 27 (12·9%) became refractory to antiepileptic drugs. Within one year of epilepsy diagnosis, 24 (11·4%) patients were assessed with EEG and 19 (9·0%) with MRI. In multivariable analysis, younger age and female sex were significant risk factors of both epilepsy and refractory epilepsy. The effects of not receiving anticoagulant medication in hospital and having a less severe stroke decreased over time after initially increasing epilepsy risk. Five-year all-cause mortality following epilepsy diagnosis was 46·2% (n=97).

Conclusions
Older adults and male stroke survivors are less likely to develop epilepsy and refractory epilepsy. Most deaths were attributed to causes other than stroke or epilepsy.

Funding: Ontario's Ministry of Health and Long-Term Care, the Academic Medical Association of Southwestern Ontario, Western University's Schulich School of Medicine and Dentistry, Lawson Health Research Institute, and CIHR.

Clinical Epilepsy / Antiepileptics

Abstract 23

The Rhyme and Rhythm of Music in Epilepsy

Marjan Rafiee[1], Edwardo Bercovici[2], Dorsa Zabihipour[1], Esther Bui[2], Peter Tai[2], Richard Wennberg[2], Peter Carlen[2], Taufik Valiante[1]

[1]*Krembil Research Institute*
[2]*Division of Neurology, Department of Medicine, University of Toronto*

Rationale
Epilepsy is the most common serious neurological condition in the world. Approximately 20% of individuals continue to have seizures despite medical and surgical treatments, suggesting alternate management strategies are required. In this study, we explore the potential therapeutic benefits of listening to Mozart K.448, which has demonstrated promise over the last 20 years.

Method
Using a randomised controlled crossover design, individuals with medically refractory epilepsy were randomly assigned to either start the intervention listening to Mozart K.448, or the control piece in 3 months intervals over a 1 year study period. Seizure diary entries were obtained from study participants, in addition to electroencephalographic (EEG) recordings at the start and end of each interval.

Results
Our preliminary results (N = 12) demonstrate a reduction in seizure frequency during the 3 months of listening to Mozart (-46 ± 12 %) compared to their baseline period, while there was an increase of 20 ± 1% for the control piece. The EEG recordings obtained during the intervention will used to explore the spectral features associated with changes in seizure frequency during the intervention time.

Conclusions
Our preliminary results demonstrate the promising effects of listening to Mozart K.448 on reducing seizure frequency. Our study contrasts with previous reports that were limited by a "no music" control condition. By using a spectrally similar control we may be able to investigate how the temporal organization of Mozart K.448 piece is associated with a reduction in seizure frequency.

This study is funded by Epilepsy Ontario.

Clinical Epilepsy / Antiepileptics

Abstract 24

Genetic Characterization and Prognosis of Adult Patients with Lennox-Gastaut Syndrome: A Prospective Case-Series Study

Robert De Santis[1], Tara Sadoway[2], Danielle Andrade[2]

[1]Schulich School of Medicine and Dentistry, Western University & Genetic Epilepsy Program, Toronto Western Hospital, UHN
[2]Genetic Epilepsy Program, Toronto Western Hospital, UHN

Rationale
Lennox-Gastaut Syndrome (LGS) is an epileptic encephalopathy that typically presents in childhood. It is characterized by intractable seizures, including atonic or tonic seizures, intellectual disability, and interictal slow spike-and-wave complexes. Patients living with LGS are often treatment resistant and comorbid with behavioural problems, making management complex. Although LGS is sometimes thought to be symptomatic to brain injury, a genetic predisposition has been proposed, but more literature is needed to establish a relationship. This study aims to analyze LGS patients for potential contributing gene mutations to the LGS phenotype and assess if they have any correlation with prognosis into adulthood.

Method
A chart review (2006-2017) was conducted to identify adult LGS patients who had either undergone or were candidates for genetic testing. Data on seizure, developmental, and intervention history was collected. Prospectively, patients and their caregivers were administered the Vineland-3 questionnaire, to evaluate the study subjects' adaptive behaviour.

Results
Genetic information was gathered from 25 adult LGS patients. Mean follow-up was 28 years (range 16-56 years) with the mean age at follow-up being 30 years old (range 19-59 years). Mean seizure frequency at follow-up was 32 seizures/month, with only 2 patients seizure free. Clinical genetic tests yielded 5 patients with a pathogenic mutation, and 10 with variants of uncertain significance. Vineland-3 questionnaires showed similarity between participants' abilities.

Conclusions
LGS is a complex epileptic syndrome with a poor prognosis. More research is needed to characterize long-term outcomes in adult patients and its association with potential genetic mutations.

No funding source to disclose.

