NEUROIMAGING

Abstract 1

3D Printed Brain Models as an Aid for Teaching Anterior Temporal Lobectomy

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Rationale
Additive manufacturing, otherwise known as 3D printing, has made it possible to create and rapidly prototype 3D designs for consumer and medical applications. Anterior temporal lobectomy (ATL) is one of the standard surgical approaches for the management of temporal lobe epilepsy, consisting of the removal of temporal neocortex and mesial temporal specimens. ATL can be challenging for neurosurgical trainees due to the complex spatial relationship between anatomical structures. Here we propose to develop a physical 3D-printed model as an aid for teaching temporal lobectomy.

Method
A left hemispheric pial surface mesh was computed using the FreeSurfer software from a T1 average of the MNI152 atlas. Using Blender and SpaceClaim, the hemispheric mesh was manually divided into three separate components: temporal neocortex, mesial temporal structures, and everything else. Each component was imported using Cura and printed independently on our in-house UltiMaker printer system using different coloured filaments.

Results
At the time of abstract submission, the initial prototype components have been printed at half the actual size with each component being easily disarticulated from the main model.

Conclusions
We have developed a prototype 3D printed model of an idealized (average) brain for facilitating the teaching of anterior temporal lobectomy. Initial experience suggests that the model can provide valuable spatial context regarding important surgical planes and neuroanatomical structures. The workflow can be easily extended for the creation of patient-specific 3D models as well as for other neurosurgical procedures.

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Abstract 2

Using Movie-Driven fMRI to Identify Abnormal Functional Connectivity in Intractable Focal Epilepsy

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The University of Western Ontario

Rationale

One third of persons with epilepsy (PWE) are medically refractory and rely on resective surgery for seizure control. Part of pre-surgical planning involves evaluating the integrity of functional networks. Given the widespread network disruptions in focal epilepsies, it is important to characterize the functionality of these networks during active engagement. We implemented a movie-driven fMRI technique that evokes reliable, time-locked BOLD signal fluctuations that are highly stereotyped across viewers [i.e., produce high inter-subject correlation (ISC)] in order to assess abnormal functional connectivity (FC) in PWE.

Method

Four pre-surgical TLE patients and 11 controls participated in resting-state (10-minute) and movie-viewing (8-minute suspenseful clip) fMRI runs in a 3T MRI system (Siemens Prisma). Representative timecourses from seven stable functional networks were extracted from participants' movie data. Mean intra-network ISC values for all participants were computed from pairwise correlations and z-scored to evaluate the degree of network asynchrony exhibited by each patient. Finally, we conducted single-subject global FC analyses within resting and movie-viewing states.

Results

The movie paradigm identified patients with significantly aberrant timecourses in seven perceptual and executive networks. Global FC analysis revealed that two patients, when compared to controls, displayed contrasting patterns of global FC abnormalities between resting and movie-viewing states. Both patients exhibited decreased FC during rest, and increased FC during movie-viewing.

Conclusions

Our findings suggest that movie-driven fMRI is sensitive to network alterations at the individual level, and that analyses of movie-driven data provide information about FC that complement those provided by resting-state data, and which may be valuable in pre-surgical evaluation.

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Abstract 3

Gradual Alterations of Structural-Functional Brain Networks in the Spectrum of Cortical Malformations

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Montreal Neurological Institute

Rationale
Malformations of cortical development (MCD) are a group of congenital anomalies recognized as a main cause of drug-resistant focal epilepsy. Emerging evidence suggests more distributed distributed pathological substrates, often exceeding the primary lesion. However, large-scale brain network organization has so far not been systematically assessed.

Method
In 154 MCD patients and 41 controls, we generated large-scale connectomes based on cortical-thickness covariance and resting-states functional connectivity. We compared network topology between groups based on clustering coefficient [Cp], path length [Lp], and rich-club indices. We divided the MCD cohorts into subgroups the histopathological subgroups based on their putative time course: focal cortical dysplasias (associated with abnormal cell proliferation), heterotopias (atypical migration), and polymicrogyrias (aberrant cortical organization). Following separate assessment of structural/functional connectomes, we evaluated network-level coupling.

Results
Structural networks in all MCD cohorts showed a more regularized topology (increased Cp and Lp) and altered rich-club organization relative to controls, with the timing of the malformative process affecting the severity of degree alterations. Specifically, cortical dysplasias showed subtle alterations, while effects were larger in heterotopias, and maximal in polymicrogyrias. While a similar gradient was present in functional networks, their topology became rather inefficient (decreased Cp, increased Lp). Patterns were supported by gradual structure-function decoupling in patients, with maximal divergence in polymicrogyrias.

Conclusions
MCDs impacts whole-brain structural and functional network organization, with changes modulated by the putative onset time window of the malformative process onset. More marked effects of polymicrogyrias relative to focal cortical dysplasias suggest increased sensitivity during late neurodevelopmental stages, where the majority of cortico-cortical connections are established.

NEUROIMAGING

Abstract 4

Arterial Spin Labeling (ASL) in the Pre-Surgical Evaluation of Pediatric Epilepsy

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Rationale
Arterial spin labeling (ASL) is a non-invasive MRI method that uses magnetically labelled blood as an endogenous tracer, producing quantitative brain perfusion maps. This technique can potentially be used as an indirect method of localizing the epileptogenic zone in epilepsy patients with negative MRIs or poorly defined lesions. While ASL has been used for this purpose in adults, little has been published in children.

Method
We prospectively applied a novel image processing pipeline to ASL data in order to visualize and quantify perfusion abnormalities in pediatric epilepsy patients. Mean cerebral blood flow was computed for the region of interest and corresponding contralateral area, followed by an asymmetry index calculation. ASL results were then compared to 3T-MRI, PET, SPECT, MEG as well as surgical pathology results in some patients.

Results
We evaluated 8 pediatric patients in the presumed interictal phase. We found that 5 patients exhibited areas of hypoperfusion, one displayed a focus of hyperperfusion, and the remaining two did not show obvious areas of abnormal perfusion. After comparison to other forms of imaging for each patient with conclusive ASL results, we found concordance in 6 out of 6 patients. Thus far, 4 patients have undergone surgical resection of the abnormality, revealing focal cortical dysplasia (FCD) in three cases and hippocampal sclerosis in the fourth. Three FCD patients are seizure free at early follow-up.

Conclusions
ASL is a useful non-invasive neuroimaging technique that can be used to help delineate the epileptogenic zone in pediatric epilepsy, possibly replacing CT-based PET and SPECT in the pre-surgical workup.

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Abstract 5

Surface-Based Integration of FDG-PET and MRI in Focal Epilepsy Syndromes

Boris Bernhardt, Seok-Jun Hong, Jean-Paul Soucy, Andrea Bernasconi, Neda Ladbon-Bernasconi

Montreal Neurological Institute

Rationale
Previous studies have suggested clinical utility of 18F-fluorodeoxyglucose positron emission tomography (FDG-PET) in drug-resistant focal epilepsy. While sensitivity of this technique to unveil metabolic anomalies proximal to the pathological substrate is unquestioned, its specificity to dissociate different epilepsy syndromes remains unknown.

Method
Using surface-based FDG-PET analysis, we mapped the divergence of cortical metabolic anomalies in patients with drug-resistant temporal and frontal lobe epilepsy (TLE and FLE). Group-level findings were complemented using an individualized prediction paradigm based on surface-wide support vector machine classification with leave-one-out cross-validation.

Results
Comparing cortical FDG uptake between both cohorts indicated bilateral temporo-polar, lateral temporal, and ipsilateral medial prefrontal decreases in TLE, whereas FLE patients presented with decreased metabolism in ipsilateral medial prefrontal regions ($P<0.05$, corrected). PET changes occurred independently of between-cohort differences in cortical morphology, quantified using cortical thickness analysis of co-registered Magnetic Resonance Imaging (MRI) data. Surface-wide statistical learning based on FDG-PET achieved high accuracy in discriminating TLE to FLE patients (96% accuracy; $P<0.01$).

Conclusions
Our multi-modal imaging findings show divergent cortical metabolic signatures across the two most common drug-resistant focal epilepsy syndromes both at the group- and individual-patient level, occurring independently from morphological anomalies. Our findings suggest that FDG-PET offers both sensitive as well as specific biomarkers in the presurgical assessment.

NEUROIMAGING

Abstract 6

In-Vivo Myelin Mapping in Temporal Lobe Epilepsy

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Montreal Neurological Institute

Rationale
Although sporadic experimental and pathological reports have indicated that temporal lobe epilepsy (TLE) may be associated with atypical mesiotemporal and neocortical myelination, the distribution of myelin changes is not well established and anatomical principles governing changes in intracortical myelin remain largely unknown.

Method
We utilized whole-brain quantitative T1 mapping to profile intracortical myelin alterations in cohorts of TLE patients and healthy controls. In addition to mapping the regional topography of myelin changes in patients, we utilized a novel multi-surface intensity profiling to assess changes along the vertical cortical axis. To model the relation between myelin changes, anatomical markers, and structural pathology, we performed a surface-wide association analysis that established the relation between T1 changes, markers of cortical atrophy, mesiotemporal connectivity, and baseline myeoloarchitecture.

Results
Compared to controls, TLE patients presented with ipsilateral mesiotemporal and temporo-polar, as well as bilateral orbitofrontal, medial prefrontal, and pericingulate T1 increases, suggestive of reduced cortical myelin content. Atypically high T1 values were seen after statistical correction for cortical thinning, suggesting only marginal links to atrophy. T1 increases were most marked in upper cortical levels, while tapering off towards the gray/white matter interface. Surface-based association studies revealed that T1 increases were higher in regions that were connected to the hippocampus and, specifically, in limbic areas with low myelin content.

