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Book of Abstracts

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Oral Presentation: Neuroimaging

Abstract 1

Is the Hemodynamic Response to Scalp Interictal Epileptic Discharges the Onset Zone of Intracerebral Interictal Discharges?

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Rationale
EEG/fMRI of scalp interictal epileptic discharges is a non-invasive tool resulting in hemodynamic responses that contribute to localize the epileptic activity generator. We sought to determine if the maximum hemodynamic response corresponds to the generator of interictal epileptic discharges (IEDs) on intracerebral EEG (iEEG).

Method
We studied patients who underwent an EEG-fMRI study showing significant hemodynamic responses, and then iEEG. We co-registered hemodynamic responses to iEEG electrodes. We included studies in which the iEEG channel closest to the peak hemodynamic response was less than 10mm away. This is the main channel of the study.
We marked IEDs in the main channel when present in other channels at roughly the same time, suggesting a widespread IED. IEDs in the main channel were aligned at their peak, and the iEEG in all channels was averaged. In resulting traces the first peak was marked in each channel showing an IED. Delays were computed from the earliest peak.

Results
Ten studies were analysed, with 105 (range 70-122) IEDs in the main channel. After averaging, 40 (25-57) channels contained IEDs. The median delay of IEDs for all channels was 76.5ms (32.8-114.2ms), and 19.5ms (16-33.5ms) on the main channel. The main channel delay is significantly smaller than expected by chance ($p=0.02$).

Conclusions
This proves that IEDs recorded close to the maximum hemodynamic response are more likely to generate widespread discharges than IEDs recorded remotely from the maximum, thus demonstrating that EEG-fMRI can reveal the source of widespread discharges, which we label the spike onset zone.

Oral Presentation: Neuroimaging

Abstract 2

Feasibility of Ultra-High Field MRI for Surgical Planning in Stereo-Electroencephalography

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Rationale
Ultra-high field (≥ 7 Tesla or 7T) magnetic resonance imaging (MRI) has important potential implications for assisting with stereo-electroencephalography (SEEG) planning as a result of increased contrast and signal compared with standard field strengths. We sought to investigate the feasibility of integrating 7T imaging into the SEEG workflow for assisting with surgical planning.

Method
In 22 controls scanned at both 7T and lower field, we evaluated local geometric changes using deformation-based morphometry (DBM), permitting voxel-level quantification of sub-millimeter to millimeter level distortions. Using our high resolution (600 micron) normative 7T template, we performed template-to-patient deformable registration in 51 SEEG patients. Electrode contacts within the hippocampus were semi-automatically labeled, propagated into 7T template space, and transformed into a recently developed intrinsic hippocampal subfield coordinate system.

Results
DBM revealed minimal (submillimeter) distortion in the mesial temporal lobe structures (e.g. hippocampus: 0.72 +/- 0.20 mm). However, pertinent regions such as the bilateral temporal poles, inferior temporal gyri, and fusiform gyri showed statistically significant distortion (effect size: 1.2-1.6 mm; corrected p-value < 0.025). 7T template-to-patient registration enabled evaluation of electrode locations relative to hippocampal subfields in 7T template space permitting group analysis of electrode locations and intracranial EEG data.

Conclusions
Ultra-high field MRI enables an unprecedented level of anatomical detail achievable in in vivo subjects that can be valuable for epilepsy investigation and surgical planning. Susceptibility artifacts and distortions remain problematic, but a multi-scale imaging approach using both standard and ultra-high field magnets may prove optimal for pre-operative planning.

Oral Presentations: Basic Science / Engineering

Abstract 3

Brainstem Seizures and Associated Cardiorespiratory Depression Following Intrahippocampal 4-AP Application in Freely Moving Rats

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Rationale
Cardiorespiratory dysfunction during or after seizures may contribute to hypoxic brain damage or, in some cases, sudden unexpected death in epilepsy (SUDEP). Lower brainstem cardiorespiratory systems are postulated to be disrupted by seizures resulting in cardiorespiratory dysfunction.

Method
Here, we explored the effects of brainstem seizures on cardiorespiratory function using a rat model of intrahippocampal 4-aminopyridine-induced acute seizures. We hypothesized that seizures, focally initiated in the hippocampus, became generalized and propagated to disrupt brainstem function leading to cardiorespiratory failure and death. Hippocampal, cortical and dorsomedial medulla electrographic recordings together with cardiorespiratory monitoring were conducted in freely moving rats.

Results
Tachypnea but unchanged heart rate occurred during isolated seizures in the hippocampus and cortex. Status epilepticus (SE) without brainstem seizures produced tachypnea and tachycardia whereas SE with intermittent brainstem seizures induced repeated cardiorespiratory depression leading to death. Respiratory arrest prior to asystole was a terminal event. Phenytoin (100 mg/kg, i.p.) terminated brainstem seizures induced cardiorespiratory depression and prevented death in 5/6 rats. Focal electrical stimulation of the brainstem also suppressed cardiorespiratory parameters.

Conclusions
We concluded that seizure propagation to the brainstem produces cardiorespiratory depression related to mortality. Although cardiorespiratory depression was observed during SE, we hope that the mechanisms causing death in our model may be shared with spontaneous seizures associated with SUDEP. These findings would add more information to a growing body of SUDEP study which could lead to preventive strategies against sudden death in people with epilepsy.

Funding source: Friends of Faces, USA

Oral Presentations: Basic Science / Engineering

Abstract 4

Repeated Attenuation of Post-ictal Hypoxia: Effect on Behaviour and Brain

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Rationale
We recently determined that following cessation of brief seizures, a long-lasting, severe hypoxic event occurs in the brain regions involved in the seizure. Repeated hippocampal seizures in rodents results in severe deficits in hippocampal-dependent tasks, and can induce pathological changes to brain structure. These behavioural disturbances are likely analogous to interictal deficits in humans. However, the contribution of the hypoxic events that follow seizures to these behavioural deficits and structural alterations ha not yet been determined.

Method
We used the electrical kindling model to induce brief seizures in the hippocampus while simultaneously recording local oxygen levels in adult male Long-Evans rats. Seizures were elicited daily until 20 post-ictal hypoxic (PIH) events occurred. We also used two pharmacological interventions to prevent the PIH: nifedipine (L-type calcium channel inhibitor) and acetaminophen (COX-1/2 inhibitor). Following this, behavioural testing was initiated (Novel Object/Context-Mismatch) followed by immunohistochemistry. We will probe for astrocyte activation (GFAP), blood-brain barrier disruption (IgG), and mossy fiber sprouting.

Results
We report a significant deficit in object/context memory in rats subjected to repeated seizures with hypoxia. Furthermore, this deficit is robustly and repeatedly ameliorated with the administration of acetaminophen or nifedipine. Preliminary immunolabelling results for astrocyte activation with GFAP indicate increased astrocyte numbers in CA1, CA3, and hilar regions of the dorsal hippocampus following repeated seizures with hypoxia. This is attenuated in rats that had PIH repeatedly blocked with acetaminophen/nifedipine. Further immunohistochemistry experiments will be performed to determine the extent of pathological disruptions due to PIH.

Conclusions
PIH can be repeatedly blocked via administration of nifedipine or acetaminophen. We have demonstrated that by preventing PIH we can also prevent deficits on a hippocampal-dependent task, and preliminary data suggests that astrocyte reactivity caused by multiple seizures may also be attenuated.

Neuroimaging

Abstract 5

Multiple Subject Barycentric Discriminant Analysis: A New Metric for Ascertaining Whole Brain Network Atypicality

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Rationale
The determination of cerebral laterality has played an important part in neurosurgical planning for children with drug-resistant focal epilepsy. Implementation of task-based fMRI language studies has reduced reliance upon more invasive methods such as intracarotid amobarbital (Wada) testing and cortical electrical stimulation mapping during awake craniotomy. Typical application of fMRI for presurgical language mapping relies upon voxel-wise or regional laterality indices [1] that may not capture the intricacies of brain network atypicality. Here, we introduce a new method of computing whole-brain network-wise atypicality across a collection of fMRI tasks.

Method
Multivariate multivoxel pattern analysis (MVPA) techniques can give whole-brain metrics of (a)typicality. Here, we use Multiple Subject Barycentric Discriminant Analysis (MuSuBADA) [2], a MVPA-like technique to simultaneously determine network atypicality across 4-tasks—semantic decision (auditory description decision task), tone detection, mental rotation, and viewing scrambled images.

Results
Results show brain network atypicality consistent with previous lateralization findings on the same cohort [1]; those with unusual lateralization patterns show greater degrees of atypicality. In addition, patterns of network activity were also sensitive to lesional pathology, with greater atypicality seen in patients with lesions on 3T MRI.

Conclusions
MuSuBADA is a useful tool for gauging whole-brain network atypicality to supplement information gained from traditional laterality indices.

Neuroimaging

Abstract 6

Postictal Hypoperfusion measured by MR Arterial Spin Labeling: Localization of the Seizure Onset Zone

Ismael Gaxiola-Valdez, Shaily Singh, Tefani Perera, Sherry Sandy, Emmy Li, Paolo Federico

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Rationale
Postictal neurological deficits are well recognized and may be associated with alterations in cerebral blood flow (CBF). Recent animal work reported hypoperfusion in the seizure onset zone (SOZ) following seizures that can last up to 60 min. Thus, postictal hypoperfusion may underlie post-ictal neurological deficits and it may identify the SOZ in patients. Thus, the aim of this study was to determine whether postictal hypoperfusion occurs in humans and whether arterial spin labeling (ASL) MRI can measure it.

Method
Twenty-one patients were recruited and underwent ASL MRI within 90 min of a habitual seizure and during a baseline, interictal period. Postictal CBF maps were subtracted from interictal CBF maps to identify areas of significant postictal hypoperfusion. The location of maximal hypoperfusion was compared to the presumed SOZ.

Results
Significant postictal CBF reductions (>15 CBF units) were seen in 15/21 patients (71.4%). In 12/15 (80%) of them, the location of hypoperfusion was partially or fully concordant with the SOZ. This technique compared favourably to other neuroimaging modalities, being similar or superior to structural MRI in 52% of cases, ictal SPECT in 60% and interictal PET in 71%. Better ASL results were obtained in patients in whom the SOZ was discernable based on noninvasive data.

Conclusions
ASL is a safe, noninvasive and relatively inexpensive tool to detect postictal hypoperfusion that may assist in identifying the SOZ. This technique may be incorporated into the battery of conventional investigations for pre-surgical evaluation of patients with drug resistant focal epilepsy.

Funded by CIHR.

Neuroimaging

Abstract 7

Temporal Lobe Epilepsy: Microscopic Hippocampal Anomalies Modulate Whole-Brain Pathoconnectomics

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Rationale
Temporal lobe epilepsy (TLE) is increasingly recognized as a disorder of large-scale networks. Considering its hippocampal epicenter, histological studies have reported variable pathological anomalies. By combining diffusion connectome analysis with high-resolution hippocampal subfield investigations, we assessed whether degrees of hippocampal pathology are mirrored in whole-brain network phenotypes.