Clinical Epilepsy / Antiepileptics

Abstract 25

Hallucinations in Kabuki Syndrome

Ran Liu[1], Elizabeth Grier[2], Lysa Boisse Lomax[3]

[1]Department of Medicine, Division of Neurology, Kingston Health Sciences Centre, Queen's University
[2]Department of Family Medicine, Kingston Health Sciences Centre, Queen's University
[3]Department of Medicine, Division of Neurology and Respirology, Kingston Health Sciences Centre, Queen's University

Rationale
KABUKI syndrome is caused by mutation in KMT2D (type 1) or KDM6A (type 2). The major clinical features include characteristic facial features, visceral malformations, short stature, abnormal dermatoglyphic patterns and intellectual disability. Although it is associated with numerous neurological complications including epilepsy, hallucinations have not been reported. Here, we report a case of psychosis with hallucinations in a patient with Kabuki syndrome and frontal lobe seizures.

Method
A 21 year old female with clinical features of Kabuki syndrome was positive for KMT2D mutation. At 17 years old, she began experiencing auditory hallucinations characterized by voices. She progressed to also experiencing vivid visual hallucinations, such as seeing frightening people. At 19 years old, she started experiencing frontal lobe seizures, characterized by stiffening of the right arm and leg, which within 2 months evolved into generalized tonic-clonic seizures. Hypermotor seizures with left frontal lobe focal onset were confirmed by intensive video EEG monitoring. No epileptiform abnormalities were captured on EEG during the patient's hallucinations.

Results
Risperidone, quetiapine and divalproex provided a limited effect on hallucinations. When topiramate was added, her hallucinations resolved although seizures persisted. Her seizures were eventually controlled with brivaracetam, topiramate, eslicarbazepine, and the Modified Atkins Diet (2:1 ratio). The patient was initiated on the ketogenic diet at a 4:1 ratio, but required a 2:1 ratio to maintain seizure control.

Conclusions
This case highlights the potential psychiatric complications of Kabuki syndrome that occurred independently of epilepsy. This is also the first case of seizures in Kabuki syndrome treated with the Modified Atkins Diet.

Clinical Epilepsy / Antiepileptics

Abstract 26

Retention Rate and Efficacy of Perampanel (PER) With a Slow Titration Schedule in an Adult Epilepsy Outpatient Clinic

Mazen Basheikh[1], R. Mark Sadler[2]

[1]*University of Jeddah*
[2]*Nova Scotia Health Authority, Central Zone*

Rationale
The manufacturer of PER suggests an initial adult dose of 2-4 mg/day and an upward dose titration of 2 mg at no more frequently than 1 or 2 week intervals when used with enzyme enhancing antiepileptic drugs (AEDs) or non-enzyme enhancing AEDs, respectively (Canadian product monograph). The general practice in our clinic is an initial dose of PER 2mg/day and titrated by 2 mg/month to an initial target of 6 mg/day.

Method
Retrospective chart audit of patients starting PER in adult epilepsy clinic between September 2013 – November 2016 with at least one 6 month followup visit. Data collection included patient demographics, seizure characteristics, remote and concurrent therapy, monthly seizure frequency before PER and at 6 months, and characteristics of PER discontinuation.

Results
N = 102 patients, mean age = 40 years and 54% females. Focal onset seizures 85 %, generalized 13%, and unknown 2%. Median prior AED exposure = 8 (range 3-20); median concomitant AED use = 2 (range 1-5). Followup range was 6-37 months. The median seizure frequency/month pre-PER treatment was 6 (range 0-30) for focal onset seizures and 1 (range 0-6) for generalized seizures. The retention rate amongst all patients at 6 months was 78.4 %. At 6 months followup 36 % of all patients achieved Engel class I (seizure freedom) (30.7 % of patients with focal onset and 63.6 % with generalized seizures).

Conclusions
Perampanel has a good retention rate when titrated slowly and encouraging seizure freedom results in an otherwise medically refractory epilepsy population.

Clinical Epilepsy / Antiepileptics

Abstract 27

Transient Epileptic Amnesia: A Variant of Temporal Lobe Epilepsy

Ana Suller Marti, Seyed Mirsattari, Jorge Burneo, Richard McLachlan

London Health Science Centre

Rationale
Transient epileptic amnesia (TEA) is a manifestation of temporal lobe epilepsy (TLE). TEA is characterized by episodes of transient amnesia with the other cognitive functions intact. Interictally, patients complain of prominent memory difficulties, but demonstrate normality in standard tests of memory. Generally TEA has a benign course and is of late onset. We suspect that this entity is underestimated, probably misdiagnosed.

Method
We reviewed the database of the Epilepsy Program at Western University between December 2016 and March 2018, to identify cases of TEA.