Conclusions
Combining quantitative analysis of T1 relaxation times with functional connectivity mapping suggests temporo-limbic network demyelination in TLE, which occurs independent of atrophy but relates to hippocampal connectivity and baseline cortical myeoloarchitecture.

NEUROIMAGING

Abstract 7

Structure-Function Analysis along Hippocampal Subfield Surfaces in Temporal Lobe Epilepsy

Boris Bernhardt, Andrea Bernasconi, Benoit Caldairou, Seok-Jun Hong, Neda Ladbon-Bernasconi

Montreal Neurological Institute

Rationale
Although most temporal lobe epilepsy (TLE) patients show marked hippocampal sclerosis (HS) upon pathological examination, 40% present with no significant cell loss but gliotic changes only. To evaluate effects of hippocampal pathology on brain structure and functional networks, we assessed multimodal MRI characteristics in patients with HS (TLE-HS) and those with gliosis only (TLE-G).

Method
In 20 TLE-HS, 19 TLE-G, and 25 healthy controls, we carried out a novel 3T MRI-based hippocampal subfield surface analysis that integrated volume, T2-signal intensity, and diffusion markers with seed-based hippocampal functional connectivity.

Results
Compared to controls, TLE-HS presented with marked ipsilateral atrophy, T2-hyperintensity, and mean diffusivity increases across all subfields, while TLE-G presented with dentate gyrus hypertrophy and focal increases in T2-intensity and mean diffusivity. A between-cohort dissociation was independently suggested by resting-state functional connectivity analysis, revealing marked hippocampal decoupling from anterior and posterior default mode hubs in TLE-HS, while TLE-G did not differ from controls. Back-projection connectivity analysis from cortical targets revealed consistently decreased network embedding across all subfields in TLE-HS, while changes in TLE-G were limited to the subiculum. Hippocampal disconnectivity strongly correlated to T2-hyperintensity and marginally to atrophy.

Conclusions
Multimodal MRI reveals diverging structural and functional connectivity profiles across the TLE spectrum. Pathology-specific modulations of large-scale functional brain networks lend novel evidence for a close interplay of structural and functional disruptions in focal epilepsy.

CLINICAL EPILEPSY / EEG / ANTIEPILEPTICS

Abstract 8

Factors Associated with Illicit Substance Use and Cigarette Smoking in People with Epilepsy

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Rationale
Substance use has a negative impact on the health status of people with epilepsy. This study aimed to explore factors associated with cigarette smoking and illicit substance use in epilepsy patients.

Method
300 consecutive epilepsy patients seen in the Calgary Epilepsy Program Clinic were approached for participation. Participants completed the Hospital Anxiety and Depression Scale (HADS) and a questionnaire examining demographics, substance use and burden of epilepsy. A physician-reported questionnaire captured clinical characteristics. Proportions and odds ratios (ORs) were calculated.

Results
279 epilepsy patients completed the questionnaires, of whom 61 (21.9%) smoked cigarettes and 44 (15.8%) used illicit substances. Illicit substance users were more frequently male (65.9%, $p<0.01$) and under 40 years of age (81.8%, $p<0.001$); these discrepancies were non-significant in cigarette smokers. A higher proportion of illicit substance users reported that their epilepsy was extremely-moderately severe (36.4%) compared to non-users (18.9%) ($p<0.05$), and that their seizures were extremely-moderately disabling (59.5% vs. 31.6%, $p<0.001$). Illicit drug users were more likely to have a HADS score suggestive of an anxiety disorder (55.8% vs 38.3%, $p<0.05$) than non-users. Cigarette smoking was associated with a HADS score suggestive of an anxiety disorder (64.4% vs 34.6%, $p<0.0001$) and a HADS score suggestive of a major depressive episode (33.9% vs 13.7%, $p<0.001$).

Conclusions
Illicit drug use and cigarette smoking are associated with increased seizure severity and seizure-related disability in epilepsy patients. Substance use has considerable overlap with anxiety and depression. Physicians should be aware of patterns of comorbidity when managing epilepsy patients.

CLINICAL EPILEPSY / EEG / ANTIEPILEPTICS

Abstract 9

International Survey on Current Use of Intracarotid Anesthetic Procedures (IAP)

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Rationale

The intracarotid anesthetic procedure (IAP) has long been considered the gold standard for presurgical cerebral dominance assessment and prediction of postoperative memory deficits. However, it is invasive, and some centers may be replacing or supplementing it with noninvasive methods, especially functional magnetic resonance imaging (fMRI). We aimed to learn the extent of IAP use in current clinical practice.

Method

We compiled 17 questions related to use of the IAP versus other options: fMRI, magnetoencephalography (MEG) or magnetic source imaging (MSI), or "other." We sent the questionnaire by e-mail to epilepsy centers in 41 countries.

Results

Responses were analyzed in total and also grouped by geographic region: 83 from North America, 46 Europe, 14 Latin America, and 23 Oceania/Asia. Altogether, 81.3% of respondents perform the IAP. This varied by geographic region, with greatest prevalence in North America (91.6%) and least in Europe (63.0%). For speech lateralization, IAP (80.1%) and fMRI (81.3%) were used to a similar degree. For memory assessment the IAP (71.7%) was used significantly more than fMRI (23.5%). The most frequently used anesthetic agent was amobarbital (55.6%), followed by methohexital (16.7%), propofol (15.3%), and etomidate (11.1%).

Conclusions

The IAP continues to be used routinely in epilepsy centers worldwide, but methodology preferences differed between North America and Europe, possibly reflecting issues in the availability of amobarbital and of training in the IAP. Although neuroimaging techniques are being used for assessing speech dominance, a reliable neuroimaging method for predicting postoperative memory status is yet to be established.

CLINICAL EPILEPSY / EEG / ANTIEPILEPTICS

Abstract 10

Epilepsy in an Elderly Population: Classification, Etiology and Drug-Resistance

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University of Saskatchewan

Rationale

The pathological processes underlying epilepsy in the elderly are often distinct from those associated with epilepsy in younger patients. For this reason, research is needed to further characterize epilepsy in the elderly population. One important feature to study is drug-resistant epilepsy (DRE), as an understanding of DRE in this population could improve individualized treatment.

Method

Using a case series design, seventy-three patients with epilepsy aged 60 and above were obtained from the Saskatchewan Epilepsy Program database. ILAE criteria were used for all study definitions.

Results

Within the study population, 59% of patients experienced the onset of epilepsy ≥ age 60 (mean 70.56 +/- 6.9). Sixty percent of patients had a good response to their first anti-epileptic drug (AED), with phenytoin being used first in 48% of cases. The majority of patients (60%) had focal epilepsy, with the remainder of cases being generalized (37%) or unclassified (3%). The commonest aetiologies of focal epilepsy were unknown (27%) and benign neoplasms (23%) followed by malignant cerebral neoplasms (9%), degenerative neurological disease (9%) and stroke (9%). For generalized epilepsy, idiopathic (93%) was the most frequent aetiology. Across all groups, 20.5% of patients met ILAE criteria for DRE.

Conclusions

In agreement with prior research, the majority of elderly participants had focal epilepsy. A high percentage of patients responded well to their first AED, with phenytoin being used first in almost half of all cases. DRE was only present in 20.5% of cases, suggesting that elderly patients are at lower risk of developing drug resistance.

CLINICAL EPILEPSY / EEG / ANTIEPILEPTICS

Abstract 11

Broken-Heart Syndrome (Takotsubo Syndrome) with Seizures (Case Report)

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Rationale
Describe the case of a patient with Takotsubo syndrome triggered seizures.

Method
We analyzed the clinical data and imaging exams of a patient with Tuberculum sellae tumor which evolved in the postoperative period with Takotsubo syndrome and seizures, correlating this case with literature.

Results
A.F.B.G., 51 years old, hypothyroidism carrier, smoker and social drinker, three months ago had a traumatic brain injury, conducted a CT scan that showed tuberculum sellae tumor. The patient underwent microsurgery and third postoperative day presented seizures being carried out emergency therapy with diazepam and phenytoin. In the post ictal period evolved with hemiparesis in left hemi body (Todd phenomenon) and hypotension refractory to volume infusion being required vasopressors (norepinephrine). Was performed sedation and intubation. Urgent CT had been demonstrated only recent surgical alterations and ultrasonography ruled out pericardial effusion. Echocardiography showed dyskinesia of all middle segments of both ventricles with an ejection fraction of 34 % suggesting Takotsubo syndrome. After three days, the patient was extubated and had visual hallucinations (insects up the body, animal attack). It was introduced antipsychotic, benzodiazepine and nicotine adhesive for treatment of withdrawal syndrome. After one week, the patient progressed with improvement in ejection fraction (54%) with mild systolic dysfunction without hemiparesis and improvement of hallucinations.

Conclusions
In this case, a chain of events could explain the seizures. The first event was the nicotine withdrawal syndrome, which generated an adrenergic release triggering Takotsubo syndrome, causing a brain hypoflow culminating in seizures.

