## Pediatric Epilepsy

Abstract #1

# Effectiveness of a Live-Online Mindfulness Intervention, Making Mindfulness Matter, for Improving Health-Related Quality of Life of Children with Epilepsy: A Pilot Randomized Trial

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### Rationale

Epilepsy detrimentally affects health-related quality of life (HRQOL), with family environment being a key determinant of HRQOL in children with epilepsy (CWE). We evaluated the feasibility of a mindfulness-based program, Making Mindfulness Matter (M3©), to improve HRQOL in CWE and their parents. This analysis examines the treatment effect of M3© on HRQOL in CWE.

### Methods

We conducted a parallel 1:1 randomized controlled trial (n=73: intervention=36, control=37) comparing the 8-week intervention to waitlist control in children aged 4-10 with epilepsy in Ontario. Non-clinician staff from a local epilepsy agency delivered M3© online, synchronously to small groups of parent-child dyads. HRQOL in CWE was measured using the parent-reported 55-item Quality of Life in Childhood Epilepsy Questionnaire (QOLCE-55). Intention-to-treat analysis using linear mixed models compared mean QOLCE-55 scores between arms 1-week post-M3©, adjusting for baseline scores and accounting for clustering of dyads who received M3© together. We then evaluated changes in mean scores in the intervention arm from baseline to 1-week and 10-weeks post-M3©.

### Results

M3© was associated with a 7-point increase in mean QOLCE-55 scores relative to controls (95% CI: 2.09-11.68). In the intervention arm, mean scores improved by 5 points at 1-week post-M3© (95% CI: 1.26-9.31) and 4 points at 10-weeks post-M3© (95% CI: -0.07-8.41).

### Conclusion

Findings provide preliminary evidence for M3©'s effectiveness in improving short-term HRQOL in CWE, suggesting the potential value of low-cost, community-based interventions to support quality of life for families and children living with epilepsy. These results, along with feasibility results, will be used to prepare a larger multi-centered trial.

Funding: Project Grant from the Canadian Institutes of Health Research (PJT 159504).

## Epilepsy Surgery

Abstract #2

# The Impact of Contralateral Electrodes in Patients Undergoing Stereoelectroencephalography

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### Rationale
Determine the impact of implanting contralateral electrodes in the suspected epileptogenic zone (EZ) in patients who undergo stereoelectroencephalography (SEEG).

### Methods
Data was collected from 109 epilepsy patients who underwent SEEG investigation at LHSC from 2018-2023. The electrode implantation for each patient was classified into one of the following categories: (i) Unilateral, in 13 patients; (ii) Sentinel, in 41 patients (iii) Bilateral with a lateralized EZ hypothesis, in 28 patients (iv) Bilateral with a non-lateralized EZ hypothesis, in 27 patients. The electrographic involvement of the contralateral electrodes was analyzed for patients with sentinel and with a bilateral with a lateralized EZ hypothesis.

### Results
Having a seizure onset and epileptiform discharges in the contralateral hemisphere to the EZ hypothesis was the most common finding associated with changing the EZ hypothesis (p=0.001) and not being eligible for surgery (p=0.001). Patients with unilateral 7 (54%), sentinel 27 (66%), and bilateral electrodes with lateralized EZ hypotheses 15(54%) were more likely to be candidates for surgery than patients with bilateral non-localized hypotheses 5 (19%) (p= 0.00178). No significant difference was found regarding seizure freedom rate depending on the type of implantation at three (p=0.867), six (p=0.994), or twelve months (p=0.867). Three (25%) unilateral, four (33%) sentinel, three (25%) bilateral electrode patients with a lateralized hypothesis and two (17%) bilateral electrode patients with a non-lateralized hypothesis had SEEG-associated complications (p= 0.501), with the majority being non-symptomatic haemorrhages.

### Conclusion
The placement of contralateral electrodes in SEEG investigations may not pose an increased risk of morbimortality; instead, it may influence surgical decision-making.

## Status Epileptics / Critical Care

Abstract #3

# Long-Term Neuropsychological Outcomes After Super-Refractory Status Epilepticus

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### Rationale

Super-refractory status epilepticus (SRSE) is a rare neurologic emergency that consists of continuous seizures despite the administration of three anti-seizure medications. SRSE may have various presentations, including new-onset refractory status epilepticus (NORSE) and febrile infection-related epilepsy syndrome (FIRES). Poor functional outcomes in SRSE survivors have been reported but specific cognitive and neuropsychological sequelae remain inadequately understood.