Method
We studied 44 TLE patients and 25 healthy controls. Postoperative hippocampal histology revealed marked cell loss and gliosis in 24 patients (TLE-HS) and isolated astrogliosis in 20 (TLE-G). After building whole-brain connectomes via systematic diffusion tractography, we assessed between-group differences in network topology and used network control theory for mechanistic predictions of brain dynamics. Multivariate correlation analysis evaluated parametric modulations of network parameters by degrees of hippocampal pathological changes, and geodesic distance mapping assessed associations between network alterations and the proximity to the hippocampal epicenter.

Results
We observed a divergence of network organization and controllability between pathologically-stratified TLE subgroups. Compared to controls, we observed a gradual pattern of changes in both TLE groups, with marked reduction in global/local network efficiency, together with decreased controllability in TLE-HS, while TLE-G showed only modest changes. Geodesic distance mapping revealed that the divergence between both TLE subgroups was indeed most marked in networks proximal to the hippocampus. Multivariate correlations indicated an association between severity of hippocampal imaging anomalies and large-scale network rearrangement.

Conclusions
Integrated hippocampal phenotyping and connectome analysis revealed a parametric modulation of whole-brain network anomalies by degrees of histopathology. Hippocampal cell loss likely exerts a cascading impact on large scale white-matter networks, likely via processes related to secondary degeneration

Neuroimaging

Abstract 8

Multimodal Neuroimaging Models for Lateralization of Temporal Lobe Epilepsy

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Rationale
Temporal lobe epilepsy (TLE) is the most prevalent type of epilepsy with the most successful surgery outcome. The neuroimaging multimodal findings concordant with EEG and neuropsychology help in decision-making prior to the resection of mesial temporal structures. We hypothesize that the development of quantitative TLE lateralization response models using MR volumetry and FLAIR, DTI and SPECT neuroimaging attributes will optimize the selection of surgical candidates and reduce the need for extraoperative electrocorticography (eECoG).

Method
Neuroimaging features of 138 retrospective TLE patients with Engel class l surgical outcomes were extracted, including the hippocampal volumes, normalized ictal–interictal SPECT and FLAIR intensities, and mean diffusivity, along with the cingulate and forniceal fractional anisotropy (FA). Using logistic function regression, univariate and multivariate models were developed.

Results
The model incorporating all multivariate attributes for 138 TLE cases that had at least one imaging attribute and imputing the missing attributes with the mean values of the corresponding attributes measured on control cohort reached the probability of detection and false alarm of 0.83 and 0.17 for all cases, and 0.90 and 0.10 for the patients who underwent eECoG.

Conclusions
Increased reliability in lateralizing TLE cases using the proposed response model involving the incorporation of the multivariate attributes reinforces the notion that eECoG in a number of cases may be circumvented. The proposed response model can be further generalized by integrating attributes of additional neuroclinical, neurophysiological, neuropsychological, and neuroimaging attributes into the presurgical decision making process.

Neuroimaging

Abstract 9

The Use of Measurements from the Temporal Lobe Pole to Posterior structures of the Temporal Lobe in Surgical Planning for Anterior Neocortical Amygdalohippocampectomy: A Magnetic Resonance Imaging Study

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Rationale
Epilepsy surgery can be an effective temporal lobe epilepsy treatment in patients affected by seizures medically refractory. The goal of this study was establish normal measures for surgical planning for anterior neocortical amygdalohippoccampectomy by Spencer's description

Method
The results showed from temporal pole to anterior end of temporal stem 22mm (18-25mm), center of amygdala 25mm (19-32mm), center of head of hippocampus 28mm (21-30mm), pies of hippocampus 58 mm(52-60mm), tip of temporal horn of lateral ventricle 30mm (22-39mm), anterior aspect of midbrain 34mm (32-41mm), posterior edge of midbrain 60mm (56-64mm).

Results
The results showed from temporal pole to anterior end of temporal stem 22mm (18-25mm), center of amygdala 25mm (19-32mm), center of head of hippocampus 28mm (21-30mm), pies of hippocampus 58 mm(52-60mm), tip of temporal horn of lateral ventricle 30mm (22-39mm), anterior aspect of midbrain 34mm (32-41mm), posterior edge of midbrain 60mm (56-64mm).

Conclusions
If we consider the anterior temporal lobectomy the distance from temporal pole to pies of Hippocampus, and anterior aspect of midbrain is very important in order to preserve the structures, however further comparison has to be done with patients harboring on sclerosis hippocampal. If we take in concern the selective amygdalohypocampectomy through middle temporal gyrus and inferior or though the collateral sulci the measurements of temporal pole to center of amygdala and head of hippocampus are very important

Neuroimaging

Abstract 10

Application of High Frequency Oscillation and Interictal Epileptiform Discharges in Simultaneous Intracranial EEG-fMRI

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Rationale

Successful surgical treatment for patients with refractory epilepsy depends upon the accurate identification of seizure onset zones (SOZ). Simultaneous scalp EEG-fMRI is a novel technique for measurement and localization of the blood oxygen level dependent (BOLD) response associated with interictal epileptiform discharges (IEDs), considered to be biomarker of the SOZ. Identification of high frequency oscillations (HFOs) recorded by intracranial EEG (iEEG) is also another biomarker of the SOZ. In this study, we performed simultaneous iEEG-fMRI to investigate the relationship between the location of the BOLD response to HFOs and IEDs to the location of the SOZ.

Method

Seven subjects with focal epilepsy underwent 60 minutes of simultaneous iEEG-fMRI acquisition at 3 Tesla. EEG and fMRI preprocessing was performed offline and IEDs were marked by two experienced electroencephalographers. HFOs were detected by an automated detection algorithm. Two parametric fMRI maps were generated for each subject: one using HFO events and the other IEDs. The location of the HFO-associated BOLD response was compared to the IED-associated BOLD response, in terms of their proximity to the SOZ.

Results

In 5/7 cases, HFO-associated BOLD signal was located immediately adjacent to the most active contact and the SOZ. In all cases, HFO-associated BOLD response was a more discrete cluster that was closer to the SOZ compared to the location of the maximal IED-associated BOLD response.

Conclusions

HFO-associated BOLD activation might be a better identification of the SOZ compared to IED-associated BOLD activations.

Funded by CIHR.

Neuroimaging

Abstract 11

Understanding Clincial Epileptogenesis – Is There any Role in Searching for Subtle Hippocampal Structural Changes in First Seizure Populations?

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Rationale
The Halifax First Seizure Clinic (HFSC) established a systematic longitudinal study of patients with first seizure (FS) in order to identify imaging biomarkers for seizure recurrence (SR). The focus of this analysis was on hippocampal malrotation (HIMAL) and loss of hippocampal internal architecture (HIA).

Method
We identified 51 adult patients (15 - 74 years) with FS or new-onset epilepsy (NOE ≥ 2 seizures in < 12 months), all of them of focal nature. 1.5 Tesla MRI imaging was performed within 6 weeks after their first index seizure. Two independent readers classified HIMAL and HIA by consensus, using a published scoring system on high resolution coronal T2 FSE images (3 mm contiguous; orthogonal to the hippocampi).

Results
There were 28 FS and 23 NOE patients. Ten FS patients converted to NOE (1-year follow-up). Eleven patients had HIMAL, and 15 patients had loss of HIA. No significant association was found between HIMAL and NOE at presentation, nor between HIMAL and conversion from FS to NOE. Loss of HIA and NOE at presentation were not significantly correlated. However, loss of HIA was significantly associated with conversion from FS to NOE ($p = 0.0427$, one-tailed Fisher's exact test).

Conclusions
Our data do not support that HIMAL plays any role in epileptogenesis. It seems to represent a normal variation. The loss of HIA however appears to be a promising early biomarker for epileptogenesis

Neuroimaging

Abstract 12

Arterial Spin Labeling (ASL) Perfusion MRI in the Pre-Surgical Evaluation of Pediatric Epilepsy: Lesional vs. Non-Lesional Cases

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Rationale
Arterial spin labeling (ASL) is a non-invasive MRI perfusion method that produces brain maps of cerebral blood flow. This technique has been used as part of the pre-surgical evaluation of epilepsy to help localize and delineate the epileptogenic zone (EZ) mainly in lesional patients, with little focus on non-lesional cases.

Method
We prospectively performed ASL in 20 consecutive pediatric focal epilepsy patients. Perfusion abnormalities were first identified through visual assessment after which asymmetry index (AI) calculations were performed between suspected abnormalities and contralateral areas. ASL results were compared to structural MRI, PET, SPECT, and MEG data as well as surgical pathology results.

Results
We evaluated 15 lesional and 5 non-lesional cases. A focal perfusion abnormality was identified on ASL in 13 of 15 lesional patients but none were seen in any non-lesional case. The perfusion abnormality was concordant with PET in 12/12, SPECT in 10/12, and MEG in 6/11. Thus far, 9 ASL-positive patients have undergone resection of the hypothesized EZ. Analysis of the resected tissue revealed 8 cases of FCD and one case of hippocampal sclerosis. Eight of 9 patients are seizure free while one patient is classified Engel 2 at a mean follow-up time of 11.27 months.

Conclusions
ASL can localize the EZ in lesional focal epilepsy cases, in particular FCD, however, it does not appear to help in non-lesional cases. In spite of this limitation, ASL is a useful noninvasive MRI perfusion sequence which can be easily added to routine MRI exams as part of the pre-surgical evaluation of focal epilepsy.

Neuroimaging

Abstract 13

Post-ictal Hypoperfusion Measured by CT Perfusion Imaging

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Rationale
Recent animal work from the Teskey laboratory has shown reduced local cerebral blood flow in the hippocampus lasting up to one hour following seizures. Using arterial spin labelling (ASL) MRI, we observed post-ictal hypoperfusion at the seizure onset zone (SOZ) in 75% of 25 patients lasting up to one hour. However, the clinical implementation of ASL is hampered by its limited availably on short notice. CT Perfusion (CTP) also measures changes in CBF and circumvents the logistical limitations of ASL. If CTP can be shown to localize the SOZ via perfusion patterns, it may provide an additional cost-effective and readily available tool to measure post-ictal CBF. We hypothesize that CTP detection of post-ictal hypoperfusion can accurately localize the SOZ.

Method
Seven patients were studied while undergoing in-patient continuous video-EEG monitoring. A CTP scan was obtained within one hour of seizure termination. While in hospital, patients underwent a baseline CTP scan following a seizure-free period of >24 hr. The CTP data were then co-registered with structural MR images, or if unavailable, structural CT images. The location of maximal hypoperfusion was then compared to the presumed SOZ.

Results
Post-ictal CTP scans were obtained 36-80 min following seizure termination. Significant hypoperfusion were seen in all seven patients and it co-localized or lateralized to the SOZ in five.

Conclusions
Significant post-ictal hypoperfusion can be detected using CTP in the majority of patients in this pilot study. CTP may be a cost-effective and more readily available alternative to ASL for investigating post-ictal perfusion changes.

Funded by CIHR.