CLINICAL EPILEPSY / EEG / ANTIEPILEPTICS

Abstract 12

Characterizing Epilepsy Phenotypes in Patients with Intellectual Disability, Autism Spectrum Disorder, Developmental Delay, Congenital Abnormalities and Chromosomes 15q11.2, 15q13.3 and 16p13.11 mi

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University of Toronto

Rationale
Microdeletions at 15q11.2, 15q13.3 and 16p13.11 have been consistently associated with a variety of epilepsy syndromes. However, most studies were performed using cohorts of patients with epilepsy.

Method
The objective of this study was to investigate the spectrum of epilepsy and EEG characteristics in patients with microdeletions at 15q11.2, 15q13.3 and 16p13.11 who were referred to chromosomal microarray for developmental delay (DD), intellectual disability (ID), autism spectrum disorder (ASD), dysmorphism and/or congenital abnormalities. Data was collected through chart review.

Results
We examined a cohort of 15,850 patients. Ninety microdeletions at 15q11.2, 28 at 15q13.3, and 22 at 16p13.11 were identified; phenotypic information was available in 20, 8 and 6 patients, respectively. Among these subjects, 12 had epilepsy: 15q11.2 (n=9/20;45%), 15q13.3 (n=2/8;25%), 16p13.11 (n=1/6;16.7%). Electroencephalographically, 15q11.2 patients had normal studies, localization-related or genetic generalized epilepsy (GGE), 15q13.3 patients had either GGE or symptomatic generalized epilepsy (SGE), and 16p13.11 had SGE.

Conclusions
This study shows that microdeletions at 15q11.2, 15q13.3 and 16p13.11 lead to the same epilepsy phenotype both in patients from large epilepsy cohorts and in patients with a mixed phenotype (DD, ID, ASD, dysmorphism and congenital abnormalities). This work also reveals a new association between 15q13.3 microdeletion and SGE.

CLINICAL EPILEPSY / EEG / ANTIEPILEPTICS

Abstract 13

Progressive Myoclonus Epilepsy Caused by SACS Mutations

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Rationale
Mutations in SACS are classically known to cause autosomal recessive spastic ataxia of Charlevoix-Saguenay (ARSACS). Recently, two patients clinically diagnosed with progressive myoclonus epilepsy (PME) were found to have probably pathogenic SACS mutations. In this report, we provide a detailed description of one of these cases of PME due to mutations in SACS.

Method
Case report.

Results
The patient is a 25-year-old female who was born to healthy, non-consanguineous parents. Psychomotor development and cognition were normal, except for a mild learning difficulty. At the age of 13 years, she began to experience spontaneous and stimulus-induced myoclonic jerks. Two years later she had her first secondarily generalized convulsive seizure. Over the years, she also presented absence, dyscognitive, atonic, and tonic seizures, as well as photosensitivity. Seizures then became pharmacoresistant, and cognitive function significantly deteriorated. Additionally, she developed exotropia, bilateral dysmetria, dysarthria, and cerebellar ataxia. The latter, in association with her severe action myoclonus, resulted in this patient being wheelchair bound. Further, she had hypertonia and hyperactive reflexes in her lower extremities, bilateral extensor plantar reflex. EEG studies showed bihemispheric slow wave background activity with multifocal interictal epileptiform discharges. Brain MRI revealed diffuse cerebral, cerebellar, and corpus callosum atrophy. Based on the aforementioned evidence, she was clinically diagnosed with PME. Genetic testing as well and skin and muscle biopsies were undertaken to investigate the most frequent causes of PME, including mitochondrial diseases, and these investigations were all normal. She finally underwent whole-exome sequencing, which revealed two rare compound heterozygous missense variants in SACS: c.1373C>T (p.Thr458Ile) and c.8393C>A (p.Pro2798Gln). Both variants were felt to be probably pathogenic and responsible for the patient's phenotype. Notably, the variants had been previously reported in patients with ARSACS.

Conclusions
We describe a patient with PME caused by alterations in the SACS gene.

CLINICAL EPILEPSY / EEG / ANTIEPILEPTICS

Abstract 14

Two Definite Sudden Unexpected Deaths in Epilepsy in a Family with a DEPDC5 Mutation

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Rationale
DEPDC5 gene, mapped to 22q12.2-q12.3, has been associated with a variety of familial epilepsies. Notably, DEPDC5 has never been linked to increased risk of sudden unexpected death in epilepsy (SUDEP).

Method
Case report.

Results
We studied a three-generation, non-consanguineous, French-Canadian family with nine clinically affected individuals. Interestingly, all but one are males. The index case is a 39-year-old man who started having seizures at the age of 13 years. His seizures were characterized by a "dream-like" aura followed by loss of consciousness and tonic-clonic movements. Initially, seizures were mainly diurnal. In his mid-20s, the episodes became exclusively nocturnal. EEGs showed interictal epileptiform discharges over the right anterior-temporal region. Brain MRI was unremarkable. Two of the index case's paternal uncles suffered definite autopsy-confirmed SUDEP, at the ages of 58 and 50 years, respectively. Seizure-history in this family can be summarized by an onset before reaching adulthood, followed by subsequent progressive decrease in seizure frequency. Seizures were predominantly nocturnal secondarily generalized tonic-clonic. All the subjects were cognitively intact. There was no history of any cardiac symptomatology, cardiovascular risk factor, or definite cardiac condition.
Genetic analysis of the index case revealed a pathogenic heterozygous variant in the DEDPC5 gene (p.Gln216, c.646C>T; ENST00000536766). The index case was also tested for genes associated with SUDEP, none of which showed mutations.
All living affected relatives, as well as four healthy family members, were clinically evaluated and had DEPDC5 Sanger sequenced. All affected subjects and one healthy individual were found to carry the same DEPDC5 pathogenic variant as the index case.

Conclusions
Several genes have been linked with SUDEP. These are associated with cardiac arrhythmias and/or severe epilepsies, both of which do not apply to this family's phenotype. The finding in this family suggests that DEPDC5 mutations may be a risk factor for SUDEP.

CLINICAL EPILEPSY / EEG / ANTIEPILEPTICS

Abstract 15

Increased Epilepsy Prevalence in Adults with 22q11 Deletion Syndrome

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University of Toronto

Rationale
Previous studies examining seizure events in patients with 22q11.2 deletion syndrome (22q11DS) have primarily focused on children and adolescents. In this study we investigated the prevalence and characteristics of seizures and epilepsy in an adult 22q11DS population.

Method
The medical records of 202 adult patients with 22q11DS were retrospectively reviewed for documentation of events suspicious for seizures, EEG reports, and MRI findings. Epilepsy status was assigned in accordance to the 2010 International League Against Epilepsy classifications.

Results
Fifty eight patients with events suspicious for seizures were further investigated. True evidence of epileptic seizures was found in 34 subjects, 24 (11.8%) of which fulfilled diagnostic criteria for epilepsy. Nine (4.4%) of these patients with epilepsy had an associated underlying structural cause and 15 (7.4%) had non-lesional epilepsy. Seizure types included generalized tonic-clonic seizures (n=21), myoclonic seizures (n=8), focal dyscognitive seizures (n=5), and focal-onset evolving to bilateral convulsive seizures (n=10). Nine patients had a history of more than one type of seizure. The lifetime seizure occurrence (21/35, 60.0 %) in patients that had received antipsychotics was similar to those who had never been treated with an antipsychotic medication (12/23, 56.5 %, p=0.79).

Conclusions
The prevalence of epilepsy in 22q11DS adult patients is much higher than in the general population (0/5-1%) and is higher than in children with 22q11DS. Our analysis showed that seizures were not significantly more common in patients with a lifetime history of antipsychotic treatment.

CLINICAL EPILEPSY / EEG / ANTIEPILEPTICS

Abstract 16

Motor Phenotype Differentiates Adult Patients with Dravet Syndrome from Lennox-Gastaut Syndrome

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[2]University of Toronto

Rationale
Distinguishing adult patients with Lennox-Gastaut syndrome from Dravet syndrome is challenging. We have previously reported that patients with Dravet syndrome present very peculiar motor phenotype. Here we sought to confirm that this association was not linked to the chronic use of antiepileptic drugs or the many lifetime seizures.

Method
We studied 14 adult patients with Lennox-Gastaut syndrome and 14 adults with Dravet syndrome as both conditions share similar seizure severity.

Results
We found that antecollis and parkinsonian gait were significantly more common in the Dravet group.

Conclusions
Thus confirming that these features are part of the Dravet syndrome adult phenotype.

CLINICAL EPILEPSY / EEG / ANTIEPILEPTICS

Abstract 17

Update of Minimal Standards for Electroencephalography in Canada: A Canadian Society of Clinical Neurophysiology Review

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Rationale
Fourteen years have passed since the CSCN Task Force published the Canadian electroencephalography standards, an initial set of guidelines for EEG in Canada.

Method
The CSCN convened an expert panel to develop new and updated national minimal guidelines. It was prepared in accordance with CAET Minimal Technical Standards and created following consultations from Canadian epileptologists, electroencephalographers, and EEG technologists. The recommendations are evidence based, however where evidence was not available, expert opinion was sought.

Results
Technological advancements in the last decades have led to improvements in the recording and reviewing quality as well as storage capabilities of EEGs. Consensus was obtained regarding laboratory standards and procedures, reporting timelines, trained personnel, LTME, cEEG, and Ambulatory EEG. Also recommended are laboratory components of a quality assurance program. The most important changes from the new guidelines will be presented.

Conclusions
The purpose of these guidelines will promote standardization and quality care in clinical neurophysiology laboratories in Canada and serve as a benchmark for future development.