Results
A total of 5 cases presented with amnesic episodes. The mean age was 75.2(70-92), four were male. The age at onset of seizures was 71.4 (61-88). The most common symptom was memory loss and the duration of the seizures was on average 111 min (40-240). The most common antiseizure medication used was levetiracetam (1000-2000 mg per day). All cases shared a history of cardiovascular disease. MoCA test was performed in 3 patients and showed an average score of 25 points (22-27). All patients complained of memory loss, 3 patients complained of long term and 2 patients complained of short term memory loss. 4 patients had neuropsychology evaluation. 3 had risk factors for seizures, but none had family history of seizures or previous epilepsy history. Interictally spikes were seen in both temporal regions (60% (N=3) right temporal and 40% (N=2) left temporal). A typical seizure was captured in one patient arising from the left Temporal,lobe but no video was available.

Conclusions
In our series, TEA presented with fewer seizures, late onset, frequent cardiovascular risk factors and normal cognition despite subjective memory complaints.

Clinical Epilepsy / Antiepileptics

Abstract 28

Valproic Acid for Women With Epilepsy: A Case Study

Melanie Jeffrey

University of Toronto

Rationale
In catamenial epilepsy seizure propensity is exacerbated by changes in ratio between estradiol (E2) to progesterone (P4) during the menstrual cycle. Modulations of excitatory and inhibitory ion channels occur as the ratios change. This case study explores the efficacy of valproic acid an adult woman with medically-refractory epilepsy.

Method
A high functioning left-handed 40 year-old female has had medically refractory, adult-onset catamenial epilepsy with partial and generalized seizures (maternal inheritance) for over 20 years. Many drug regimens were unsuccessful. Phenytoin, a broad spectrum sodium channel inhibitor, was an effective anticonvulsant drug for this patient, however, it caused a pro-arrhythmic effect and was discontinued. In addition, her seizure focus was in the eloquent frontal cortex, preventing surgical resection.
Hormonal fluctuations due to early perimenopause could contribute to the patient's worsening seizure control. A bilateral salpingo-oophorectomy was performed, with micronized progesterone and topical estradiol as hormone replacement therapy.
Genetic testing indicated that she had SCN3A and PDHA1 X-linked mutations. A ketogenic diet was initiated.

Results
The ketogenic diet was unsuccessful, suggesting the PDHA1 mutation did not affect seizure control. A low-glycemic index diet was initiated to limit the potential for energy crises in the brain.
Valproic acid, which binds specifically to SCN3A (Nav1.3) has greatly improved seizure control in this patient without the arrhythmic side effects of phenytoin. This suggests that the SNC3A mutation significantly contributes to her seizure propensity.

Conclusions
As genetic testing becomes more accessible, specific channelopathies can be targeted, such as SCN3A, which is treatable with valproic acid. Hormone replacement therapy after a bilateral salpingo-oophorectomy can stabilize hormone levels, decreasing catamenial/perimenstrual seizure exacerbation, and increasing quality of life.

Paediatric Epilepsy

Abstract 29

Trajectories of Depressive Symptoms Among Mothers of Children with Newly Diagnosed Epilepsy: A Longitudinal 10-year study

Klajdi Puka[1], Mark Ferro[2], Kelly Anderson[2], Kathy Speechley[2]

[1]*Western University*
[2]*University of Waterloo*

Rationale
Up to 50% of mothers of children with epilepsy (CWE) have depression, although past studies have been cross-sectional and none has evaluated long-term outcomes. Importantly, parental depression significantly impacts children's health and well-being. This study prospectively followed families with newly-diagnosed CWE over 10-years to identify distinct trajectories of maternal depressive symptoms and associated prognostic factors.

Method
Data came from the Health-Related Quality of Life in Children with Epilepsy Study (HERQULES), a prospective cohort study of children with newly diagnosed epilepsy. Maternal depressive symptoms were measured at diagnosis, and 0.5, 1, 2, 8, and 10 years later using the Center for Epidemiological Studies Depression Scale (CES-D). Scores ≥16 indicate risk for major depressive disorder. Trajectories of depressive symptoms were evaluated using latent class growth modeling, and prognostic factors were evaluated using multinomial logistic regression.

Results
A total of 356 mothers were included. Four unique trajectories were identified: 37% were 'Low-Stable' (scores of ~6 at each time), 39% 'Borderline-Stable' (scores of ~12 at each time point), 20% 'High-Stable' (scores of ~23 at each time point), and 5% 'High-Decreasing' (scores of ~38 at diagnosis and ~5 at last follow-up). Older maternal age ($p=.003$), better family functioning ($p=.012$), and greater family resources ($p<.0001$) at baseline were associated with better depressive symptom trajectories; epilepsy-related variables were not statistically significant predictors.

Conclusions
Mothers were not a homogeneous group and showed distinct trajectories of depressive symptoms over time. Depressive symptoms were pervasive, persistent over time, and may be amenable to interventions targeting family environment. Funding: CIHR.