Neuroimaging

Abstract 14

At our Institution, Does Repeat 3T MRI Improve Diagnostic Yield when Compared with 1.5T in Patients with Refractory Epilepsy?

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Vancouver General Hospital

Rationale
Standard epilepsy studies are performed at 1.5T in our institution and throughout the province of BC.

In patients with refractory epilepsy, we now can offer a repeat scan performed at 3T to attempt to increase our yield for diagnosis of radiologically apparent lesions.

We reviewed the results of the 3T MRIs performed since the commencement of the service.

Method
We audited the first 16 months of the service.

Literature review to assess the accepted rate of new pick ups from repeat 3T MRI, standard of between 5% and 10%.

Prior and current studies were compared in all 122 cases. If there was a new finding on the repeat scan, the prior images were reviewed to assess whether the finding was also present on the prior.

Results
122 3T MRIs were performed with prior 1.5T for comparison.

Overall rate of new pick up was 12%. All 1.5T studies at our institution was read by a neuraradiologist, whereas most from elsewhere were read by general radiologists.
When the prior scan was read by a neuroradiologist, the pick up was 6%. We showed that studies performed outside our institution by non neuroradiologists had a 26% increase in diagnostic yield, most of which were in retrospect visible on the original 1.5T scan.

Conclusions
1. Our yield of new findings was 6%, which is within the range in the current literature.

2. Prior scans read by non neuroradiologists should be reviewed by a neuroradiologist prior to repeat scan at 3T.

Neuroimaging

Abstract 15

Seizure Onset Zone Localization by Comparing Patient Postictal Hypoperfusion to Healthy Controls

Tefani Perera[1], Ismael Gaxiola-Valdez[1], Shaily Singh[1], Madison Milne-Ives[1], Sherry Sandy [1], Emmy Li[2], Paolo Federico[3]

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Rationale
We have shown that arterial spin labeling (ASL) MRI can be used to detect postictal hypoperfusion localizing to the seizure onset zone (SOZ). Clinical implementation of this technique is limited by current need to obtain two scans per patient: a postictal scan and an interictal, baseline scan. The two maps are then subtracted to identify regions of postictal hypoperfusion. Thus, we aimed to determine whether it is possible to limit the number of ASL scans to one per patient by comparing patient postictal ASL data to that of 100 healthy controls. We hypothesize that statistical comparison between patient postictal maps and control maps would provide similar localizing information as provided by subtraction.

Method
Twenty-one patients were prospectively recruited and underwent ASL MRI within 90 min of a seizure. The data were statistically compared to average baseline maps from 100 healthy controls to identify significantly hypoperfused brain regions in patients. The location of maximal hypoperfusion was compared to the presumed SOZ to assess concordance.

Results
The area of maximal postictal hypoperfusion was concordant with the suspected SOZ in 10/21 patients versus 12/21 patients in subtraction. Two patients that showed no or discordant changes by subtraction had concordant findings by the statistical method. Both patients had very active interictal EEGs.

Conclusions
Comparing postictal hypoperfusion maps to controls is more sensitive but less specific than our original subtraction method, thereby affecting localizing ability for certain patients. However, the statistical method is better suited than subtraction for patients with active interictal EEGs.

Neuroimaging

Abstract 16

High Field Structural MR Imaging in Focal Epilepsy: Do 3 T Scans Improve Diagnostic Yield over 1.5T Scans?

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Rationale
As surgery is the only curative strategy in refractory epilepsy, it is vital to accurately and precisely delineate the seizure onset zone (SOZ) to maximize surgery outcome. Structural magnetic resonance (MR) imaging is an important component to the surgery workup, serving to identify epileptogenic lesions to guide resective surgery. With 3 T MR scanners now available across Canada, high field structural MR scans have become more common despite mixed evidence regarding their efficacy compared to standard 1.5 T scans.

Method
107 patients who had undergone both a 1.5 T and 3 T epilepsy protocol scan were selected. The scans were randomized and examined by two neuroradiologists. Results were analyzed for any significant difference between the field strengths and compared to the patient's EEG findings, the gold standard in SOZ localization.

Results
A modest but significant increase in both tissue contrast (1.5 T : x = 2.965, SEM = 0.038 ; 3 T : x = 3.675, SEM = 0.033) and also artifact (1.5 T : x = 3.231, SEM = 0.047 ; 3 T : x = 3.486 SEM = 0.044) quality was observed at 3T. More lesional scans were detected with the higher field strength, and rater agreement was modestly increased (1.5 T: 0.59; 3 T: 0.66).

Conclusions
A modest increase in epileptogenic lesion detection rate was seen at 3T compared to 1.5T.

Clinical Epilepsy / EEG / Antiepileptics

Abstract 17

The Creation and Early Life of an Adult Epilepsy Monitoring Unit

Gillian Reid McDonald

The Ottawa Hospital

Rationale
Epilepsy monitoring units (EMU) are seen as a valuable component of successful epilepsy programs. In Ontario, a provincial framework was established to maximize value and effectiveness in epilepsy care. One component was further supporting existing Epilepsy Monitoring Units along with the creation of new units in Ontario.

Method
The poster will provide a review of the first three years of such a unit in an Ontario hospital; identifying the key elements considered in its creation and the ongoing progress of the unit. The poster will review what was considered in setting up the unit; such as finding any best practices, linking with existing units, adapting to hospital centric needs and the consideration of Ontario provincial guidelines on Epilepsy monitoring units. There will be a focus on the patient centred care model that is adopted in the hospital and the overall positive impact on the patient experience.

Results
The poster will allow the viewer to see the journey, lessons learned, patient experiences, small and large pearls discovered along the way.

Conclusions
The aim of the poster is to provide an insight into Epilepsy monitoring units, their creation and provide further input on what the novice unit looked to gain from long standing units, and vise versa.

Clinical Epilepsy / EEG / Antiepileptics

Abstract 18

Standardizing Practice for Safety in the EMU: Describing the Quality Improvement Initiative for Nursing Practice Recommendations by the Canadian Epilepsy Nursing Group (CENG)

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Rationale

A recent study by CENG highlighted that variability in Epilepsy Monitoring Unit (EMU) composition, nurse – patient ratios, and nursing skill mix were often independent of patient acuity [1]. Findings spoke to the need for a national strategy to develop nursing practice guidelines to standardize care and improve patient safety.

Method

In 2011, CENG was formed to consolidate knowledge as it became clear there was little evidence to inform nursing practice in EMUs. This was further supported by an Ontario expert nursing panel, including CENG members, who contributed to a broader multidisciplinary provincial EMU guideline project [2]. These simultaneous projects resulted in a national working group being established. Informed by a quality improvement framework [3] and practice guideline development tool [4], an expert panel reviewed literature and workplace practices and developed a comprehensive list of nursing practice recommendations. Using a modified Delphi approach [5], each recommendation was evaluated and formalized after it received 85% or above approval from the expert panel.

Results

A systematic stratified through-put model was developed with over 100 nursing practice recommendations, chronologically organized from pre-admission through discharge focusing on the domains of safety, patient care, patient education and staff education. Pre- admission covers formal written communication to patients about EMU stay and risks including medication weaning. Upon-Admission highlights continuation of formal communication tools for nurses, such as check lists, to ensure there is a concrete documented team-based plan of care, comprehensive nursing and seizure histories, with tailored baseline assessments and education also completed. During-Admission addresses continuous patient monitoring, specific ictal monitoring, medication administration and invasive monitoring. At- Discharge ensures clear follow up instructions, medication reconciliation and a concrete emergency response plan.

Conclusions

This is the first ever comprehensive national set of Canadian nursing practice recommendations developed for epilepsy monitoring units. Further research should explore their implementation through an evaluative quality improvement process.

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Clinical Epilepsy / EEG / Antiepileptics

Abstract 19

Vulnerability to Mania: a Lower Threshold for Concern on the Epilepsy Monitoring Unit

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Rationale
Both sleep deprivation and discontinuation of mood-stabilizing antiepileptic drugs (AEDs) are well-described triggers for manic episodes in individuals with vulnerability to bipolar affective disorder. These two measures are routinely instituted on epilepsy monitoring units (EMUs). However, there is sparse literature describing the risk of manic episodes as an adverse event in EMUs.

Method
We report a case and review the literature.

Results
A 20-year-old man with idiopathic generalized epilepsy and no prior history of manic or hypomanic episodes was admitted to the EMU. He was sleep deprived and doses of mood-stabilizing AEDs were reduced. On the fourth day of admission, he experienced a manic episode. This resolved within four days with sedatives and reinstatement of his pre-admission AED regimen. Psychiatric history included a past major depressive episode and family history of psychosis. Continuous EEG showed no seizures throughout the admission.

Patients with bipolar disorder are commonly initially diagnosed with major depressive disorder because the first manic episode may only present after several major depressive episodes. Knowledge of predisposition to bipolar disorder could influence the extent of measures on the EMU such as sleep deprivation and AED dose reduction, to avoid triggering mania with its associated risks. The psychiatric literature describes clinical features that can offer clues to bipolarity even before the first manic episode.

Conclusions
In some patients admitted to the EMU, screening for subtle clues to vulnerability to bipolar disorder might be recommended to avoid the risk of mania induced by sleep deprivation and/or AED tapering.

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Abstract 20

Thought Disturbances in Epilepsy: A Dimensional Approach

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Rationale
In some patients with epilepsy and neuropsychiatric symptoms, boundaries can be blurred between several abnormalities of thought content, including preoccupations, overvalued ideas and delusions. There is limited literature to guide the approach to this diagnostic challenge.

Method
We present a case report and review related literature.

Results
A man with independent bitemporal epileptic foci experienced a constellation of neuropsychiatric symptoms including peri-ictal visual hallucinations and postictal psychotic episodes. Seven years after the onset of seizures, he developed a range of persistent beliefs that were mostly bizarre. These beliefs were persistently preoccupying and distressing, but not always held with absolute conviction. The degree of conviction, preoccupation, distress, and overall functioning considerably improved on olanzapine. The phenomenology of these beliefs is explored in detail. Related differentials include a range of non-psychotic phenomena, chronic psychosis with an element of retained insight, the effects of frontal network behavioural syndrome, and/or the controversial Waxman-Geschwind syndrome. Furthermore, the phenomenology can change as these conditions evolve over time and potentially overlap with one another. The literature lacks extensive descriptions of variation across the above syndromes in terms of the degree of conviction, preoccupation and distress associated with beliefs. Dimensional psychometric instruments may help characterize the differential in such presentations.

Conclusions
The use of dimensional psychometric instruments can provide further insight into the phenomenological differences between the above conditions, their potential interaction in terms of comorbidity and longitudinal evolution, and also the response of different aspects of phenomenology to treatment.

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Abstract 21

Resolution of Pseudobulbar Affect due to Petrous Meningioma After Temporal Lobectomy for Epilepsy

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Rationale
Pseudobulbar affect (PBA) is a disabling condition which can be refractory to pharmacological intervention. However, there have been very few reports of surgical intervention resulting in resolution of PBA.

Method
We present a case report and review pertinent literature.