CLINICAL EPILEPSY / EEG / ANTIEPILEPTICS

Abstract 18

Long-Term Outcomes of Vagus Nerve Stimulation and Its Impact for Patients with Medically Refractory Epilepsy

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Rationale
The number of cases treated by vagus nerve stimulation (VNS) therapy is gradually expanding as a palliative treatment option for medically refractory epilepsy in Japan. To clarify the impact of VNS on the comprehensive approach for patients with medically refractory epilepsy, its efficacy and indications of VNS were well investigated.

Method
We reviewed retrospectively 104 patients who underwent VNS implantation from February 2010 through February 2015 in our hospital. Outcomes of VNS therapy were evaluated using the McHugh (MH) outcome classification.

Results
In patients treated by VNS, a more than 80% reduction in seizure frequency (MH class 1) was achieved in 38 patients (37%), and a 50-79% seizure reduction (MH class 2) in 16 patients (15%). In terms of indications, VNS implantations were carried out for 50 (48%) cases of generalized epilepsy, 29 (28%) cases of multifocal epilepsy, 10 (10%) cases of unilateral diffuse hemispherical epilepsy, 7 (7%) cases of bilateral independent foci, and 5 (5%) cases with residual seizures after focus resections.

Conclusions
VNS therapy was an effective treatment option as palliation for pediatric and adult patients with medically refractory epilepsy. Ninety-seven out of 104 patients (93%) would not be ideal candidates for intracranial epilepsy surgery. Then they could not obtain seizure reduction and better QOL without VNS. Therefore VNS has produced great benefits for these patients.

CLINICAL EPILEPSY / EEG / ANTIEPILEPTICS

Abstract 20

Cortical Thickness Analysis in Operculo-Insular Epilepsy

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Rationale
In temporal lobe epilepsy (TLE), advanced neuroimaging techniques reveal anomalies extending beyond the temporal lobe such as thinning of frontocentral cortices. Operculo-insular epilepsy (OIE) is an under-recognized and poorly characterized condition with the potential of mimicking TLE. In this work, we investigated extra-insular cortical thickness (CT) and volume changes in OIE

Method
All participants (14 patients with refractory OIE, 9 age- and sex-matched patients with refractory TLE and 26 healthy controls) underwent a T1-weighted acquisition on a 3T MRI.Anatomical images were processed with Advanced Normalization Tools. Between-group analysis of CT was performed using a two-sided t-test (threshold of $p<0.05$ after correction for multiple comparisons;cut-off threshold of 250 voxels) between (i) patients with OIE vs TLE, and (ii) patients with OIE vs healthy controls.

Results
Significant widespread thinning was observed in OIE patients as compared with healthy controls mainly in the ipsilateral insula, the prefrontal and temporo-limbic areas, and the peri-Rolandic region. Contralateral cortical shrinkage followed a similar albeit less diffuse pattern.
The CT of OIE patients was equal or reduced relative to the TLE group for every cortical region analyzed. Thinning was observed diffusely in OIE patients,predominantly involving the bilateral insulae, anterior cingulate gyri, paracentral lobules and precunei.

Conclusions
Our results reveal structural anomalies extending beyond the operculoinsular area in OIE. Although more work is necessary, the differential morphologic pattern of cortical atrophy, likely resulting from seizure propagation and disease chronicity, could constitute a complementary tool to differentiate OIE from TLE.

CLINICAL EPILEPSY / EEG / ANTIEPILEPTICS

Abstract 21

The Role of Positron Emission Tomography (PET) in the Pre-Surgical Evaluation of Patients with Refractory Epilepsy

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Rationale
Pre-surgical localization of the epileptogenic focus is critical in the success of epilepsy surgery. Traditionally, the localization of the epileptogenic focus depends on seizure semiology, scalp video-electroencephalogram (vEEG), magnetic resonance imaging (MRI), neuropsychological assessment, and when needed, intracranial EEG (iEEG). We aimed to explore the role of positron emission tomography (PET) in the pre-surgical evaluation of patients with refractory epilepsy.

Method
A retrospective review was conducted on patients with refractory epilepsy who underwent PET at London Health Sciences Centre (London, Canada) from 2011-2016. MRI, vEEG, iEEG, PET results were obtained. The accuracy of epileptogenic focus localization was compared between different investigative modalities and the surgical outcome was documented.

Results
We identified 62 patients with refractory epilepsy who underwent PET. The mean age was 34. 4 patients had surgical resection of the epileptogenic focus and became seizure free with matching PET and vEEG (bypassed iEEG). 5 patients are anticipating surgical resection bypassing iEEG. 9 patients had surgical resection and became seizure free with matching PET and vEEG/iEEG. The outcome of the other 13 patients who had matching PET and vEEG were heterogeneous. There were mixed results with the accuracy of PET compared to traditional investigative modalities in the remaining 31 patients.

Conclusions
PET has a vital role in the pre-surgical evaluation of patients with refractory epilepsy. It may either allow resection of the epileptogenic focus without the need for iEEG, or it may guide intracranial electrode placement for further localization of epileptogenic focus.

CLINICAL EPILEPSY / EEG / ANTIEPILEPTICS

Abstract 22

Quantification of Stigma Perception in Patients with Epilepsy of the National Institute of Neurology and Neurosurgery "Manuel Velasco Suárez"

Rossmery Espinosa, Mariana Espínola

National Institute Neurology And Neurosurgery Manuel Velasco Suarez

Rationale
Identify the prevalence of stigma in patients with epilepsy from the National Institute of Neurology and Neurosurgery Manuel Velasco Suarez "INNN" by revised epilepsy stigma scale . Determine the relationship of stigma with demographic and clinical variables , depression , anxiety , quality of life and degree of discrimination.

Method
Observational, cross-sectional, descriptive study. Scales stigma in epilepsy, quality of life in epilepsy, depression Beck, Hamilton anxiety and discrimination, were applied in patients ≥ 16 years of age both genders diagnosed with epilepsy treated at the INNN who agreed to participate and have clinical conditions to answer.

Results
78 patients, 46 women and 32 men. Mean age 35.7 years. Most are single (70.5%), mean scholarship of 4 years. Only 16 of the 78 patients (20.5%) have job. Degree of stigma found: no stigma 2.6%, mild stigma 35.9%, moderate 50%, severe 11.5%. Overall quality of life 55.7%, being more affected by cognitive impairment concern and preoccupation crisis. Degree of discrimination: "sometimes". Dominant neuropsychiatric comorbidities: 53.8% depression, anxiety 33.3%, psychosis 16.7%, personality change 7.7%, cognitive impairment 6.4% and 5.1% conversion disorder convulsive.

Conclusions
The degree of stigma found in Mexican population is moderate. Also they suffer psychiatric comorbidities that contribute to the deterioration in their quality of life. We propose to include comprehensive approach to the assessment of stigma and inclusion programs that strengthen the biological-physical, social and psychological areas.

CLINICAL EPILEPSY / EEG / ANTIEPILEPTICS

Abstract 23

Does Correlation Structure of Multichannel Intracranial EEG Data Characterize the Seizure Behaviour and Dynamics?

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Rationale
We studied seizure behaviour and dynamics from the correlation structure of multichannel intracranial electroencephalogram (iEEG) data.

Method
One patient with left frontal lobe epilepsy underwent implantation of an 8x8 subdural grid and two 4-contact depth electrodes for clinical purposes. iEEG data were collected continuously at 2000 Hz. Two segments of iEEG data, one including a generalized tonic-clonic seizure, and the other a focal seizure, were selected for analysis.

1. We implemented a novel and comprehensive method to despike the data such that any desired portion of removed spiked noise, if needed, could be put back into the despiked data for detailed iEEG processing.
2. We investigated the correlation connectivity matrices during the pre-ictal, ictal, and the post-ictal periods, computed at every time sample over the duration of the recording.
3. We used this correlation structure to construct eigenvector centrality and spectral gap maps, and the anticorrelation index.
4. We analyzed the seizure characteristics of the two data sets in different frequency bands, namely alpha, beta, gamma, theta, delta, and ripple bands.

Results
1. We observed different brain network states over time, albeit in a local region of the brain.
2. We tracked the sensitivity of the electrode regions to energy attribute of the iEEG data.

Conclusions
Eigenvector centrality and spectral gap maps, and neuronal dynamics associated with anticorrelation structure after ictal offset stress the significance of the correlational structure. Further generalization of the results would require additional studies with available iEEG data from potential patients.

CLINICAL EPILEPSY / EEG / ANTIEPILEPTICS

Abstract 24

Improving Neuropsychological Markers of Frontal-Lobe Dysfunction

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Rationale
Experimental studies have shown that two neuropsychological tests are sensitive to damage in different regions of frontal cortex. The Self-Ordered Pointing Task assesses the ability to monitor internally-generated actions and is sensitive to lesions within the mid-dorsolateral prefrontal region. The Conditional-Associative Learning Task examines the ability to learn arbitrary associations and has been associated with damage to posterior dorsolateral areas. To date, these tests cannot be used for routine clinical assessment due to a lack of adequate normative data. The current study aimed to establish a database on neurologically-healthy individuals against which the performance of patients with suspected brain damage can be compared and to examine the influence of age on these two abilities, while controlling for memory and estimated intelligence.

Method
Healthy individuals (n=128), aged 18 to 67 years, were recruited to participate. They were given the two target tasks, Conditional-Associative Learning and Self-Ordered Pointing. They subsequently completed two control tasks from a standardized intelligence battery and a test of face recognition.