Paediatric Epilepsy

Abstract 30

Long-Term Quality of Life (QOL) Trajectories Among Individuals Diagnosed with Epilepsy in Childhood

Klajdi Puka[1], Mark Ferro[2], Carol Camfield[3], Simon Levin[1], Mary Lou Smith[4], Samuel Wiebe[5], Guangyong Zou[1], Kathy Speechley[1]

[1]*Western University*
[2]*University of Waterloo*
[3]*Dalhousie University*
[4]*University of Toronto*
[5]*University of Calgary*

Rationale
Past studies evaluating long-term QOL in children with epilepsy have been cross-sectional, and unable to assess QOL changes since diagnosis. This study prospectively followed children with newly-diagnosed epilepsy over 10 years to identify distinct trajectories of QOL and associated prognostic factors.

Method
Data came from the Health-Related Quality of Life in Children with Epilepsy Study (HERQULES), a prospective cohort study of children (aged 4-12 years) with newly-diagnosed epilepsy. Parents reported on children's QOL using the QOLCE-55 at diagnosis, and 0.5, 1, 2, and 8-years later. Youth self-reported on QOL 10-years after diagnosis using QOLIE-AD-48 or QOLIE-31. Latent class growth models were used to identify trajectories of parent-reported QOL and estimate youth's self-reported QOL associated with each trajectory. Multinomial logistic regression was used to identify factors associated with each trajectory.

Results
367 families were included. Five unique trajectories of QOL were identified: 11% 'Low-Stable' (scores of 48), 19% 'Low-Increasing' (scores 62–73), 14% 'Intermediate-Decreasing' (scores 73–57), 43% 'Intermediate-Increasing' (scores 78–86), 14% 'High-Increasing' (scores 87–90). For each trajectory group, youths' self-reported QOL at the 10-year follow-up are discussed. Absence of cognitive problems (p=.001) and fewer family stressors/demands (p=.007) at time of diagnosis were associated with better QOL trajectories (higher scores).

Conclusions
Children with epilepsy are not a homogeneous group and showed distinct trajectories of QOL over the long-term. Interventions that address epilepsy-related comorbidities and support families to reduce stress early may help individuals diagnosed with epilepsy in childhood achieve more favourable QOL into young adulthood.
Funding: CIHR.

Paediatric Epilepsy

Abstract 31

"Programme Épilepsie Passage "(PEP): Development and Evaluation of a Nursing Innovation to Facilitate the Transition of Young People with Epilepsy from Pediatric to Adult Care

Dominic Chartrand[1], Vanessa Léger[2], Anne Lortie[1], Patrick Cossette[2], Keezer Mark[2], Johanne Déry[3], Beaudet Line[2]

[1]CHU Sainte-Justine
[2]Centre Hospitalié de l'Université de Montréal (CHUM)
[3]Université de Montréal

Rationale
The transition from pediatric to adult epilepsy care is challenging. Educational programs coordinated by nurses are seldom evaluated. We developed a joint psycho-educational program to influence the behaviour of young people and their caregivers. Our aims are to: 1) improve young people's and caregivers' knowledge of epilepsy; 2) promote among young people the development of self-care and management of their epilepsy; 3) optimize and standardize the exchange of information between the pediatric and adult care setting, as well as the preparation of these young people and their caregivers for the transition period.

Method
This will be a prospective study (pre-posts tests X4) with mixed methodologies selected to examine the program implementation and benefits. Sample: 200 young people with epilepsy aged 14-19 years and their caregiver(s). Settings: CHUSJ / CHUM Neurology Clinics, and community network partners. Instruments: sociodemographic questionnaire, Epilepsy Knowledge Scale (May and Pfäfflin, 2002), Epilepsy Self-Management Scale (Dilorio, 2010), and "Transition Responsibility to Adult Care" questionnaires (BC Children's Hospital, 2017). Analysis: paired t-test and McNemar's test to measure the impact of the PEP program on the described instruments. Thematic content analysis of semi-structured interviews: 20 young people / 20 caregivers + 8 health professionals from the adult care setting.

Results
We have completed the refinement of PEP program and are beginning the recruitment of participants. We will present the details of the PEP program, our study protocol, and available preliminary results.

Conclusions
Understanding which factors are critical will facilitate care planning and a successful transition experience.

Paediatric Epilepsy

Abstract 32

Intellectual Functioning in Children with CSWS

Taryn Fay-McClymont[1], William MacAllister[2], Brian Broons[2], Kim Deschamps[1], K. Morris Scantlebury[3], J.P. Appendino[1], Luis Bello-Espinosa[1]

[1]*Alberta Children's Hospital*
[2]*Alberta Children's Hospital University of Calgary*
[3]*University of Calgary*

Rationale
Children with CSWS (Continuous Spikes and Waves during Slow wave sleep) are known to have substantial cognitive impairments. The purpose of the current investigation is to assess intellectual functioning in a sample of clinically referred children with CSWS.

Method
25 children (aged 2.4-13.8 years at the time of the assessment) received an intellectual functioning assessment as part of a comprehensive neuropsychological assessment at a tertiary care center. A subset (N=12) of children were followed longitudinally.