Results
A 60-year-old woman with medically refractory epilepsy since age 47 years had been diagnosed with an unresectable left petrous apex meningioma extending inferiorly along the clivus at age 37 years. Neuroimaging revealed mass effect laterally towards the mesial temporal region, medially upon the midbrain and pons, and encasement of the left cavernous internal carotid artery. Disabling features of PBA were persistent for the past five years, without evidence of other psychiatric differentials such as bipolar disorder. Electroencephalography characterized seizures of left temporal origin, which continued to occur every three days despite extensive anti-epileptic drug trials. She underwent anterior temporal lobectomy and mesial temporal resection for seizure control. By two weeks postoperatively, the PBA had subsided. Neuroimaging showed slightly less mass effect from the meningioma on the brainstem. Resolution of PBA has been previously reported on resection of a petroclival meningioma. In our patient, although resection of the meningioma was not possible, PBA resolved on resection of adjacent temporal lobe structures. We discuss the possible mechanisms of this improvement, including decompression and relief of mild ischemia.

Conclusions
This is the first case, to our knowledge, of resolution of PBA after temporal lobectomy for epilepsy associated with an unresectable petrous meningioma. We hope that this will help guide future care in similar presentations.

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Abstract 22

Transient Resolution of Motor and Vocal Tics following Left Temporal Lobectomy for Treatment of Refractory Epilepsy

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Rationale
Tic exacerbation after non-dominant temporal lobectomy is reported, this case elucidates the role of dominant temporal lobe in tic circuitry.

Method
Case Report and review of literature

Results
We present a 23-year-old right-handed male with developmental delay, frequent partial seizures, and a longstanding Torrett's syndrome. His seizures involved activity arrest, delayed forced right head and gaze version and right arm extension before secondary generalization. His MRI of brain indicated bifrontotemporal cortical malformation more severely affecting the left side. Video-EEG monitoring captured four left temporal seizures and frequent interictal left temporal epileptiform discharges. Neuropsychology battery indicated more prominent dysfunction of the dominant temporal lobe. Left hemispheric language dominance was confirmed by fMRI. The patient underwent a standard left anterior temporal lobectomy with intraoperative electrocorticography and language mapping. Postoperatively, he became seizure free for four weeks and for six weeks there was full resolution of his motor and vocal tics. However, after the sixth week, patient's vocal and motor tics recurred and gradually progressed to baseline intensity.

Conclusions
A resection of the dominant anterior temporal lobe in this patient resulted in temporary suppression of his motor and vocal tics. Nucleus accumbens, in association with mesial temporal structures, is involved in the tic circuitry in monkeys. Therefore, we hypothesize that the dominant anterior temporal lobe may provide a positive feedback into the circuitry involved in the activation of the motor and vocal tics. Conversely, resection of the non-dominant temporal lobe aggravates tics suggestive of providing negative feedback into the tic circuitry.

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Abstract 23

Carbamazepine-Induced Dyskinesias Confused for Seizures

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University of British Columbia

Rationale
Carbamazepine increases dopamine transmission and may contribute to movement disorders such as dyskinesias.

Method
Case report and literature review.

Results
A woman with childhood-onset biopsy-confirmed left hemispheric Rasmussen's encephalitis did not receive disease-specific treatment until presentation at age 47 years with a spastic right hemiparesis, hemisensory deficit and hemianopia correlating with marked left hemisphere cerebral atrophy. Right hemibody clonic seizures co-occurred with bilateral asymmetric tonic seizures, right hemiballismus, hyperkinetic oral movements and head drops without EEG correlate. Immunotherapy was ineffective, hence she underwent a functional hemispherotomy at age 48 years. While the surgery resolved her right hemiclonic seizures and hemiballismus, she remained disabled by innumerable daily paroxysmal head drops which co-occurred with involuntary non-suppressible mouth movements, grunting and variable alterations in responsiveness, verbal output and swallowing. The spells clustered over hours and comprised the bulk of her waking day, yet resolved in sleep. While these were originally suspected to reflect ongoing seizures, they were unresponsive to benzodiazepines or AED adjustments. Video EEG did not show any electrographic ictal correlate and clarified that the 'head drops' were related to involuntary activation of neck flexors as opposed to cervical atonia. Her longstanding carbamazepine was weaned in the context of symptomatic toxic drug levels (dizziness, diplopia, nausea). Thereafter, the spells have improved dramatically such they now occur only briefly every 7-10 days while off carbamazepine.

Conclusions
Very limited evidence is available on the dyskinesia-inducing potential of anti-seizure medications, yet this instructive case highlights that such symptoms may be confused for seizures and improve with medication discontinuation.

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Abstract 24

The Critical Importance of Implementing a First Seizure Clinic in a Comprehensive Epilepsy Program: Key Learnings from the Halifax Experience

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Rationale
Streamlining patient flow in epilepsy programs (EP) has been identified as a priority to improve quality of care for people with epilepsy (PWE). First Seizure Clinics play a critical role in this scenario. The Halifax First Seizure Clinic (HFSC) was developed systematically to serve as an innovative portal to an existing EP.

Method
The HFSC was implemented in 2008 following a systematic approach with a database, multimodal assessment, an integral research component, and a shared specialist-nurse practitioner care model.

Results
The HFSC was well received by patients and the referring networks. Wait times for first seizures (FS) assessments reduced from > 6 months to less than 2 weeks. Total registered patient visits almost tripled within 5 years; 2010 (n= 322) versus 2015 (n=828). Clinical pathways were entirely redesigned to increase efficiency with special focus on new Emergency Department referral algorithms. Time to identifying potential surgical candidates and patients with psychogenic non-epileptic seizures dramatically improved. A grant-based research component was essential; providing early MRI and epilepsy syndrome classification and compensating for health care insufficiencies . 19 publications resulted from the prospective cohort approach with new perspectives on clinical outcomes, mechanisms of pharmacoresistance, role of psychiatric comorbidities and cognition, epileptogenicity of focal cortical dysplasias, and early occurrence of SUDEP.

Conclusions
The HFSC experience underlines the importance of new service portals in EPs and provides longitudinal systematic follow-up of PWE. The learnings were significant with regards to health care system performance and challenges and new insights in disease evolution and care models.

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Abstract 25

A Patient-General, Low-Complexity Seizure Anticipation Algorithm

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Rationale
Responsive electrical neurostimulation is an emerging therapy for epilepsy. This technology works by detecting that a seizure is imminent or has just begun, and then electrically stimulating the brain to prevent or abort the seizure. Current commercially available devices are effective at reducing seizure frequency but are very unlikely to produce seizure freedom, which is critical to significantly improving patient quality of life. Current devices use very simple algorithms for seizure anticipation/detection in order to minimize device energy demands and could likely perform much better with more sophisticated detectors. The goal of this project was to develop a next-generation seizure anticipation algorithm that uses more sophisticated pattern classification techniques, while still being simple enough to meet the physical constraints of an implantable device.

Method
We trained a support vector machine classifier on archived intracranial electroencephalographic (iEEG) seizure recordings from eight patients (61 seizures). The input features consisted of bandpassed signal magnitude in conventional frequency bands, with five different degrees of temporal smoothing. The classifier was trained to detect any time point between -4 and +9 seconds of the clinician defined seizure onset.

Results
Algorithm balanced accuracy performance was 80%. All seizures were detected within 3 seconds of onset on average but with frequent false positives.

Conclusions
Our current algorithm achieves excellent sensitivity but with mediocre specificity. We will attempt to improve specificity by adding additional features, training on more data, and causally smoothing classifier output.

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Abstract 26

Amygdalar Physiological Alterations Parallel Interictal Emotional Impairment Associated with Seizures

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University of Calgary

Rationale

Comorbid psychiatric disorders are common in patients with epilepsy. These comorbidities include depression, anxiety, psychoses, and cognitive dysfunction. It has been extensively documented that temporal lobe epilepsy, the most prevalent form of adult epilepsy in humans, is often associated with interictal memory deficits and negative emotional disturbances. However, the underlying mechanism of seizure-induced emotional impairment is still unclear. We investigated whether amygdala kindling caused chronic interictal behavioural alterations in memory and emotionality. We then correlated the seizure-induced behavioural changes with alterations in excitatory and inhibitory transmission within the amygdala.

Method

Kindling procedure consisted of 20, once daily electrical stimulation (1 ms, biphasic square-wave pulses, 60Hz for 1s) with a stimulation current 20% above the initial afterdischarge threshold. One week after the last evoked sham or kindled seizure rats were tested in the elevated plus maze task to assess anxiety and fear conditioning to test fear memory dynamics. In the same rats, patch clamp recordings of pyramidal neurons of the basolateral amygdala were performed to parallel behavioural alterations with changes in intrinsic neuronal excitability and glutamate and GABA transmission.

Results

Preliminary data show alterations of the emotional behaviour and fear memory in rats subjected to amygdala kindling relative to the sham group. Moreover, behavioural emotional alterations were associated with dysregulation of the GABA synaptic transmission, increased glutamate transmission and increased basal neuronal excitability.

Conclusions

These results demonstrate that repetitive seizures cause long-lasting changes in amygdala physiology, which is paralleled with emotional disturbances.

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Abstract 27

Carbon Dioxide and Oxygen as a Potential Treatment for Postictal Hypoxia

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Rationale
Seizures result in various postictal behavioural alterations, including limb weakness (Todd's Paresis) and memory deficits (amnesia). These alterations result from a postictal hypoxic/hypoperfusion event caused by local vasoconstriction (Farrell et al., 2016). A mixture of 5% carbon dioxide (CO2) and 95% oxygen (O2) may be a viable treatment method for the postictal hypoperfusion event. CO2 acts a potent vasodilator that may attenuate local vasoconstriction allowing greater delivery of the exogenous O2 to the site of hypoxic insult. This study examined whether a combination of CO2 and O2 could attenuate the local postictal hypoperfusion event.

Method
Rats had seizures elicited in the hippocampus while local oxygen levels were recorded before, during, and after seizures. Shortly after seizure termination, rats were placed in a chamber and administered atmospheric gasses (control group) or gas mixtures of CO2 and O2 (experimental group). Local oxygen profiles were evaluated to determine efficacy of treatment.

Results
A mixture of CO2 and O2 raises hippocampal oxygen levels

Conclusions
A mixture of CO2 and O2 can raise hippocampal O2 levels and may be a viable treatment for postictal behavioural alterations that could potentially be translated to a clinical setting.

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Abstract 28

Ictal Magnetoencephalography in Children Undergoing Presurgical Evaluation for Intractable Epilepsy

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Rationale
Ictal events are rarely captured in routine magnetoencephalography (MEG) recordings due to the typically short duration of such recordings. However, captured seizures could be of considerable value for outlining the seizure onset zone non-invasively given the unique combination high temporal resolution and good spatial resolution afforded by MEG.

Method
We recorded MEG in 25 children (age range 5-18 y.o.) with intractable epilepsy who underwent presurgical evaluation at the Montreal Children's Hospital from 2015 to 2017. Simultaneous EEG and video were recorded together with the MEG. Recording duration ranged from 45 minutes to 7 hours (one patient was recorded overnight sleeping in the MEG). PET, SPECT, and 3T MRI were obtained for all patients. Magnetic source imaging of MEG data and time-frequency analyses of preictal and ictal time windows contrasted to baseline recordings were performed to localise the seizure onset zone.