Results
The oldest group of subjects made more errors on the self-monitoring task and took longer to learn the stimulus-response associations in comparison with all the younger groups. No important differences amongst the groups were observed on the control tasks.

Conclusions
The executive skills measured here are vulnerable to normal aging, underlying the importance of comprehensive age-matched norms. Clinical adaptation of experimental measures known to be sensitive to damage in particular brain regions is a critical step towards localization of focal cortical epilepsy.
Funded by NSERC.

CLINICAL EPILEPSY / EEG / ANTIEPILEPTICS

Abstract 25

High-Channel-Count Wearable fNIRS-EEG System for Long-Term Clinical Monitoring

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Rationale

The monitoring of neurological pathologies such as epilepsy as well as neuroimaging protocols involving movement requires continuous and noninvasive brain imaging techniques. Among existing ones, functional near infrared spectroscopy (fNIRS) and electroencephalography (EEG) have the advantage of being inexpensive, may yield portable solutions and offer complementary monitoring of electrical and local metabolic/hemodynamic activities. Combining both techniques could provide useful complementary information. Unfortunately, current fNIRS systems are bulky, have poor spatial sampling and do not include EEG. Our goal was to develop a light, portable, wireless, high-channel count fNIRS-EEG monitoring system.

Method

Our system is composed of 128 fNIRS channels and 32 EEG electrodes to cover the entire adult superficial cortex, light and battery-powered to improve portability, transmitting data wirelessly to an interface for real-time display of electrical and hemodynamic activities. Two analog channels for auxiliary data, eight digital triggers for event-related protocols and an accelerometer for movement artifacts removal contribute to improve acquisition quality. The prototype was tested on 10 healthy subjects using visual and language tasks and 4 neurological patients.

Results

The system weighs 650g, can operate up to 24h on battery and is adapted to include 32 EEG electrodes and up to 128 fNIRS channels for full head coverage by various photoemitter/detector combinations. Data analysis confirmed expected hemodynamic variations during validation recordings and useful clinical information during in-hospital testing.

Conclusions

Preliminary results indicate that our portable multichannel and combined EEG-fNIRS system can be used for simultaneous electrical and hemodynamic information in patients with neurological disease.

CLINICAL EPILEPSY / EEG / ANTIEPILEPTICS

Abstract 26

Incidence and Prevalence of Epilepsy in the Province of Saskatchewan, Canada (2001-2010)

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University of Saskatchewan

Rationale
To measure incidence and prevalence of epilepsy between 2001 and 2010 in the province of Saskatchewan, Canada.

Method
A population-based retrospective cohort was created from an administrative database linked by a unique health services number. This cohort included individuals with the first identification of epilepsy from January 01, 2001 to December 31, 2010, based on case definition of epilepsy met with any one of two administrative health databases (Hospital separation data and Physician's service data). The case definition was fulfilled if the subject had, at least, one hospital separation with a diagnosis of epilepsy (ICD-9 345 or ICD-10-Ca G40)during the ten years period or had two physician visits within 730 days before or within the ten-year period of the study.

Results
A total of 7,930 incident cases of epilepsy were identified during 2001/2010. The incidence rate between 2001 and 2005 range from 78.27 to 109.14 per 100,000 people but between 2006 and 2010 they range from 43 to 61.84 per 100,000 people. The incidence of epilepsy was higher in elderly, but not in early life. Also was higher in Registered Indian, and slightly more frequent in males than in females. Prevalence of epilepsy for 2001 was 3.02 per 1000 people.

Conclusions
This is the first Canadian study of the incidence of epilepsy involving the entire age spectrum. We did not find a classical U shape incidence curve as it has been found in other developed countries, finding only a high incidence in the elderly population. Our new finding are foundational for public awareness and policy recommendations, health promotion and prevention strategies, appropriate health resource planning, and research priorities.

PEDIATRIC EPILEPSY

Abstract 27

The Influence of Child, Caregiver and Family Factors on Symptoms of Anxiety and Depression in Children and Adolescents with Intractable Epilepsy

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[2]*Hospital for Sick Children*

Rationale
The impact of family and caregiver factors on symptoms of anxiety and depression in children with epilepsy has not been adequately addressed. This study evaluated these relations in a cohort of children with medically refractory epilepsy.

Method
Data were derived from a multicenter prospective cohort study evaluating 46 children (ages 6-11 years) and 68 adolescents (ages 12-18 years) with epilepsy. This study is unique in evaluating the impact of multiple child, caregiver and family characteristics on self-reported symptoms of anxiety and depression.

Results
Among children, depression symptoms were associated with a higher proportion of life with seizures (β=.360, p=.014), caregiver depression (β=.405, p=.005), poor family functioning (β=.405, p=.005) and poor family mastery and social support (β=.326, p=.027); in multivariable analyses, proportion of life with epilepsy remained significant. No significant predictors of anxiety were found. Among adolescents, depression was associated with caregiver unemployment (β=.345, p=.004) and anxiety (β=.371, p=.002), low household income (β=.301, p=.016), poor family mastery and social support (β=.303, p=.012) and greater family demands (β=.290, p=.017); in multivariable regression, caregiver anxiety remained significant. Greater anxiety symptoms among adolescents were associated with females (β=.337, p=.005) and caregiver depression (β=.247, p=.043) and anxiety (β=.401, p=.001); in multivariable analyses female sex and caregiver anxiety remained significant.

Conclusions
These finding highlight the central role of caregiver and family characteristics, which are amenable to intervention, on patient – particularly adolescent – symptoms of anxiety and depression.
Study funding provided by the Canadian Institutes for Health Research.

PEDIATRIC EPILEPSY

Abstract 28

Role of White Matter Synaptic Plexi in Pathogenesis of Focal Epilepsy

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University of Calgary

Rationale
Excessive white matter neurons beneath focal cortical dysplasias (FCD) may contribute to epileptic circuitry. Synaptic plexi can be demonstrated is tissue resections by synaptophysin immunoreactivity. Origin of subcortical neurons can be either from tangential migration/fetal subplate zone (calretinin reactivity) or from radial migration (calretinin nonreactivity). Mitochondrial enzymes can demonstrate neuronal hypermetabolism. Glial αBcrystallin identifies active epileptic foci.

Method
Synaptophysin, calretinin, NeuN, GFAP and αBcrystallin antibodies were applied to sections of surgical resections at epileptic foci with focus on subcortical axonal networks in 19 infants and children, ages 3 months to 17 years: 10 FCD I; 6 FCD II; 3 tuberous sclerosis. Ten normal fetal brains 18-22wk gestation, 6 of 37-41wk. Eight age-matched postnatal brains provided controls. Frozen section histochemistry demonstrated mitochondrial enzymes.

Results
Subcortical and deep white matter in FCD exhibited excessive neurons, mostly scattered but focally clustered. Most neurons were reactive for NeuN, but rarely for calretinin. Elaborate axonal plexi showed connections between heterotopic neurons and also with overlying cortex. Axons were oriented randomly and frequently projected to and entered the cortex; subcortical axons of controls ran parallel to cortex. Some neurons had intense mitochondrial activity. All foci exhibited αBcrystallin.

Conclusions
Subcortical white matter neurons in FCD have elaborate synaptic plexi that probably contribute to epileptic circuitry. They are not derived from the subplate zone, hence contribute to excitatory rather than inhibitory networks. Actively discharging heterotopic white matter neurons are hypermetabolic. Neurosurgical FCD resections should include some adjacent white matter. Neuropathology reports should describe white matter plexi.

PEDIATRIC EPILEPSY

Abstract 29

Clinical Evolution in SCN1A Positive Dravet Syndrome Patients Across the Lifespan

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Rationale
To characterize the clinical evolution of patients with Dravet syndrome.

Method
Retrospective review of the clinical and EEG records of patients with Dravet syndrome and SCN1A mutations. The study population was subdivided into 4 groups for data analysis; during the 1st year of life, 2nd to 5th year, 6th to 16th year and 17th year onwards.

Results
The study population comprised 24 patients (14 males) aged 2-29 years at most recent follow-up (mean16.3 years) with Dravet syndrome. 23 had normal development prior to seizure onset. All had intellectual impairment; moderate to severe in 21 and mild in 3. Autism spectrum disorder was diagnosed in 50%. Seizures were recorded in 18/24 (75%) of patients. During the first 5 years of life, myoclonic seizures were the most common and occurred daily or weekly. From the 6th year onwards, focal seizures were the most commonly recorded followed by tonic seizures. In the third decade seizure frequency decreased to monthly or several/year. All failed 5-12 AEDs, and the longest seizure free interval was 10 months to 3 years seen in 4 patients, 3 of whom were on the ketogenic diet. 8 patients (aged 10-28 years) had a crouch gait.

Conclusions
All patients had treatment resistant epilepsy and the ketogenic diet resulted in the longest seizure-free interval. Myoclonic seizures were most common in the first 5 years and focal seizures and tonic seizures in older patients. Seizure frequency decreased with increasing age. Crouch gait was observed in 30% of patients.

PEDIATRIC EPILEPSY

Abstract 31

Long-Term Academic Outcomes in Pediatric Epilepsy: Mediating Effects of Working Memory

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Rationale
Academic difficulties are common in pediatric epilepsy (for review see Reilly & Neville, 2011), although little is known about long-term academic outcomes in this population, and how these may be impacted by epilepsy factors (e.g., seizure status) and cognitive factors (e.g., working memory). The purpose of this study was to examine the potential indirect relationship between seizure status and long term academic outcomes as mediated by working memory.