Results
The mean full scale intellectual quotient (FSIQ) of the total sample was 78.96 (19.34). 32% of children had FSIQ in the "very low" range (FSIQ=70-79) whereas 20% of the sample had FSIQ in the range associated with intellectual disability (FSIQ <70) at the time of the assessment. FSIQ was not related to age at assessment or gender, but children with MRI abnormalities (48% of the sample) showed more significant cognitive impairment (FSIQ=73 vs. 84; Cohen's d=0.58; moderate effect size). Twelve children were followed longitudinally, with four children (33%) showing significant decline over time as defined by a one standard deviation (15 points) or greater decline in FSIQ. Of those showing decline, three children (75%) had abnormal MRI.

Conclusions
Assessment of intellectual functioning is critical in the care of children with CSWS. These children should be monitored carefully over time, particularly when abnormalities are seen on neuroimaging.

Paediatric Epilepsy

Abstract 33

Have You Seen This Person Before? Face Recognition in Children With Epilepsy Undergoing Temporal Lobe Resections

Mary Lou Smith

University of Toronto and the Hospital for Sick Children

Rationale
Research on face memory in children undergoing temporal lobe surgery has yielded conflicting results on whether lateralized effects are evident and whether there are changes after surgery, possibly due to small samples, grouping of left and right-sided cases, and the inclusion of extra-temporal cases within some of the temporal lobe samples. Here, with a larger sample than previously investigated, we explored change over time, laterality of excision, and whether excision of mesial temporal structures had an effect on face memory.

Method
Participants were 68 children and adolescents (IQs ≥ 70) who underwent temporal lobe surgery, subdivided into those with sparing of the mesial structures (lateral group; n=29, 20 left), and those whose temporal lobectomy included resection of mesial structures (n=39, 19 left). Participants completed standardized tests of face memory before and 1 year following surgery.

Results
Before surgery, all groups obtained mean scores within the average range on immediate recognition of faces. A Time x Resection Type x Laterality ANOVA yielded no significant effects. For delayed recognition, the right lateral group has a somewhat (albeit not statistically significant) lower score at baseline (within the low average range) compared with the other groups, but again, the analysis did not yield any significant effects.

Conclusions
Face recognition tests do not appear to be sensitive to laterality of temporal lobe lesion or to resection of mesial temporal lobe structures. Scores did not change significantly after surgery, suggesting a good outcome with respect to this aspect of visual memory.

Paediatric Epilepsy

Abstract 34

Cognitive Outcome in Children With Epileptic Spasms Using a Standardized Treatment Protocol: A Five-Year Longitudinal, Multicenter Study

Jonathan Y Bitton[1], Béatrice Desnous[1], Lionel Carmant[1], 10 other members of the Canadian Pediatric Epilepsy Network[2]

[1]Research Centre of Sainte-Justine Hospital, Montreal
[2]Pediatric hospitals in Halifax, Ottawa, Hamilton, Toronto, Calgary and Vancouver

Rationale
The aim of this study was to improve cognitive outcome in children with epileptic spasms (ES).

Method
During the first two years, we evaluated the effect of the calcium blocker L-flunarizine as adjunctive therapy to our standard protocol, followed by an open label study for an additional 3 years. The children received vigabatrin as first-line treatment. Non-responders were switched to ACTH, and failing this, to topiramate. Cognitive development and social adaptation were assessed on the Bayley, Stanford-Binet and Vineland scales, respectively, 1-, 2- and 5-years post-diagnosis.

Results
Of 68 children enrolled, 41 completed the 5-year follow-up. Of the initial cohort, 96% became spasm-free within two months, 57% on vigabatrin, 34% on ACTH and 4% on Topiramate. Lead-time to diagnosis was not a factor influencing outcome. Significant cognitive improvement was observed between 2 and 5 years with an average gain of 25 points in developmental quotient. Socialization skills failed to improve. Children showing improvement were mostly those without identified etiology. Factors impeding cognitive improvement included developmental delay due to symptomatic etiology and presence of other seizure types prior to diagnosis, as well as persistent EEG abnormalities and the emergence of new seizure types.

Conclusions
Our findings show significant and progressive long-term improvement of cognitive functions in children with ES following our treatment protocol, especially in those without an identifiable etiology. This stresses the importance of aggressive treatment at onset and periodic re-assessment of cognitive development in order to adjust cognitive, social and educational interventions to changing needs.

This study was supported by grants and scholarships from the Savoy Foundation (LC & JB), CURE Foundation (LC), and Canadian Institute of Health Research (CPEN).