Results
Clinical seizures were recorded in 4/25 (16%) of patients, including 14 seizures in the one patient that was recorded overnight. All seizures were confirmed by the patient or their caregiver and semiology was recorded on video. Preictal spiking had the highest value for localising the seizure onset zone, but time-frequency analyses of activity in the beta to gamma range also proved valuable.

Conclusions
Ictal MEG in children is feasible and could contribute to the localisation of the seizure onset zone as part of the presurgical evaluation. Overnight MEG recordings are proposed as a way to increase the yield of the technique. Further work will explore concordance with post-surgical outcomes.

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Abstract 29

Social Outcomes of Adults with Childhood-Onset Epilepsy: A Systematic Review and Meta-Analysis

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Rationale
Population-based studies of adults with childhood-onset epilepsy find an overall favorable outcome in terms of seizure control. Although social outcomes in this group are often poor, some studies find social outcomes similar to matched controls. The goal of this study was to systematically evaluate the literature evaluating social outcomes, namely education, employment, income, romantic relationships, and independence, of adults with a history of childhood-onset epilepsy.

Method
A comprehensive search of MEDLINE, EMBASE and PsycINFO for studies published in English between January 1, 1987 to January 30, 2017 identified 4517 articles. All articles were screened by two independent reviewers. We present preliminary results relating to education, employment and income; 360 articles underwent full-text screening, yielding 17 eligible articles. Data extraction relating to romantic relationships and independence are ongoing.

Results
Among population-based studies, 52-78% of patients had completed secondary school, 31-73% had completed some post-secondary education and 23-24% completed college or university. Similarly, 53-77% were currently employed or enrolled in full-time education. Studies with matched controls showed that patients had poorer education attainment, employment and annual income. Among patients with "epilepsy-only" (no neurological history and/or no intellectual disability), 60-98% had completed secondary school and 66-97% were employed. Results were similar among studies evaluating adults who underwent epilepsy surgery in childhood.

Conclusions
This is the first systematic review evaluating the social outcomes in adults with childhood-onset epilepsy. Preliminary results suggest that patients with "epilepsy-only" have similar social outcomes to matched controls. Factors associated with social outcomes will be evaluated.

This project has not received any funding.

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Abstract 30

Recognition of Psychogenic Nonepileptic Seizures Based on Semiology

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Rationale
Psychogenic nonepileptic seizures (PNES) are similar in semiology to epileptic seizures (ES), but are caused by a psychological process rather than abnormal electrical discharges in the brain. Ictal semiology interpretation is important for correct diagnosis and adequate treatment, whether in the context of an acute or elective setting. No study has evaluated the ability of different Canadian health care professionals to distinguish PNES from ES based on seizure semiology.

Method
In our study, we showed in a random mix 36 videos of PNES or ES (18 each) and asked 198 participants to classify each seizure. The performance regarding PNES diagnosis was calculated for each group using sensitivity, specificity and area under curve (AUC) values. AUC values were derived from summary receiver operating characteristic curves (SROC). Furthermore, the statistical difference between AUCs of epileptologists (as the reference) and the other groups of health care professionals was calculated.

Results
The ascending order of correct recognition of PNES from ES was the following: undergraduate medical students, emergency physicians, neurology residents, neurologists and epileptologists. Furthermore, undergraduate medical students' performance was worse than luck whereas epileptologists' performance (AUC=95%) was significantly better compared to the other health care professionals ($p<0.01$).

Conclusions
These results indicate that a higher level of medical knowledge allows for better visual recognition of PNES. On the contrary, a lower level of medical knowledge may lead to a tendency to incorrectly diagnose PNES as ES. This underscores the importance of medical education and has practical implications for the management of patients with seizures.

Funding sources : Canadian League Against Epilepsy (CLAE) (Canadian Epilepsy Alliance, UCB Canada and Sunovion Pharmaceuticals)

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Abstract 31

An Assessment on the Efficacy of VNS in Generalized Epilepsy

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Rationale
The VNS (Vagus Nerve Stimulation) is a type of neuromodulation therapy used in patients with focal epilepsy, usually reserved for those who are not candidates for resective surgery. However, there is not clear evidence if it has the same effect in all types of epilepsy. Our aim is to assess how effective this treatment is in those with generalized tonic-clonic (GTC) seizures in the context of generalized epilepsy.

Method
We interrogated the database of the Epilepsy program at Western University and identified those patients with generalized epilepsy, who underwent VNS implantation, since this treatment became available in Canada, until March 2017.

Results
A total of 16 patients with history of generalized epilepsy, underwent VNS implantation in our center. The mean age of implantation was 27.9 years (range:18-51), 10 patients (62.5%) were male. Mean follow up was 61.9 (5 to 192 months). Mean number of previously tried antiepileptic drugs was 3.4 (range: 2-9) and mean number of AEDs currently in use was 2 (range: 2-6). The frequency of GTC seizures range from daily to several per year. After the implantation, none of the patients was GTC seizure free. Five (31.3%) had a more than 50% reduction in the frequency of seizures. Only one patient developed an infection, while 8 of them had either pain in the neck or voice changes. None of them required explantation. The average output current was 2mA, signal frequency of 30 Hz, pulse width of 500μSec, signal on 45 sec, signal off 5 min.

Conclusions
VNS appears to be a therapy effective not only in focal epilepsy, but also in reducing the number of GTC seizures in those with generalized epilepsy.

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Abstract 32

Differences in Sudep Identification Among Neurologists and Pathologists

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Rationale
Sudden unexpected death in epilepsy (SUDEP) is the sudden, unexpected death of a person with epilepsy when a post-mortem examination does not reveal a cause of death. Researchers classify SUDEP as Definite, Definite Plus (when a comorbidity may have contributed to death) and Non-Definite (autopsy not done or revealed competing cause of death). Pathologists do not use a standard approach for SUDEP classification. To understand how pathologists classify SUDEP, we examined the cause of death on post-mortem reports in cases of sudden death in people with epilepsy.

Method
To identify potential SUDEP cases, we screened autopsy summaries of deaths investigated by the Ontario Forensic Pathology Service between January 2014 and June 2016 using a language processing script. We manually reviewed those identified, and using post-mortem reports, classified into above categories. Pathologist determination of cause of death was compared to research classification.

Results
From 15229 autopsies, we identified 499 cases of epilepsy- or seizure-related deaths. Manual review identified 258 potential SUDEP cases. After post-mortem review, 82 were classified as Definite, 29 Definite Plus, 32 Non-Definite. Among Definite SUDEPs, pathologists classified cause of death as SUDEP (72%), epilepsy (6%), seizure disorder (6%), and unascertained (7%). Slight regional variances were detected across Ontario.

Conclusions
Ontario pathologists classify most Definite SUDEP cases as SUDEP. However, 19% of SUDEP cases were not identified by pathologists, suggesting a different approach to death determination between SUDEP-focused researchers and forensic pathologists. Standardization of SUDEP identification could improve consistency, allowing for better case ascertainment, and facilitating collaborative research opportunities.

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Abstract 33

Systematic Review of Unmet Healthcare Needs in Patients with Epilepsy

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Rationale
Patients with epilepsy (PWE) are more likely to have unmet healthcare needs than the general population. This systematic review assessed the reasons for unmet needs in PWE.

Method
Medline, Embase, PsycINFO, Cochrane and Web of Science databases were searched using keywords: unmet healthcare needs, treatment barriers, and access to care. The search included all countries, adult and pediatric populations, survey and qualitative studies, but excluded non-English articles and articles published before 2001. Reasons for unmet needs were extracted.

Results
Nineteen survey and 22 qualitative studies were included. Three survey and five qualitative studies excluded patients with comorbidities. There were twice as many studies on unmet mental healthcare needs as there were on unmet physical care needs in PWE. Poor availability of health services, accessibility issues, and lack of health information contributed to unmet needs in both Western and developing countries. Lack of health services, long wait lists, uncoordinated care and difficulty getting needed health information were prevalent in the United States (U.S.) as well as countries with universal healthcare systems. However, unmet needs due to costs of care were reported more commonly in studies from the U.S.

Conclusions
This systematic review identified reasons for unmet needs in PWE across different countries, which will inform specific interventions required to address these unmet needs. Unmet needs may have been underestimated due to exclusion of PWE with comorbidities in some studies. Additional studies are needed to understand the contribution of comorbidities to unmet needs, and their interaction with caregiver and family factors.

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Abstract 34

Assessing Cognitive Reserve in Patients with First Seizure or Newly Diagnosed Epilepsy

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Rationale
Many patients with epilepsy will develop some degree of cognitive impairment, but there is no reliable way to identify those who are at increased risk. 'Cognitive reserve' (CR) has been proposed to explain the finding that people with extensive neuropathology may be cognitively normal. There is no consensus around how to accurately measure CR, and there are few studies applying this concept to predicting cognitive impairment in patients with epilepsy. We are developing a composite measure of CR that reflects the diverse ages and developmental stages of this population.

Method
16 participants were recruited as part of a larger study evaluating early cognitive changes in patients with first seizure or newly diagnosed epilepsy. During a tailored neuropsychological assessment, we collected data on the following measures of cognitive reserve: occupational attainment, verbal IQ, years of education, and engagement in leisure activities.

Results
Occupational attainment is significantly correlated with years of education ($r=-0.7$, $p<0.01$). However, there are no significant correlations between either verbal IQ or engagement in leisure activities and any of the other measures of CR.

Conclusions
We propose that there are independent mechanisms underlying CR, which may vary across a broad range of age, educational, and occupational development. An assessment of CR must therefore account for multiple protective factors. We are applying this new concept of CR to testing i) whether patients with low CR are more likely to demonstrate cognitive dysfunction at the time of first assessment, and ii) whether low CR predicts a more complicated clinical course.

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Abstract 35

The Burden and Predictors in Drug Resistant Epilepsy: A Systematic Review and Meta-Analysis

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Rationale
A proportion of patients continue to have recurrent seizures despite optimal pharmacological treatment. The burden of drug resistance and its predictors remain uncertain. Different studies have reported widely varying estimates, using varying definitions of drug resistance. We aim to conduct a systematic review and meta-analysis to identify the incidence and prevalence of drug resistant epilepsy as well as the predictors and correlates for this condition.

Method
For this study, we developed a search strategy in consultation with a medical librarian. We searched the electronic databases Ovid Medline, Ovid Embase, and Web of Science. We hand-searched relevant journals and conference proceedings. The full study protocol is published in the PROSPERO international prospective register of systematic reviews.

Results
Two reviewers independently screened each of the 8,873 titles and abstracts followed by 485 full-text articles. After exclusions were made, 95 relevant articles were identified. Thirty-four articles report the prevalence and or incidence of drug resistance, 17 report predictors and correlates of drug resistance, and 44 report on both. Full analysis of these articles and a meta-analysis are underway.