Method
All participants were patients with epilepsy at the Hospital for Sick Children who underwent neuropsychological (baseline) evaluations to determine surgical candidacy between 2002 and 2009. Follow-up evaluations occurred 4 to 11 years after surgery (or baseline assessment for non-surgical patients). Seizure status was defined as the presence/absence of seizures in the year preceding follow-up assessment. Working memory was defined as the Working Memory Index standard score on the age-appropriate version of the Wechsler Intelligence Scale. The academic skills assessed included word reading, spelling, and arithmetic on the Wechsler Fundamentals Academic Skills.

Results
Persistent seizures at long term follow-up were associated with poorer working memory, which in turn led to lower word reading (n=68), spelling (n=64), and arithmetic (n=67) scores, controlling for baseline academic performance. Bootstrap estimates of the indirect effect between seizure status and academics (via working memory) suggest significant mediation effects across areas assessed.

Conclusions
Patients with seizures at long-term follow-up had reduced working memory ability, which then negatively impacted academic skills. Therefore, for children with epilepsy and academic difficulties, working memory interventions may be a useful adjunct to direct academic remediation.

PEDIATRIC EPILEPSY

Abstract 32

Heart Rate Variability in Patients with Sodium Channel Mutations Who Suffer SUDEP

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Rationale
The significance of heart rate variability (HRV) in sudden unexpected death in epilepsy (SUDEP) has been a recent topic of interest. From a mechanistic perspective, altered autonomic function is an appealing candidate as a contributing factor in SUDEP, as HRV abnormalities have been noted in at least two patients in the period immediately before death. Retrospective cardiac evaluation of those who die of SUDEP is challenging as people with epilepsy do not routinely have Holter monitoring or other cardiac evaluations.

Method
We reviewed ECG tracings from available EEG recordings of all patients with Dravet syndrome and other epileptic encephalopathies secondary to sodium mutations from our centres, Austin Health (Heidelberg, VIC, Australia) and the Alberta Children's Hospital (Calgary, AB, Canada). Inter-beat intervals were manually extracted over 5 minute periods in wakefulness and stage 1/2 sleep (when available) for each patient. Time domain HRV measures (SDNN and RMSSD) were calculated and statistical comparisons made between patients who had died of SUDEP and those who were still alive or who had died from other causes.

Results
Considerable inter-patient variability in HRV measures was observed; however awake HRV tended to be higher in individuals who went on to die of SUDEP.

Conclusions
Altered patterns of HRV may be a biomarker for SUDEP risk in patients with Dravet syndrome and other sodium channel mutation-associated epileptic encephalopathies. Although further research is needed, HRV should eventually be incorporated into clinical evaluation of people with epilepsy in order to improve counseling related to SUDEP risk.

This collaborative research project was supported by funding from the Alberta Children's Hospital Foundation.

PEDIATRIC EPILEPSY

Abstract 33

Transition from Paediatric to Adult Health Care: Readiness and Experiences of Adolescents and Young Adults Diagnosed with Epilepsy in Childhood

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Rationale
Transition from paediatric to adult health care results in better long-term patient outcomes than transfer alone. Assessing transition readiness is important to guide healthcare. Despite concern that transfer is insufficient, transition readiness of adolescents with epilepsy has not been formally assessed.
Objectives: 1. document transition readiness of adolescents and young adults (AYAs) with epilepsy; 2. explore its association with individual and familial factors; 3. describe transition experiences for AYAs with epilepsy and their parents.

Method
Families enrolled in the Health-Related Quality of Life in Children with Epilepsy Study were followed for ten years after their children were diagnosed. Data were collected from parents, AYAs, and physicians using questionnaires. AYAs are currently ages 13 to 24 years. AYAs reported on transition readiness using the Transition-Q, an assessment of self-management skills that has sound psychometric properties. Questions about transition experiences were included in parent and AYA questionnaires.

Results
Return rates for parents and AYAs were 79% (169/215) and 73% (129/176), respectively. Preliminary analysis indicates that 17% of AYAs have transferred to adult care, 8% see a paediatric neurologist, and 63% no longer see a physician for epilepsy. Mean Transition-Q scores for these sub-groups were 64, 53, and 68 respectively (possible scores: 0 – 100).

Conclusions
This is one of the first studies to measure the extent of transition readiness in AYAs with epilepsy using a psychometrically sound scale. Results will inform development of transition programs for AYAs with epilepsy as an essential step in achieving better long-term outcomes.

PEDIATRIC EPILEPSY

Abstract 34

Population-Based Registry of SUDEP in Children

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Rationale
Risk factors for SUDEP are known in adults; however, pediatric factors are not well established. We aimed to identify potential pediatric risk factors through the development of a national, multi-centered, prospective population based registry for SUDEP.

Method
Children with epilepsy with unexpected death from January 1, 2014 - December 31, 2015 were sought for enrollment. Inclusion criteria were: age at death ≤ 18 years, history of epilepsy (≥ 2 seizures), death that was sudden and unexpected and when available autopsy that determined no anatomical or toxicological cause of death. Trauma or drowning related deaths were excluded. Cases were collected from: Ontario Forensic Pathology Service, Canadian Pediatric Epilepsy Network and Canadian Pediatric Surveillance Program.

Results
Twenty-one cases of pediatric SUDEP were identified. Forty-eight percent were males. Median age at death and duration of epilepsy were 8.3 years and 5.2 years. Age of seizure onset was known in sixteen, 94% had onset before 5 years. At death, 62% were on two or more AEDs. Fifteen were globally delayed. In eighteen, the state before death was known. Sixteen children (89%) were asleep, two (11%) were awake; death was unwitnessed in fourteen (78%) and witnessed in four (22%). Seventeen children had information regarding the presence of recent infection and eight (47%) had a recent infection.

Conclusions
Most SUDEP deaths were unwitnessed, in sleep, and occurred in children with global delay, early onset epilepsy and seizures requiring polytherapy. Nearly 50% of cases had a recent infection, which may potentially favour increased surveillance around illness.

PEDIATRIC EPILEPSY

Abstract 35

The Value of "Negative" MEG Studies: Defining the Functional Deficit Zone Using Spontaneous MEG in Children with Intractable Epilepsy

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Rationale
The usefulness of MEG for the definition of the irritative zone through localisation of interictal epileptiform discharges (IEDs) in focal epilepsy is well established. However, IEDs occur infrequently in many patients, and it is not uncommon for MEG studies to turn out "negative" because an insufficient number of IEDs could be recorded within a practical amount of time. We hypothesise that MEG recordings devoid of paroxysmal epileptiform events are not without value, and may in fact serve the secondary purpose of helping define the functional deficit zone.

Method
We computed metrics of spontaneous (task-free) activity in MEG recordings across all healthy controls in the Open MEG Archive (OMEGA) database. The same metrics were computed in 10 paediatric intractable epilepsy patients. Co-registration and statistical contrast between individual patients and healthy controls was then undertaken, resulting in maps showing areas where individual patients' brains differed from the norm.

Results
Contrasts against controls from the OMEGA database revealed differences in regions corroborating results from interictal FDG PET and SPECT in a subset of patients. The frequency band in which differences were observed depended on the region of functional deficit.

Conclusions
Preliminary results suggest that spontaneous MEG recordings can be used to define the functional deficit zone in at least a subset of patients. This could potentially be of value both for indirectly helping in identifying the epileptogenic zone, and for localising abnormally functional cortex. Further study will be needed to characterise the sensitivity and specificity of the proposed method.

PEDIATRIC EPILEPSY

Abstract 36

Validating the Shortened Quality of Life in Childhood Epilepsy Questionnaire (QOLCE-55) in Children with Drug Resistant Epilepsy

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[4]*Western University*
[5]*University of Toronto*

Rationale
This study aimed to validate the newly developed shortened Quality of Life in Childhood Epilepsy Questionnaire (QOLCE-55) in a sample of children with drug resistant epilepsy.

Method
Data came from 136 children enrolled in the Impact of Pediatric Epilepsy Surgery on Health-Related Quality of Life Study (PEPSQOL), a multicenter prospective cohort study. Confirmatory factor analysis was used to assess the higher-order factor structure of the QOLCE-55. Internal consistency reliability was evaluated for the original QOLCE and the QOLCE-55 using Cronbach's alpha and the Spearman-Brown prophecy formula. Convergent and divergent validity were assessed by correlating subscales of the KIDSCREEN-27 (parent report) with the QOLCE-55.

Results
The higher-order factor structure of the QOLCE-55 demonstrated adequate fit: Comparative Fit Index = 0.948; Tucker-Lewis Index = 0.946; Root Mean Square of Approximation = 0.060 (90% CI 0.054–0.065); Weighted Root Mean Square Residuals = 1.247. Higher-order factor loadings were strong, ranging from λ = 0.74 to 0.81. Internal consistency reliability was excellent (α = 0.97, subscales α > 0.82), showing improvement over the original QOLCE. QOLCE-55 subscale scores demonstrated moderate to strong correlations with similar subscales of the KIDSCREEN-27 (ϱ = .43-.75) and weak to moderate correlations with dissimilar subscales (ϱ = .25-.42).

Conclusions
The findings provide support for the factor structure of the QOLCE-55 and contribute to its robust psychometric profile as a reliable and valid instrument. Researchers and health practitioners should consider the QOLCE-55 a viable option to reduce respondent burden when assessing health-related quality of life in children with epilepsy.