Paediatric Epilepsy

Abstract 35

Stiripentol Efficacy and Safety in Dravet Syndrome: A 12-Year Observational Study

Kenneth Myers[1], Paul Lightfoot[2], Shekhar Patil[3], Helen Cross[4], Ingrid Scheffer[5]

[1]McGill University, Montreal Children's Hospital
[2]Austin Health
[3]Apollo Paediatric Centre
[4]UCL Institute of Child Health & Great Ormond Street Hospital for Children NHS Foundation Trust
[5]Austin Health, University of Melbourne

Rationale
Stiripentol is a medication for which short-term clinical trials have shown safety and efficacy in control of seizures for people with Dravet syndrome. However, there are very few data on the long-term safety and efficacy of stiripentol in this patient population.

Method
We conducted a prospective, observational open label study (2003–2015) of the efficacy and long-term safety of stiripentol in patients with Dravet syndrome and ongoing seizures. Frequency of generalized tonic-clonic seizures, focal seizures, status epilepticus, and adverse events were recorded.

Results
Forty-one patients started stiripentol, with median age at enrolment 5 years 7.2 months (range 11 mo–22 y) and median duration of treatment 37 months (range 2–141 mo). Twenty out of 41 patients had greater than or equal to 50 percent long-term reduction in frequency of generalized tonic-clonic seizures. Frequency of focal seizures was decreased by greater than or equal to 50 percent in 11 out of 23 patients over the long-term. Frequency of status epilepticus was decreased by 50 percent or more in 11 out of 26 patients.

The most common adverse events were anorexia, weight loss, sedation, and behavioural changes. One patient had worsening of absence and myoclonic seizures. Another developed recurrent pancreatitis on concurrent valproate.

Conclusions
Stiripentol improves long-term seizure frequency in approximately 50 percent of patients with Dravet syndrome, when used as part of unrestricted polytherapy. Long-term use appears safe. In more more than 40 percent of patients, episodes of status epilepticus markedly decrease after stiripentol initiation.

Paediatric Epilepsy

Abstract 36

Post-Hoc Analysis of Rufinamide Study 303: Seizure-Free Days in Patients With Lennox-Gastaut Syndrome (LGS)

Stéphane Auvin[1], Betsy Williams[2], Rob McMurray[3], Dinesh Kumar[2], Carlos Perdomo[2], Manoj Malhotra[2]

[1]Pediatric Neurology Department & INSERM U1141, Robert-Debré University Hospital, APHP
[2]Eisai Inc.
[3]Eisai Ltd.

Rationale
Although drop seizures impact quality of life (QoL) in LGS patients, total number of seizures impacts QoL more globally, as seizure frequency usually correlates with cognitive function. This investigation evaluated two novel seizure assessment parameters in pediatric patients with LGS.

Method
Seizure diary data were obtained from Study 303, a Phase III, randomized, controlled, open-label study of patients (1–<4 years) with inadequately controlled LGS treated with 1–3 antiepileptic drugs (AEDs), which evaluated cognitive and behavioral effects of adjunctive rufinamide. Screening/Baseline visits preceded a 106-week Treatment Phase (rufinamide [≤45 mg/kg/day], or any other AED for control). Baseline versus post-Baseline comparison for mean number of seizure-free days was performed for rufinamide only. Time-to-event analysis assessed median number of days during treatment to reach Baseline seizure frequency for both groups.

Results
Patients were randomized to rufinamide (n=25) or any other AED (n=12). For rufinamide, mean number of seizure-free days was 42.2% greater post-Baseline versus Baseline (P<0.0001, parametric and non-parametric tests). Median number of days of seizure diary data collection at Baseline was 53.5 for the any-other-AED group and 35.5 for rufinamide. Median time to reach Baseline number of seizures increased by 0.5 days for the any-other-AED group and 10.5 days for rufinamide during treatment.

Conclusions
Both endpoints showed a change from Baseline after Randomization in seizure burden. Rufinamide was associated with improved outcomes. Robustness of the comparison between Baseline and post-Baseline number of seizure-free days was indicated by similar parametric/non-parametric test outcomes. These parameters might represent new clinically significant primary endpoints.

Funding: Eisai Inc.

Paediatric Epilepsy

Abstract 37

Identification of Two Copy Number Variants in Genetic Epilepsy With Febrile Seizures Plus (GEFS +) Families

Olivier Fortin[1], Christian Vincelette[2], Kenneth Alexis Myers[3]

[1]Montreal Children's Hospital
[2]Université de Sherbrooke
[3]McGill University Faculty of Medicine, McGill University Health Center

Rationale
Genetic epilepsy with febrile seizures plus (GEFS+) is a familial epilepsy syndrome in which affected individuals within a family may have a variety of epilepsy phenotypes, the most common being febrile seizures and febrile seizures plus. This syndrome exhibits considerable genetic heterogeneity, with most identified genetic causes being point mutations, including in genes such as SCN1A, SCN1B and GABRG2. In this study, we investigated the possible contribution of copy number variants in GEFS+ families.