Conclusions
Drug resistant epilepsy is a major challenge but uncertainty remains. The findings of our study will allow clinicians and researchers to better understand the burden of drug resistant epilepsy as well as help predict its occurrence. Such better understanding will help provide for the best care of these people.

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Abstract 36

A Longitudinal Cohort Study on the Impact of the Clobazam Shortage on Patients with Epilepsy: A Patient Perspective

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Rationale
Drug shortages in Canada are occurring at an increasing rate. From May to October 2016 there was a shortage of the Level I critical antiepileptic drug, clobazam. Therefore, we aimed to study the impact of the clobazam shortage on patients with epilepsy.

Method
Calgary's Comprehensive Epilepsy Program patients who were taking clobazam were approached to participate in the study. Baseline data included clinical variables and pre-survey patient-reported outcomes (PROs) from the clinic prospective registry. We used a mixed methods cross-sectional questionnaire via telephone. We analyzed quantitative data using descriptive methods and qualitative data using a phenomenological approach.

Results
Of the 85 eligible patients, 71 (84%) agreed to participate. Participants ranged from 18-78 years old and 59.2% of participants were female. Overall, 80% of participants were subjected to some form of medication change due to the shortage. No significant differences were found in the pre- and during-shortage PRO data for the medication change subgroup. However, six important themes emerged regarding the impact of the AED shortage on patients: (1) communication and awareness (2) burden on patients and caregivers (3) physical impact (4) psychological impact (5) health care provider assistance in navigating the shortage and (6) policy change.

Conclusions
There is a lack of research on the impact of drug shortages from patients' perspective. We identified important themes on the impact of drug shortages on epilepsy patients and make recommendations on how to mitigate this impact. Further research is needed to better understand drug shortages from the patient's perspective.

Pediatric Epilepsy

Abstract 38

The Psychodevelopmental Impact of Epilepsy: Eriksonian Formulations at Different Ages

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Rationale
Early influences in psychological development can confer vulnerability to adult psychiatric presentations. However, few studies have explored the psychological impact of epilepsy arising in youth on adult presentations with neuropsychiatric aspects of epilepsy.

Method
We present two case reports and compare them from the perspective of Erikson's stages of psychosocial development.

Results
Two women with medically refractory epilepsy experienced onset of seizures at different ages. Patient 1, with eyelid myoclonia with absences, had seizure onset at age 7 years. She presented with social anxiety disorder since her teens which was ongoing into her late twenties. Patient 2, with non-lesional left temporal epilepsy, had seizure onset at age 15 years. She presented with a major depressive episode at 21 years in the context of interpersonal experiences which recapitulated earlier life challenges related to her schoolmates' initial reaction to her diagnosis with epilepsy. The cases are explored in detail. From an Eriksonian perspective, these patients experienced onset of seizures in the stages of 'Industry versus Inferiority' and 'Identity versus Role Confusion', respectively. The different psychiatric outcomes in these two cases are compared against the background of the different psychodevelopmental tasks which epilepsy interfered with in each developmental stage. This includes symptom chronicity and development of self-image versus perceived image in the eyes of others.

Conclusions
An Eriksonian approach can be useful in understanding the psychodevelopmental influence of epilepsy on adult psychiatric presentations. We encourage further studies to better characterize these dynamics and to inform developmentally sensitive psychotherapy.

Pediatric Epilepsy

Abstract 39

Intracranial Infraslow Activity Using Depth Electrode Recordings of Eight Pediatric Patients with Frontal Lobe Epilepsy

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Rationale
Analysis of infraslow EEG activity (ISA) has shown potential in the evaluation of patients with epilepsy. Infraslow EEG activity analysis may also provide insights in determining the origin of focal epileptogenic focus

The purpose of this report is to present our experience of eight children with drug-resistant epilepsy, who underwent robotic-guided intracranial depth electrodes placement whose intracranial recording demonstrated lateralized infraslow ictal pattern changes that preceded the onset of the recorded clinical seizures

Method
The continuous prolonged intracranial depth EEG recording of eight children with severe drug-resistant epilepsy were obtained as part of the intracranial evaluation to determine the epileptogenic zone. During the recording multiple habitual seizures were captured. In addition to the conventional settings, analysis of the EEG infraslow (ISA) activity was undertaken using LFF 0.01 AND HFF of 0.1 Hz respectively to determine the presence of infraslow activity

Results
Focal unilateral infraslow activity was identified in all cases. The recorded lateralized/focal infraslow activity preceded the onset of the clinical seizures in all the recorded habitual seizures. The identified infraslow activity was concordant with the conventionally identified epileptogenic zone.

Conclusions
Ictal infraslow activity can be detected prior to the onset of clinical seizures in children with drug-resistant epilepsy. Identification of focal infraslow activity (ISA) can help in determining and localizing the epileptogenic zone in patient with drug-resistant epilepsy

Pediatric Epilepsy

Abstract 40

Psychosocial and Dietary Support Group for Caregivers of Patient's on the Ketogenic Diet: Topics and Caregivers' Feedback

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Rationale

The ketogenic diet is an effective therapy for children with refractory epilepsy, yet there are factors that may impact the experience of the diet, and complicate compliance. McNamara et al. (2012), identified ways medical providers can better support families, including tele-practice resources, mentors, improved food selection, and formal classes. In addition to ketogenic related stressors, parents of children with epilepsy experience major psychosocial stress related to decreased participation in social and leisure activities, increased emotional disturbances (frustration, anger, guilt feelings), as well as economic problems (Thomas et.al., 1999).

Method

The social worker and ketogenic dietitians at McMaster Children's Hospital, organized a focus group to identify the relevant topics. Once topics were identified, parents of children on the ketogenic diet were invited to meetings, where a topic was discussed. Parents from twelve families attended the ketogenic parent group over the previous year.

Results

The focus group discussion highlighted four main areas of interest, including: ketogenic diet strategies (illness management, holiday tips, eating out), financial subjects (tax implications, government financial support programs), community support programs/services (epilepsy community agencies, home care) and miscellaneous topics (caring for the caregiver, database for diet related products). Parents from twelve families have attended ketogenic parent group over the previous year. Preliminary feedback is that attendance of this support group is both informative and an excellent avenue of support.

Conclusions

The ketogenic parent group is of significant value in allowing caregivers to network amongst themselves which helped to increase their social/leisure activity, while learning about ketogenic diet implementation strategies and resources.

Pediatric Epilepsy

Abstract 41

Mutations in Infants 0 to 3 Years of Age with New Onset Epilepsy

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CHU Ste-Justine

Rationale
The growing availability of genetic testing has considerably increased the number of genes recognized as having causal links to epileptic encephalopathies. We sought to describe the frequency and types of genetic mutations in infants 0 to 3 years old with new-onset epilepsy.

Method
We prospectively recruited infants with new-onset epilepsy seen at Ste-Justine Hospital. Etiological investigation included metabolic workup, 3T-MRI, and CGH. Targeted sequencing was completed on a clinical basis in select cases.

Results
Forty-six infants with seizure onset within 3 years of life were recruited. Genetic variants were identified in 8 children (17.4%). Three mutations were identified among the 18 infants with infantile spasms, 4 among the 7 with generalized epilepsy, and 1 mutation was found in the 21 infants with focal epilepsy. All infants with genetic mutations had critical developmental delay in at least 2 spheres, whereas 47% of infants without genetic findings had normal developmental or delay in only one sphere.

Conclusions
Although genetics are believed to play a causal role in 40 to 70% of epilepsies, we were able to identify genetic variants in fewer than one fifth of children using CGH and selective targeted sequencing. Our data also suggests that performing copy number variant analysis may not be cost-effective in children with normal development or isolated developmental delay. We believe that additional testing using whole exome analysis would allow identification of underlying causes in a higher proportion of infants. These discoveries will allow elucidation of the neurobiology behind more epilepsy disorders, paving the way for personalized treatments.

Pediatric Epilepsy

Abstract 42

The Efficacy and Tolerability of the Ketogenic Diet in Treatment of Epileptic Spasms after Failure of Steroids and Vigabatrin

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Rationale

To evaluate the efficacy and tolerability of the early use of the ketogenic diet (KD) in infants with Epileptic Spasms (ES) who are refractory to Vigabatrin and/or steroids (ACTH/oral prednisolone)

Method

This is a retrospective study of all infants with ES who received the KD at our hospital between 2014 to 2016. All infants with ES with severe epileptic encephalopathy refractory to vigabatrin and/or steroids were treated with the KD. The information of efficacy and side effects of KD were obtained. Secondary outcomes of EEG results and neurodevelopment status were collected. The cessation of ES was defined as the absence of clinical spasms from within 14 days of commencement of treatment while electroclinical cessation of ES with resolution of hypsarrhythmia

Results

A total 10 infants were included in this study (8 males). The mean age of at onset of ES was 3.8 months (95% CI 0.8-6.8), and mean age at initiation of KD was 6.7 months (95% CI 3.4-10.0). Seven cases had West syndrome and three had Ohtahara syndrome. Among these, 3 (30%) had cessation of ES and hypsarrhythmia, 1 (10%) case had ES cessation for 3 months and then recurrence with improvement of hypsarrhythmia. In other 3 cases , they had >50% reduction of spasm with EEG improvement, 2 cases had no response and 1 case had deterioration. Nine infants tolerated the KD well and one cases experienced failure to thrive.

Conclusions

Ketogenic diet is a safe and potentially effective treatment for infants with epileptic spasms after steroid and vigabatrin therapy

Pediatric Epilepsy

Abstract 43

Targeted Therapy for Treatment Refractory Epilepsy in a Neonate with KCNT1 Mutation Associated with Poor Response to Quinidine but Marked Improvement to Potassium Bromide

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Rationale

The KCNTI gene is widely expressed in the human central nervous system. This gene encodes a Na+ activated K+ channel.One of the phenotypes is Malignant Migrating Partial Seizures of Infancy (MMPSI). It is characterized by polymorphous multifocal seizures and arrest of psychomotor development in the first six months of life. The previous case reports show quinidine is an efficacious treatment for seizures.

Method

We report a case who had poor response to quinidine, but had marked improvement with potassium bromide.

Results

Term baby boy was born at term followed by unplaned pregancy. He developed seizures shortly after birth. Following ineffective trials of 6 anti-seizure medications, this patient was trialed on oral quinidine which titrated up to a dose of 52mg/kg/d over time in a monitored setting. His seizures had no improvement. He subsequently had a trial of potassium bromide. The dosage of potassium bromide was gradually increased till reaching 3.5 mL twice a day, which is about 80 mg/kg. His mom noticed his seizure frequency has more than 50% reduction from 7 to 5 seizures per hour just to about 1 to 3 seizures an hour. They are all about 10-30 seconds in duration. She is not needing to provide any rescue medications. He is also wake in the daytime for several hours, and he can go a few hours without having any seizures.

Conclusions

We report a case of MMPSI and KCNT1 mutation R428Q with poor clinical response to quinidine, but his seizure had an apparent improvement,<50% reduction after the trial of potassium bromide.