BASIC SCIENCE / ENGINEERING

Abstract 37

Changes in Pentylenetetrazole-Induced Convulsion Threshold Following Chronic Caffeine and Taurine Administration to Rats

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Rationale

Moderate consumption of caffeine, a xanthine alkaloid, is sufficient to induce behavioral stimulation, which is mainly due to its antagonism of all adenosine receptors that function as neurotransmission and neuronal excitability modulators. In contrast, taurine, a neurotransmitter itself has a more regulatory effect on the CNS by reducing spontaneous neuronal firing, hyperpolarizing the resting membrane potential and increasing the membrane's conductance for Cl-.

Method

The effect of caffeine and taurine on PTZ-induced convulsion parameters was measured following a one-month treatment of caffeine (0.2g/L, Caf) and taurine (1000mg/kg, Taurine) dissolved in the rats' (n=136) drinking water, as the only source of water available. Furthermore, the probability, latency and type of convulsions were recorded following the administration of the intraperitoneal PTZ doses.

Results

The caffeine treated group showed a significant change in convulsion latency in contrast to the taurine treated group, mainly with the two highest doses of PTZ: 50mg/kg (control 376.7±63.7s, Caf 132.4±21.1s, $P<0.05$. Taurine 368.4±88.4s, $P>0.05$) and 80mg/kg (control 281.9±63.2s, Caf 127.9±44s, $P<0.05$. Taurine 298.4±88.5s, $P>0.05$). Furthermore, caffeine treated group also showed a higher probability of convulsion when given the aforementioned doses of PTZ: 50mg/kg (control 50%, Caf 100%, Taurine 56%) and 80mg/kg (control 67%, Caf 100%, Taurine 67%).

Conclusions

Chronic administration of caffeine has a significant effect on the PTZ-induced convulsion threshold. It also shows a higher susceptibility to PTZ than both the control and chronic taurine groups. On the other hand, the chronic administration of taurine seems to have no significant effect on the PTZ-induced convulsion threshold.

BASIC SCIENCE / ENGINEERING

Abstract 38

Effects of Acute Caffeine and Taurine Administration on Pentylenetetrazole-Induced Convulsion Parameters in Rats

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Rationale

Primarily, caffeine's behavioral stimulation is related to its antagonizing effect on the adenosine receptors that modulate neurotransmitter release and neuronal excitability. Taurine, on the other hand, acts as a neuroprotector against glutamate-induced neurotoxicity and increases the membrane conductance of Cl-, thus reducing the spontaneous firing of neurons.

Method

In this study we measured the pentylenetetrazole-induced convulsion threshold in 120 rats after acute administration of caffeine (0.2g/L of water for two days, Acute Caf) and taurine (1000mg/kg/day for two days, Acute T). The probability, type, latency and duration of the convulsions were recorded after the administration of five different doses of pentylenetetrazole intraperitoneally.

Results

The results showed significantly lower latencies for convulsions in the acute caffeine groups, especially with the 50mg/kg dose of PTZ (control latency 376.7±63.7s, Acute Caf 296.9±88.9s, Acute T 269±86.2s $P<0.05$, ANOVA) and 80mg/kg of body weight dose of PTZ (control latency 281.9±63.2s, Acute Caf 152.4±51.7s $P<0.05$, ANOVA, Acute T 281.4±97.1s $P>0.05$, ANOVA). By comparing the durations of the convulsions, the results showed the same pattern response, whereas the convulsion duration was significantly higher in caffeine treated animals. No significant responses were recorded in the acute taurine group when compared to the control or acute caffeine group.

Conclusions

Acute administration of caffeine has shown to increase the PTZ-induced convulsion threshold, which suggests an increased level of neuronal excitability. In contrast, acute administration of taurine has a non-significant to minimal effect on the PTZ-induced convulsion threshold.

BASIC SCIENCE / ENGINEERING

Abstract 39

Susceptibility of Aging Hippocampal Circuitry to Epileptogenesis: Evidence from a Mouse Model of Hippocampal Kindling

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Rationale
An increased incidence of seizures and epilepsy is associated with old age. However, due to the common presence of comorbidities such as stroke, tumours, brain injuries, and dementias, the role of aging on epileptogenesis, in and of itself, remains unclear. In order to separate the effects of aging and other pathologies on susceptibility to epileptogenesis, a mouse model of hippocampal kindling was used.

Methods
Aging and young mice (male, C57BL/6, ≥20 months and 3-5 months of age, n=8 for each group) were used. These animals received bilateral hippocampal electrode implantation and underwent daily electrical stimulation via using a classical kindling protocol. Behavioural seizures and evoked hippocampal discharges were recorded to assess seizure progression. The mice were considered to be fully kindled if stage 5 seizures were elicited over 5 consecutive days.

Results
In comparing two successfully kindled groups of aging and young mice (n=8 each), the process of reaching the fully kindled state was faster in aging mice than in young mice. The duration of hippocampal discharges was also longer in the group of aging mice.

Conclusions
These pilot data suggest that the hippocampal circuity of aging mice is more susceptible than that of young mice to the kindling epileptogenic process. Works are in progress to verify these data in other cohorts of aging and young mice and to explore potential factors that may promote the kindling process in aging mice.
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BASIC SCIENCE / ENGINEERING

Abstract 40

Resting State Functional Network Disruptions in a Kainic Acid Model of Temporal Lobe Epilepsy

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Rationale
Mesial temporal lobe epilepsy (mTLE) is the most common form of drug-resistant epilepsy (DRE). The clinical application of non-invasively mapped networks using resting-state functional magnetic resonance imaging (rsfMRI) in humans has been rather limited due to heterogeneity of the patients. We employed a status epilepticus (kainic acid) rodent model of TLE to measure the extent of functional network disruptions using rsfMRI.

Method
Functional connectivity was determined by temporal correlation of the resting-state Blood Oxygen Level Dependent (BOLD) signals between two brain regions during 1.5% and 2% isoflurane, and analyzed as networks in epileptic and control rats.

Results
Graph theoretical analysis revealed a significant increase in functional connectivity between brain areas in epileptic than control rats, and the connected brain areas could be categorized as a limbic network and a default mode network (DMN). The limbic network includes the hippocampus, amygdala, piriform cortex, nucleus accumbens, and mediodorsal thalamus, whereas DMN involves the medial prefrontal cortex, anterior and posterior cingulate cortex, auditory and temporal association cortex, and posterior parietal cortex.

Conclusions
These results suggest extensive disruptions in the functional brain networks, which may be the basis of altered cognitive, emotional and psychiatric symptoms in TLE.

BASIC SCIENCE / ENGINEERING

Abstract 41

Relation Between Epileptogenesis and Delta Power in Mice

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Rationale
Severe brain damage leads to epilepsy several months to years after the trauma. The mechanisms leading to epileptogenesis are unknown.

Method
We used deafferented (undercut) cortex mice as a model of cortical trauma epilepsy (TIE). TIE propensity is low in young animals, and it increases with age. We performed undercut in the somatosensory area in young and adult C57/BL6 mice and implanted LFP and EMG electrodes for continuous electrographic recordings for at least two months.

Results
In the following weeks, we found only isolated interictal spikes in young animals, but all old mice revealed recurrent seizure activities. We evaluated seizure occurrence and calculated the delta power of sleep LFP (area of 0.2-4 Hz in spectrogram) in each animal. Delta power was much lower in control adult mice as compared to control young mice and it was relatively stable over weeks for the same animals. The delta power increased with time in undercut old mice and this increase was much more pronounced during light period. Previous studies showed that delta power depends on neuronal silence and neuronal silence leads to progressive increase in excitability. Therefore, using DREADD technology we decreased the excitability in a given cortical area (no undercut) and the animal became epileptic. In other experiments, using DREADD technology that locally increases excitability, we were able to prevent epileptogenesis in the undercut mice.

Conclusions
We concluded that TIE is age-dependent and is correlated with the amount of delta activity in areas surrounding the undercut, so epileptogenesis might be controllable by manipulating excitability.

EPILEPSY SURGERY

Abstract 42

Successful Surgical Treatment of Praxis-Induced Reflex Seizures Mainly Precipitated by Writing

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Rationale
The association between praxis-induced reflex seizures and idiopathic generalized epilepsy has been established in previous studies. Whereas focal lesions were found in other subtypes of reflex epilepsy in which surgical approaches were attempted, no such findings allowed a surgical approach in praxis-induced epilepsy yet.

Methods
We report the case of a 23-year-old left-handed woman with medically intractable praxis-induced reflex seizures mainly precipitated by writing.

Results
Selective resection of subtle end-of-sulcus cortical dysplasia in the right inferior parietal lobule resulted in freedom from seizures.

Conclusions
To the best of our knowledge, this is the first case of praxis-induced reflex seizures mainly precipitated by writing in which a focal lesion was found, and treated successfully by surgery.

EPILEPSY SURGERY

Abstract 43

Forced-Choice Recognition Memory Performance Facilitates Lateralization of Memory Functioning

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Rationale

A key contribution of neuropsychology in temporal lobe epilepsy surgery is determining the extent to which memory performance is consistent with laterality of the seizure focus and MRI evidence. While those with dominant temporal lobe epilepsy (typically left) show characteristic verbal memory deficits, a consistent finding of non-verbal memory impairment in those with non-dominant temporal lobe epilepsy has been elusive (e.g., Lee, 2010). The existing clinical tasks emphasize one aspect of hippocampal function, pattern completion (list learning and free recall). We examined whether including tests that emphasize another aspect, pattern separation based on fine-grain discrimination of perceptual features, would enhance identification of non-dominant profiles.