Method
We reviewed the cases of patients in GEFS+ families followed in a pediatric epilepsy clinic of a tertiary healthcare center who received chromosomal microarray analysis. Parents were tested for genetic confirmation, usually with fluorescence in situ hybridization. When possible, we reviewed microarray results in other family members.

Results
Of seven small GEFS+ families followed in the clinic, two had individuals carrying at least one copy number variant. Five individuals (including the proband) in the first family and two individuals (including the proband) in the second family had various types of seizures previously associated with GEFS+. Microarray analysis showed a maternally-inherited 0.880 Mb duplication on Xq11.2q12 in proband one and his half-brother, and a maternally-inherited 0.263 Mb deletion on 15q11.2 in proband two.

Conclusions
We identified two copy number variants of uncertain significance in two unrelated families with GEFS+. The pathogenicity of these variants is unclear; however, in this small study there appeared to be an overrepresentation of copy number variants. These findings suggest chromosomal microarray could be considered as part of the workup in GEFS+ families.

Paediatric Epilepsy

Abstract 38

Gender Disparity, Income Adequacy, and Geographic Location among Neurodevelopmental Disabilities in Canadian Children; Data from the National Longitudinal Study of Children and Youth

Zaid Salaheen[1], Bradley Corbett[2], Asuri Prasad[3]

[1]*Western University*
[2]*Ivey School of Business, Western University*
[3]*Division of Paediatric Neurology, Schulich School of Medicine, Western University*

Rationale
Canada's National Longitudinal Study of Children and Youth survey 9NLSCY)data provides insights into chronic health conditions in children. Research into socioeconomic factors influencing burden of chronic neurological disease in children is critical to understanding cause effect relationships in health policy planning.

Method
We analyzed data from a cross sectional sample of 31963 respondents in cycle 3 of the NLSCY. The presence of neurodevelopmental disabilities (NDD) was self-reported and included; Epilepsy, Cerebral palsy, Intellectual disability, Learning disability, Emotional and nervous difficulties. Information on parental income status (income adequacy groups; Low, Middle, High) and residence (Rural versus Urban location) was also surveyed. Stepwise logistic regression models were developed to examine the relationships of gender, income adequacy, and geographic location with the five neurodevelopmental disabilities surveyed in Cycle 3 respondents.

Results
There was a clear male preponderance observed across the five neurological conditions surveyed. There was a statistically significant relationship between income adequacy and epilepsy (Low Exp (B)=2.11 95%CI 1.25, 3.54) p=0.005), and emotional nervous disorders (Low, Exp(B)=1.50 (95% CI 1.03, 2.18; p=0.035) High, Exp(B)=-0.55 (95% CI 0.41, 0.75; p=0.001). Children in rural locations had lower odds of being identified with learning disability (Exp(B)=-0.73; 95%CI 0.58; 0.91, p=0.005), and emotional nervous difficulties (Exp(B)=-0.68; 95% CI 0.48, 0.96; p=0.030).

Conclusions
Male children are more likely to report NDD than females across the spectrum. Income adequacy (low income groups) carries higher odds of epilepsy and emotional nervous problems) while children in rural locations carry lower odds for learning disabilities and emotional behavioural problems.

Basic Science / Engineering

Abstract 39

The Role of Seizures and Spreading Depolarizations for Injury

Karl Schoknecht[1], Majed Kikhia[1], Coline Lemale[1], Alon Friedman[2], Jens P Dreier[3]

[1]Neurology and Experimental Neurology, Charité - University Medicine
[2]Department of Medical Neuroscience, Dalhousie University
[3]Center for Stroke Research & Department of Neurology and Experimental Neurology, Charité - University Medicine

Rationale
Stroke is a leading cause of death and disability and early seizures are common after stroke. Here we investigated the influence of epileptic seizures and spreading depolarizations (SDs) on the progression of injury using the photothrombosis model (PT).

Method
Cerebral ischemia was induced by the Rose bengal PT model in anaesthetized male Wistar rats. Excitability was increased by topical perfusion of 4-aminopyridine (4-AP) and neuronal activity was modulated by different anesthetics, i.e. urethane and ketamine. Blood-brain barrier (BBB) permeability and cerebral perfusion were assessed through a cranial window following intravenous injection of fluorescein sodium salt until 4 hours post PT. Neuronal injury and lesion volume were quantified using hematoxylin & eosin stained coronal slices and ex-vivo T2-weighted magnetic resonance imaging.

Results
PT was characterized by an expanding hypoperfused primary lesion surrounded by BBB-dysfunctional cortex. 4-AP induced repetitive seizures and neuronal injury was mildly, yet insignificantly, elevated in epileptic compared with non-epileptic animals under urethane anesthesia. MRI-based lesion volume assessment correlated with neuronal injury. BBB permeability rapidly increased irrespective of the electrophysiological phenotype. Ketamine significantly reduced neuronal injury although seizure duration and power were elevated compared with urethane-anesthetized animals. The number of SDs prior to 4-AP application and SD complexes were however reduced by ketamine.