Pediatric Epilepsy

Abstract 44

Determining the Needs of Epilepsy Patients, Caregivers and Healthcare Providers using the Ketogenic Dietary Therapy

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Rationale
The Ketogenic Diet is commonly used to treat specific types of treatment-refractory childhood epilepsy. Medical institutions worldwide have implemented diet clinics and administrative protocols specializing in the ketogenic diet. To date, there have been no nationwide studies performed to identify potential challenges and boundaries met by healthcare professionals and primary caregivers.

Method
We conducted a nationwide healthcare provider survey and patient/caregiver–focused interviews. The survey gathered data on current practices and protocols in ketogenic diet clinics across Canada. The interviews were semi-structured and discussed various aspects of the caregivers' process and experience with the ketogenic diet such as the initiation process, sources of information and ongoing support, financial impact, and impact on daily life.

Results
Twelve out of eighteen clinics responded to the survey. The data highlighted significant variation in resources, efficiencies, and quality of care amongst diet clinics. Other areas of improvement identified were related to methods of initiation, home monitoring and funding. Results of the phone interviews showed that parents/caregivers have positive perceptions of the care received during ketogenic diet administration. However, multiple areas for improvement were also identified. Caregivers reported challenges related to preparatory knowledge, side effects, measuring effectiveness and personal barriers.

Conclusions
Based on our results, the data collected and analyzed can be used to identify key problem areas for caregivers and healthcare providers administering the ketogenic diet. In order to deliver optimal care for children on the ketogenic diet and their families, targeted efforts at improving care in the aforementioned areas may be taken.

Pediatric Epilepsy

Abstract 45

Is a Single-Item Measure as Valid and Reliable as Multi-Item Scales in Assessing Quality of Life in Children with Epilepsy?

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Rationale
There is a need for brief, practical measures of quality of life (QOL) that can be used by health-practitioners aiming to monitor treatment progress of children with epilepsy. The current study investigated the psychometric properties of a single-item QOL measure, the Global Quality of Life in Childhood Epilepsy Scale (G-QOLCE).

Method
Data came from the Impact of Pediatric Epilepsy Surgery on Health-Related Quality of Life Study (PESQOL), a multicenter prospective cohort study (N = 118) with observations collected at baseline and 6-months follow-up on children aged 4 – 18 years. QOL was measured with the QOLCE-76 and KIDSCREEN-27. The G-QOLCE was an overall QOL question derived from the QOLCE-76. Construct validity and reliability were assessed with Spearman's correlation and intraclass correlation coefficient (ICC). Responsiveness was examined through distribution-based and anchor-based methods.

Results
The G-QOLCE showed moderate ($r \geq .30$) to strong ($r \geq .50$) correlations with composite scores and most subscales of the QOLCE-76 and KIDSCREEN-27 at baseline and 6-months. Caregiver anxiety and family functioning contributed most strongly to G-QOLCE scores over time. The G-QOLCE had moderate test-retest reliability (ICC range: 0.49-0.72) and was able to detect clinically important change in patient QOL (standardized response mean: 0.38; probability of change: 0.65; Guyatt's responsiveness statistics: 0.62 and 0.78).

Conclusions
Results offer promising preliminary evidence regarding the validity and reliability of the proposed single-item QOL measure. The G-QOLCE is a potentially useful tool that can be administered in a busy clinical setting to evaluate clinical status and impact of treatment outcomes in pediatric epilepsy.

Basic Science / Engineering

Abstract 46

EEG Changes after Repetitive Mild Blast Injury in Rats

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Rationale
Blast injury has become a more frequent cause of traumatic brain injury (TBI) with the increased use of explosive devices during war. Some soldiers are exposed to multiple blast injuries a day. In a study of veterans with a diagnosis of both epilepsy and TBI, blast exposure was the most common mechanism of injury, implicating a strong association with post-traumatic epilepsy (PTE) that needs to be investigated further. The purpose of this pilot project was to characterize the EEG changes in a rat model of repetitive, mild blast injury.

Method
Experimental blast injury was induced in rats twice daily for five days (repetitive blast group) versus chamber placement without delivery of blast pressure (sham group). Rats were implanted with electrodes and monitored with continuous video-EEG recordings for up to six months.

Results
50% of the repetitive blast group developed spontaneous spike wave discharges which were recorded from bifrontal electrodes, but not from the hippocampal or parietal electrodes. Animals exhibited freezing behavior but no other behavioral changes during these events which lasted up to 10 seconds. These discharges were not seen in sham animals.

Conclusions
Mild repetitive blast injury leads to EEG abnormalities in 50% of rats, consisting of runs of bifrontal spike wave discharges with accompanying freezing behavior. These preliminary data suggest that repetitive blast injury alters normal brain electrophysiology and may predispose to spontaneous seizures. Further investigation is needed to determine whether increased number or severity of repetitive blast injuries, or increased time post-injury, leads to the development of PTE.

Basic Science / Engineering

Abstract 47

Postictal Hypoperfusion/Hypoxia as a Mechanism of Sudden Unexpected Death in Epilepsy and Pharmacological Intervention with a COX-2 Inhibitor

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Rationale

Sudden Unexpected Death in Epilepsy (SUDEP) occurs when someone with epilepsy, who is otherwise healthy dies suddenly with no known cause. Our lab recently discovered a COX-2 mediated period of severe hypoxia during and following a seizure in the brain regions involved in the seizure which can cause cellular and behavioural dysfunction. We hypothesize that SUDEP occurs when seizure activity propagates to brainstem breathing centers causing severe local hypoxia leading to dysfunction of breathing and death. Further, that inhibition of COX-2 activity could rescue this severe hypoxia.

Method

Animals were treated with either ibuprofen (15mg/kg) 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 thoracic cavity.

Results

In both groups, 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. Preliminary data is suggestive that those mice who received ibuprofen survived several bouts of brainstem seizures and associated hypoxic events.

Conclusions

Our model replicates previous studies in persons with epilepsy showing that breathing failure is the precipitating cause of seizure-induced death. The severe local hypoxia observed in brainstem breathing centers immediately prior to apnea and death indicates seizure- induced brainstem hypoxia may be involved SUDEP. Moreover, this severe hypoxia may be rescued via the COX-2 inhibitor ibuprofen.

Basic Science / Engineering

Abstract 48

Vagal TRPV1-Mediated Respiratory Alkalosis Increases Susceptibility to Hyperthermic Seizure

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Rationale

Hyperthermia-induced respiratory alkalosis is linked to febrile seizures (FS). As transient receptor potential vanilloid-1 (TRPV1) receptors are expressed in peripheral and central structures involved in the respiratory response to hyperthermia, and are implicated in their heat sensitivity, we hypothesize that TRPV1 activation enhances hyperthermia-induced respiratory alkalosis, which in turn triggers FS in immature rodents.

Method

FS was induced in postnatal day 10 rats by the heated dry air method, and threshold temperature and latency assessed following i.p. or i.c.v. injection of TRPV1 agonist, piperine, and/or antagonist, AMG-9810, 5% CO2 exposure, TRPV1 deletion, bilateral vagotomy or DREADD-mediated inhibition of vagal TRPV1-containing cells. The ventilatory response to hyperthermia and consequent expired CO2 (indicative of respiratory alkalosis) were assessed with head-out plethysmography.

Results

Peripheral but not centrally administered piperine decreased seizure thresholds and exaggerated the hyperthermia-induced respiratory alkalosis. This pro-convulsant effect was attenuated by pre-treatment with AMG-9810, and completely abolished in TRPV1 KO mice, demonstrating that the piperine effects were mediated entirely by the TRPV1 receptor. 5% CO2 abolished seizures in 44% of piperine-treated animals and prolonged the seizure thresholds in the remainder. Bilateral vagotomy reversed the effects of piperine on FS expression and respiratory alkalosis, and DREADD-mediated inhibition of vagal nodose ganglia TRPV1-containing cells also reversed the pro-convulsant effects of piperine.

Conclusions

These data suggest that sensitization of TRPV1 receptors prior to hyperthermia, increases susceptibility of immature rodents to FS via a vagally-mediated mechanism involving respiratory alkalosis, thus identifying a novel peripheral anatomical and molecular target for FS drug development.

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Basic Science / Engineering

Abstract 49

COX-2 Oxygenation of Endocannabinoids Mediates Postictal Hypoxia

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Rationale
Recent studies have implicated COX-2 in the metabolism of the endocannabinoid, 2-arachadonoylglycerol (2-AG). This novel pathway produces prostaglandin glycerol esters (PG-Gs). A biological setting in which the brain produces PG-Gs is unknown and their physiological effects remain elusive. Since both COX-2 activity and endocannabinoid production occur in an activity-dependent manner, seizures may be a setting where PG-Gs are synthesized. Our previous research revealed that COX-2 plays a major role in mediating postictal hypoxia, but how COX-2 signals is unknown. Here we tested the hypothesis that COX-2 oxygenation of 2-AG, and not the conventional substrate arachidonic acid, mediates hypoxia following seizures.

Method
We measured local tissue oxygenation in the hippocampus following electrically-induced seizures in awake, freely-moving rats. We pre-administered substrate-selective COX-2 inhibitors and manipulated the endocannabinoid enzyme systems with pharmacological tools to observe their effect on postictal hypoxia. Lastly, we used mass spectrometry to measure eicosanoid levels before and after seizures.

Results
Mass spectrometry revealed that seizures transiently and profoundly promote the synthesis of endocannabinoids and engagement of COX-2 activity. Furthermore, selective inhibition of endocannabinoid oxygenation, while leaving the arachidonic acid pathway intact, prevented postictal hypoxia. Subsequent pharmacological experiments pointed to 2-AG as being the chief endocannabinoid involved.

Conclusions
This research provides a key advance in our understanding of brain COX-2 signaling and identifies more targeted treatments for postictal hypoxia.

Basic Science / Engineering

Abstract 50

Potassium Redistribution in Neocortex in Vivo: the Role of Gap Junctional Communication

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Rationale
Resting extracellular potassium (K+) is strongly regulated by inter-astrocytic gap junctions. Seizures raise extracellular potassium. In turn, raised K+ increases brain excitability, triggering seizures, and in higher concentrations, blocking seizures. Hence K+ redistribution is a critical but poorly understood seizure process.

Method
Two double-barrelled potassium or 2 field potential electrodes were implanted 4mm apart in vivo in mouse neocortex. 50mM K+ was injected focally near one of the electrodes, and extracellular K+ levels or the local field potential were measured before and after gap junctional blockade.

Results
Focal application of 50 mM K+ could not maintain a sustained rise in K+ due to powerful local K+ buffering, but did cause a transient increase in K+ (e.g. from 1.2 to 8.9 mM lasting for 5.1 min) associated with a transient hyperpolarized local field potential (-20mV, 1.2min). In the remote electrode, following a delay (~20 sec), there was a smaller rise in K+ (7.4mM, 3.6min) and a hyperpolarized field potential (-16mV, 1min), hypothesized due to K+ redistribution via inter-astrocytic gap junctions.