Method

We evaluated clinical data in temporal lobe epilepsy cases whose laterality was confirmed at surgical rounds (n=181). Difference scores on three matched memory measures (Rey Auditory Verbal Learning Test vs. Rey Visual Design Learning Test; Warrington Words vs. Faces; and Doors vs. Names) were calculated as a z-score for each patient (verbal minus non-verbal) and entered into a binary logistic regression to predict either left or right hemisphere dysfunction.

Results

As expected, left ATL candidates had negative difference scores indicating weaker verbal memory while right ATL candidates had positive scores indicating stronger non-verbal memory. List learning and Warrington were unique predictors of seizure laterality, but not the Doors and Names difference score.

Conclusions

Preliminary findings indicate that evaluating both pattern separation and pattern completion aspects of hippocampal function is useful in identifying memory profiles characteristic of right mesial temporal lobe dysfunction.

EPILEPSY SURGERY

Abstract 44

Magnetic Resonance Guided Laser Interstitial Thermal Therapy for Medically Intractable Epilepsy: An Individual Participant Data Meta-Analyst

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Rationale
MRgLITT has emerged as a minimally invasive alternative to open resection for DRE patients and has rapidly gained in popularity. However, there is uncertainty as to whether MRgLITT is in fact safe, efficacious, and whether the results obtained are comparable to standard epilepsy surgery.

Method
Systematic review and individual participant data meta-analysis to determine the efficacy and safety of MR-guided laser interstitial thermoablative therapy (MRgLITT) for drug-resistant epilepsy.

Results
Of 4308 citations, 10 articles reporting on 92 participants were eligible. The median duration of follow-up was 12 (range 1-38.5) months and 53 (57.6%) participants were seizure-free (Engel class 1) at follow-up. The mean duration of seizure freedom following MRgLITT was 19.4 months (95% CI, 15.0-23.8). Patient age and history of prior surgery were not predictors of outcome on Cox regression univariate analysis. We identified a difference in efficacy dependent on etiology but we were underpowered to conclude a statistically significant difference. Hypothalamic hamartoma had better seizure freedom than MTS/MTA, and both were superior to FCD, although this was not statistically significant. There was no procedure-related mortality, but morbidity was experienced in 14 (15.2%) of participants mainly comprising probe/device malfunction, unexpected neurological deficit, hemorrhage, or cerebral edema.

Conclusions
MRgLITT is safe and associated with reduced hospital stay compared to standard epilepsy surgery. It should be considered a first line surgical treatment for HH as it is associated with superior efficacy and a reduced complication profile. For cases of drug-resistant MTLE, the reduced rate of visual field deficit make it an appealing alternative to standard SAH. The role for MRgLITT in extra-temporal FCD is less clear and may be best suited for deep (e.g. depth of sulci) and reoperation cases.

EPILEPSY SURGERY

Abstract 45

SEEG and Subdural Electrodes: Analyzing the Trend of Their Use in a Large Canadian Epilepsy Program

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Rationale
Stereo-electroencephalography (SEEG) has begun to displace subdurally-placed electrode monitoring despite concerns of being a more invasive technique. In our center, the use of subdural electrodes and grids had been the gold standard of invasive monitoring in refractory epilepsy, but the placement of depths electrodes is becoming more common. This study reviews the transition of our practice into SEEG, and how SEEG has been used to investigate those patients who were previously assessed with subdurals and/or grids, but in whom an epileptogenic focus was not found.

Method
We reviewed the epilepsy surgery database since the inception of our epilepsy program (1977) until December of 2015. All patients who underwent a second phase of assessment with the use of intracranially-placed electrodes were included. Then, we assessed the trend on the usage of SEEG, and analyze the sub-group of patients who underwent SEEG after they had subdurals and/or grids.

Results
A higher number of SEEG cases were seen in the last 2 years. Eight patients underwent SEEG after an initial investigation with subdural electrodes. We will present detailed clinical information, including surgical procedure (if performed). The outcome following SEEG, allowed surgery in 3 cases, while in the other ones did not, because of evidence of multifocality or an epileptogenic area over an eloquent area. Those who underwent surgery became seizure free. Complications following insertion of depth electrodes were seen in only 2 patients.

Conclusions
There is a increasing trend toward the use of SEEG over investigation with subdural electrodes in our center. There is a benefit in reassessing with SEEG those cases in whom the epileptogenic focus was not found with the use of subdural electrodes. The use of depth electrodes appears to be a safer procedure than subdurals and/or grids.

EPILEPSY SURGERY

Abstract 47

An Assessment of Patient Barriers to Accessing Surgical Care in Epilepsy Surgery

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Rationale
Less than 1% of patients with pharmacorresistant epilepsy are referred to specialized centers. The average wait-time from seizure-onset to epilepsy surgery is 20 years in adults. Few studies have explored barrier access to epilepsy surgery.

Method
This is a cross-sectional study that recruited 101 patients with focal epilepsy. Patients answered a 33-item questionnaire that assessed knowledge and perceptions about surgical options and risks. The answers from patients who had epilepsy surgery were compared with those who did not have. Mean, SD and intervals were used to describe numerical variables and frequencies and proportions for categorical variables. Analysis of Chi square and t-student were used to explore differences. P value was established at <0.05.

Results
Mean age of patients was 38.6±12.9 (17-75). 55% were male and the mean duration of epilepsy was 16.2 years±13.0. 31 patients (30.7%) had previous epilepsy surgery. Mean time from epilepsy onset to epilepsy surgery was 16.1±12.1. The answers that were different between the two groups were as follows: knowledge about if brain surgery was an option to treat epilepsy and who told them, risk of serious side effects after epilepsy surgery and questions about travel for surgery and costs. In general, patients who had epilepsy surgery had a lower negative perception of epilepsy surgery (p 0.02).

Conclusions
We identified important negative perceptions for epilepsy surgery in patients who have not had epilepsy surgery. These perceptions can potentially become barrier of access for the best treatment for epilepsy.

EPILEPSY SURGERY

Abstract 48

Long-Term Outcomes after Gamma Knife Surgery for Hypothalamic Hamartomas Causing Refractory Epilepsy - A Prospective Observational Study

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Rationale
This prospective observational study, conducted at the CHUS between 2005 and 2016, aims to examine the outcomes of patients who underwent radiosurgery for hypothalamic hamartomas (HHs).

Method
Patients were included in the study if they were diagnosed with an HH and refractory epilepsy, without any other suspected seizure focus. After radiosurgery, seizure status was assessed periodically using the Engel Classification. Neuropsychological and quality of life evaluations were performed at baseline and thereafter. A follow-up evaluation was completed ten years after the first Gamma-knife treatment.

Results
Thirteen patients, refractory to medical treatment, were included in the study, ranging in age from 12 to 57 years. Using the Régis Classification, ten patients had smaller hamartomas (Grade I-III) and underwent treatment of the entire lesion. Radiosurgical disconnection was attempted in three patients with larger lesions (Grade IV-VI). One patient was lost to follow-up, and one died from seizure complications following an open surgery for HH. Disconnection was ineffective. Radiosurgery was repeated in three patients in which the first intervention had failed to reduce the seizure burden. After 5.7 years in average, seven patients (58%) had a good outcome (Engel I-II), including five patients who were seizure-free after a mean time of 6.4 months. Five patients (42%) had Engel classification of III or IV. Adverse events included psychotic depression and radiation necrosis.

Conclusions
We consider radiosurgery as a first-line surgical therapy for patients suffering from refractory epilepsy secondary to HHs, as it has shown long-term efficacy in our population, principally in cases where the entire lesion could be targeted.

EPILEPSY SURGERY

Abstract 49

Temporal Lobe Epilepsy Surgery in Patients with Co-Existent Psychogenic Non-Epileptic Seizures

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Rationale
Psychogenic non-epileptic seizures (PNES) may co-exist in patients with epileptic seizures. Patients with PNES and concurrent drug resistant epilepsy can be a particular challenging group for surgical decision-making due to concerns about post-surgical outcomes, higher prevalence of psychiatric comorbidities and the fear that sustained PNES following a successful surgery could impose obstacles for additional impact in quality of life. The aim of this study is to report the clinical characteristics and post surgical outcomes of patients with temporal lobe epilepsy and concomitant PNES (TLE+PNES), and compare them with surgical TLE patients without PNES (TLE-PNES).

Method
This is a retrospective observational study. TLE patients who underwent surgery from 1999 to 2014 were identified from the database at the University of California San Francisco (UCSF) and from one neurosurgeon's database at the Montreal Neurological Institute. Demographic information, seizure frequency, presurgical psychiatric comorbidities and post-surgery psychiatric complications were reviewed. Seizure outcomes were evaluated using Engel's classification.

Results
From 279 TLE cases, 9 (3.2%) had a presurgical concomitant diagnosis of PNES demonstrated by video-EEG. From the remaining 270 patients, 45 were randomly selected to constitute a comparison group. We found no significant differences in gender, presence of pre surgical psychiatric comorbidities, mean age at seizure onset and duration of epilepsy until surgery between the patients with and without PNES. Post-surgery seizure outcomes were similar in both groups.

Conclusions
When compared to TLE-PNES, patients with TLE+PNES have similar post-surgical psychiatric and seizure outcomes. Adequate preoperative psychiatric evaluation and clarification of clinical characteristics of PNES by video-EEG monitoring are helpful for decision towards surgery.