Conclusions
Our results implicate robust SD- and seizure-independent BBB dysfunction and a greater impact of SDs compared with seizures on lesion progression in the hyper-acute phase in this stroke model. Our data further suggest ketamine as a therapeutic to reduce early injury progression.

Basic Science / Engineering

Abstract 40

Isoflurane Reduces Paraoxon-Induced Brain Damage

Evyatar Swissa[1], Guy Bar-Klein[2], Lyna Solomon Kamintsky[3], Ofer Prager[1], Arik Eisenkraft[4], Alon Friedman[5]

[1]Departments of Brain and Cognitive Sciences, Physiology & Cell Biology, Zlotowski Center for Neuroscience, Ben-Gurion University of the Negev, Beer-Sheva, Israel
[2]McKusick-Nathans Institute of Genetic Medicine, Johns Hopkins University School of Medicine and Howard Hughes Medical Institute, Chevy Chase
[3]Department of Medical Neuroscience, Dalhousie University
[4]The Institute for Research in Military Medicine, Hebrew University, Jerusalem
[5]Departments of Brain and Cognitive Sciences, Physiology & Cell Biology, Zlotowski Center for Neuroscience, Ben-Gurion University of the Negev, Beer-Sheva, Israel / Department of Medical Neuroscience, Dalhousie University

Rationale
Organophosphates (OPs) are widely used as pesticides, but can also be misused as warfare agents. OPs inhibit acetylcholinesterase leading to over-stimulation of cholinergic synapses. OPs cause status epilepticus (SE), which lead to irreversible brain damage. Therefore, there is high interest in rapid termination of status epilepticus, prevention of recurrent seizures and associated brain damage. We report a rat model of OP-induced SE and epileptogenesis using paraoxon, and test the efficacy of anti-seizure and anti-inflammatory drugs in suppressing paraoxon-induced SE and preventing late brain damage.

Method
Electrocorticographic recording were performed using epidural electrodes 24 hours prior, during and up to 48 hours after injection of 4.5 LD50 paraoxon. One and Five minutes after poisoning rats were injected with atropine and toxogonin to prevent death, and 30 min later treated with midazolam to terminate SE, together with different anti-seizure (lorazepam, valproic acid, phenytoin) or anti-inflammatory (losartan, isoflurane) drugs. Outcome measures included SE duration, number of recurrent seizures, and duration of epileptiform brain activity 24 hours after poisoning. Brain damage was assessed by T2-weighted magnetic resonance imaging (MRI) one month after poisoning.

Results
There was no significant difference in SE duration and the number of recurrent seizures between rats treated with single midazolam injection, and any of the drugs tested. Brain imaging revealed the most prominent changes in the midbrain, septum, striatum, hippocampus and fornix. Isoflurane, but not anti-seizure medications significantly reduced these structural lesions.

Conclusions
We show that acute treatment with isoflurane, but not anti-seizure medication, reduces brain damage following SE. These results are consistent with the recently reported anti-epileptogenic effect of isoflurane.

Basic Science / Engineering

Abstract 41

Multi-Electrode Array Detection of Excitatory Synchronous Activity in a Slice model of Epilepsy

Adam Ravalia, Matthew Parsons

Memorial University of Newfoundland

Rationale
One of the benchmarks of epileptiform activity is anomalous synchronous firing across extensive brain regions. Traditionally, this synchrony is assumed to be too high and too extended, resulting in the wide range of symptomologies associated with epileptic activity. In order for researchers and clinicians to continue to explore therapeutic avenues that minimize hyper-synchronous activity in the epileptic brain, precise screening tools devised to quantify synchrony must be developed.

Method
We utilized 4-aminopyridine(4-AP) in-situ to induce synchronous firing in the hippocampus of 2-4-month-old C57BL/6 mice while simultaneously recording spontaneous activity via a multi-electrode array (MED64). This approach allows for simultaneous recording of 64 electrodes within hippocampus proper. The spatial expansiveness of this array grants much more widespread and accurate screening of synchronous activity compared to conventional electrophysiological methodologies.

Results
We report that the multi-electrode array recordings of spontaneous activity proved to be an incisive and comprehensive screening tool of synchrony within hippocampus. Furthermore, application of 4-AP results in a concentration dependent increase in amount and length of epileptic-like events, as well the spatial spread of this pathological synchronous activity. We also found that application of glutamate transport blockers in conjunction with 4-AP exacerbated synchronous activity observed in hippocampus.

Conclusions
Multi-electrode array technology can be utilized as a capable and robust screening tool for the detection and subsequent analysis of synchronized bursting activity in a slice model of epilepsy. This methodology has the potential to act as a preliminary step toward more targeted reduction of hyper-synchronous activity in the epileptic brain.