Gap junctional blockade simultaneously increased the amplitude and duration of the local K+ response, and the local field response was moderately attenuated but greatly prolonged. From the remote K+ and field potential electrodes, both the K+ and field potential responses sometimes disappeared or were significantly attenuated in amplitude, and increased in duration.

Conclusions
Spatial buffering of raised extracellular K+ is mediated through gap junctional communication, most likely via astrocytes.

Epilepsy Surgery

Abstract 51

Canadian Pediatric Epilepsy Surgery Survey: Are We Doing More Surgery in Children? A Long-Term Follow-up Study

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Rationale
Despite evidence on the efficacy of epilepsy surgery in appropriately selected individuals and guidelines supporting its use, rates of epilepsy surgery have remained stable or have even declined. To date, a limited number of studies have examined nationwide utilization patterns of pediatric epilepsy surgery. Our objective is to compare the frequency of pediatric epilepsy surgery in Canada over a greater than 10-year period.

Method
All pediatric epilepsy centres (patients <18) in Canada were asked to complete a questionnaire to identify the number and type of epilepsy surgery procedures completed in 2015. Data was compared to a similar survey from 2003.

Results
Eleven centres were identified (100% response rate). A total of 201 procedures were performed in 2015, compared to 191 in 2003. Five centres were considered high volume (>15 procedures/year), compared to four in 2003. In 2015, lesionectomy and vagus nerve stimulator implantation (VNS) were the most common resective and non-resective surgeries, respectively. Compared to 2003, case volumes increased for lesionectomies and hemispherectomies. The frequency of temporal lobectomies, cortical resections, and palliative procedures were slightly lower over time, while VNS and intracranial investigations were relatively stable.

Conclusions
This study provides the first set of long-term data from all pediatric epilepsy centres in Canada and demonstrates that over a 12-year period the total number of pediatric epilepsy surgical procedures performed has modestly increased. This study offers an evidence-based examination of the utilization of pediatric epilepsy surgery in Canada, which may help inform decisions about future changes in the distribution of pediatric epilepsy surgical care.

Epilepsy Surgery

Abstract 52

A Nation-Wide Audit of Epilepsy Surgery for Adults

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Rationale
Epilepsy surgery is likely underutilized.1 The number of surgeries performed in adults has not only stagnated over the last few decades, but has begun to decrease.2,3 Our goal is to study the utilization of epilepsy surgery, using Canada as a model of a high-income country with ready access to comprehensive pre-surgical assessments and epilepsy surgery.

Method
We systematically identified all active adult epilepsy surgery centres in Canada. Our audit aimed to answer two questions: in 2015, what were the number and character of the epilepsy surgery procedures carried out; the human and physical resources available at each centre.

Results
A total of 12 adult centres were active in Canada in 2015, located in 6 of 10 provinces. We obtained complete data from all centres. Five provinces had 1-2 centres while Quebec had five. Eight centres performed > 15 therapeutic surgeries (curative or palliative). Per capita volume per province varied between 7.0 and 20.5 therapeutic surgeries per million adult residents (mean: 14.6; standard deviation: 3.9). Temporal lobe resections accounted for 59.8% of all treatments. Eleven of the 12 adult centres possessed facilities to carry out intracranial investigations. The number of therapeutic surgeries performed at a centre relative to the number of intracranial investigations varied between 1.4 and 9.0 (mean: 3.5; standard deviation: 2.2).

Conclusions
This study provides the first set of complete data regarding epilepsy surgery in adults in Canada. There is dramatic inter-centre and inter-province variability in the services provided. Further work is required to ensure optimum care for this vulnerable patient population.

Epilepsy Surgery

Abstract 53

Depth Versus Subdural Electrodes for Intracranial Electroencephalographic Monitoring in the Presurgical Investigation of Drug-refractory Epilepsy

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London Health Sciences Centre

Rationale

Intracranial electroencephalographic monitoring in the presurgical investigation of drug-refractory epilepsy can be performed using stereotactically implanted depth electrodes, or subdural electrodes and grids. At the London Health Sciences Centre Epilepsy Program, the practice has shifted from using subdural to depth electrodes starting in 2013. Only a few studies have compared both techniques with respect to feasibility and complications.

Method

Patient characteristics, periprocedural parameters and complications were acquired from a retrospectively-managed databank to compare depth and subdural electrode cases.

Results

A total of N=275 intracranial electroencephalographic monitoring cases were analyzed (n=101 depth and n=174 subdural electrodes). Both groups were of equal age (mean 33.8±11 and 32.1±12.6 years) and gender distribution (49.5% and 50.6% male). Patients undergoing stereoelectroencephalography had a mean duration of epilepsy of 18.7±12.4 years, used 2.4±1 antiepileptic drugs, and had a radiological focus in 69/101 (68.3%) compared with 104/174 (59.8%) in subdural cases. A third of the depth electrode patients had previous cranial surgery. There was no difference in length of stay (12.4±6.6 and 12.9±6.3 days). Implantation of one depth electrode took 14.8±4.6 min and exposed the patient to 3.7±2.6 rad*cm2 (dose area product) on average. Complications were generally low in both groups (hemorrhage 3% and 1.2%; infection 0% and 1.2%). Depth electrode deviation or postoperative inaccuracy was noted in 13/101 cases (12.9%).

Conclusions

For their equal safety profile, good feasibility and high patient acceptance, we prefer stereotactically implanted depth over subdural electrodes at our institution and aim to improve accuracy with our newly introduced stereotactic robot.

Epilepsy Surgery

Abstract 54

First Institutional Experience with Robot-assisted Implantation of Depth Electrodes for Stereoelectroencephalography

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London Health Sciences Centre

Rationale
Since the first implementation of a stereotactic robot for a brain biopsy by Kwoh in 1985, robots in neurosurgery have been further developed; among them, the NEUROMATE (RENISHAW), an image-guided, five degrees-of-freedom, computer-controlled robotic system is currently the most widely used. In the field of neurosurgery, one of its multiple applications entails the implantation of depth electrodes for stereoelectroencephalography (SEEG), but only few clinical studies have highlighted its advantages.

Method
The transition from 'manual' stereotactic Leksell frame-based to robot-assisted SEEG at the London Health Science Centre Epilepsy Program was analyzed with the main focus on databank-acquired operative time and complications.

Results
A cohort of N=101 patients with drug-refractory epilepsy undergoing depth electrodes implantation were reviewed (n=91 before and n=10 after the introduction of the robot). Baseline characteristics were well-balanced between groups. Operative time was significantly reduced from 142.9±44.5 to 98.3±36.3 min (15.3±4.5 to 9.3±2.5 min per electrode format; both $p<0.01$). Dose area product (16.8±28 vs. 10.38±3.6 rad*cm2 per electrode) and fluoroscopy time (41±67.5 vs. 36.8±13.8 sec per electrode) remained similar. There was no increase in the rate of complications, however, the first robot-assisted cases were challenged by inaccurately placed electrodes due to technical difficulties.

Conclusions
In our preliminary institutional series, robot-assisted SEEG reduces human error, enhances patient safety, and is less time-consuming than 'manual' Leksell frame-based SEEG after the learning curve has been overcome.

Epilepsy Surgery

Abstract 55

Technical Note: Stereotactic Leksell Frame-Based Depth Electrodes Implantation for Stereoelectroencephalography

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Rationale
For intracranial electroencephalographic monitoring, stereotactically implanted depth electrodes are increasingly used at epilepsy centres around the world. While the technical principles have essentially remained the same over the past 50 years, some technical nuances were modified with the progress in technology over time.

Method
Pearls and pitfalls from our experience with stereotactic Leksell frame-based depth electrodes implantation were identified and presented in a short technical note supported by an intraoperative video.

Results
A detailed description and a 60-second video on how to implant depth electrodes using the stereotactic Leksell frame is presented followed by an overview of the literature.

Conclusions
Neurosurgeons implanting depth electrodes for stereoelectroencephalography might find the technical nuances and caveats described in this technical note useful for their practice to avoid technical difficulties, hasten their learning curve and save time, improve accuracy and avoid complications resulting in higher patients' safety.

Epilepsy Surgery

Abstract 56

Filling the Gap in Post-Surgical Epilepsy Care: A Needs Assessment Study of Post-Surgical Epilepsy Patients

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Rationale
A good psychosocial outcome is not necessarily contingent on a good seizure outcome. Increasingly, "successful" epilepsy surgery is believed to be a combination of an acceptable seizure status and an individual's perception of an improved quality of life (QOL). Despite well documented issues of "the burden of normality" and "forced normalization" following surgery, and recommendations for a pre-surgical intervention, no study has specifically addressed the factors/variables necessary to design such an intervention.

Method
This is a qualitative study involving semi-structured interviews with post-surgical epilepsy patients from Toronto Western Hospital. A content analysis methodology was used to establish emerging themes derived from patients' experiences. A quantitative component involved administrating the QOLIE-31 questionnaire.

Results
Seventy-three patients ages 18-80 were interviewed and completed the QOLIE-31 survey. In this group 46 (63%) participants were female, with no significant difference in QOLIE-31 scores between genders (67.91 +/- 20 and 64.42 +/- 17, for males and females respectively; $p = 0.42$). To date, forty-five interviews have been analyzed with preliminary themes categorized into; 1) pre- and post-surgical concerns, 2) adjustment and coping strategies and; 3) recommendations. Different individual clusters, based on social locations, are being identified and compared.

Conclusions
These results may have profound implications for improving the surgical management of epilepsy and providing a platform for the creation and implementation of a pre-surgical intervention. In conjunction with our recently proposed predictive coding model of post-epilepsy surgery adaptation (submitted), our results lay out the groundwork for developing an intervention addressing patient predictions and expectations to fully realize the benefits afforded by epilepsy surgery.

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Epilepsy Surgery

Abstract 57

Anatomical Study of Complete Callosotomy in Fresh Cadaveric Brain Specimens: Technical Note

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Rationale
Patients affected by intractable seizures who are not candidates for focal resective surgery are indicated for a palliative surgical procedure, the callosotomy. In the majority of refractory epilepsy cases with significant atonic seizures callosotomy is accomplished over the anterior one half or two thirds of extension. Rarely the seizure spreads in posterior brain areas when we should perform the callosotomy posteriorly. Callosotomy has been performed in sequential operations (multistaged), but few authors have advocated to accomplish it in a single operation. It may be useful in severe Lennox Gastaut patients, although a few patients experience complete seizure control after callosotomy

Method
This study was accomplished from by dissecting and performing callosotomy in fresh cadaveric brain specimens

Results
In order to improve this technique the authors approached 2 heads of cadaveric specimens in a neutral position, with a bicoronal incision, and bifronto parietal craniotomy and through right interhemispheric approach, with a catheter placed in right lateral ventricle (simulating a live aptient) we can reach the whole extention of callosum body and perform the microsurgical section.

Conclusions
We must remind that the neuronavigation system may be useful in planning of the surgery, determining the size and side of craniotomy depending on the predominance of drainaing veins. Corpus callosotomy is usually intended to alleviate-not to achieve total control of epileptic seizures.