### Methods

We are the primary site for a retrospective multicentre study for SRSE patients that were admitted to the intensive care unit between 2000 and 2023 and received neuropsychological testing post-SRSE. We are considering acute and long-term clinical outcomes and neuropsychological assessment results.

### Results

At our site, four of 22 patients who were admitted with SRSE received neuropsychological testing at our site (two males; median age = 35 years, IQR=9.25 years). All patients had NORSE, with three being classified as FIRES. All patients developed drug-resistant epilepsy (multi-focal (N=2) and bilateral temporal lobe (N=2)). Results from neuropsychological evaluations (completed a median of 2 years (IQR=0.5 years) post-SRSE onset) were variable. General intellectual functioning was impaired for two participants, and broadly average and low average for the remaining two. Results from neuropsychological assessments will be presented, along with data from three international sites. A comparison of how various centres measure cognitive outcomes will also be presented.

### Conclusion

This international study will provide insight into neuropsychological outcomes among SRSE survivors and the assessments that provide a detailed outline of abilities post-SRSE. This study may inform the assessments used in future work to harmonize international research initiatives.

## Neuroimaging

Abstract #4

# Structural Compromise in Spiking Epileptic Cortex and Connected Tissue: A Combined MRI and HD-EEG Study

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## Rationale

Developing non-invasive cartographies of the epileptic brain is critical to understanding epilepsy pathophysiology and ultimately improving diagnostics. Here, we mapped alterations in cortical structure within and beyond spiking tissue.

## Methods

We studied 25 patients with focal epilepsy (12F, mean±SD age = 31.28±9.30 years) and 30 controls (15F, mean±SD age = 31.40±8.74 years). All underwent 3T MRI (T1-weighted, diffusion, quantitative relaxometry, and resting-state functional). We derived maps of mean diffusivity (MD), cortical thickness (CT), quantitative T1 relaxometry (qT1), intrinsic neural timescales (INT), connectivity distance coefficient (CDC), and node degree (ND). We derived vertex-wise structural alteration multivariate scores (from MD, CT, and qT1 maps) and functional alteration scores (from INT, CDC, and ND maps). Using HD-EEG, the average preponement spike type was localized at maximum amplitude time using coherent maximum entropy on the mean. We quantified alteration scores within spiking regions, their functional, structural, and geodesic neighbors, and the rest of the brain.

## Results

HD-EEG spiking regions showed increased structural MRI alterations: group-wise analyses revealed a significantly greater percentage of structurally altered vertices within the spiking region than in the rest of the brain, paired t-test, $p < 0.05$. Structural compromise extended to all close functional neighbors of spiking regions and to 80% of close structural neighbors, but not to geodesic neighbors, paired t-tests, FDR-corrected $p < 0.05$.

## Conclusion

Mapping alterations in cortical microstructure and morphology carries potential to help localize the epileptogenic zone noninvasively. Functional and structural relationships to the epileptic focus may impact the magnitude of structural changes in other cortical regions.

## Neuroimaging

Abstract #5

### Atypical Signal Flow in Episodic Memory Associated with Temporal and Frontal Lobe Epilepsy

Donna Gift Cabalo[1], Jordan DeKraker[1,2], Ke Xie[1,2], Jessica Royer[1,2], Raul Rodriguez-Cruces[1,2], Thaera Arafat[2], Neda Bernasconi[2], Raluca Pana[2], Jonathan Smallwood[3], Boris Bernhardt[1,2]

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### Rationale

Temporal and frontal lobe epilepsy[1] (TLE; FLE) are associated with significant but differential episodic memory impairments[2]. TLE patients exhibit marked episodic memory difficulties[3], while FLE experience mild impairment[4]. This study examines the directionality of signal flow between two models of epilepsies with variations of structural alterations, to assess how local disruptions due to lesions integrate with broader cognitive architectures and impact global brain function.

### Methods

We studied 20 TLE (left/right=12/8, age=32±7 years; F/M: 13/7), 15 FLE (left/right=8/7, age=30±8 years; F/M: 9/6) and 78 controls (age=32±9 years, F/M: 38/40). Effective connectivity[5] (EC) was computed from neocortical and hippocampal episodic fMRI data to infer out/in degree (signal) scores. Group differences in signal flow and its association with memory impairments were evaluated.

### Results

Behaviorally, patients exhibited markedly reduced episodic accuracy relative to controls. In TLE, atypical signal flow was observed in ipsilateral lateral-temporal, fronto-parietal and hippocampal lateral regions. In FLE, disrupted signal flow was observed in the ipsilateral anterior hippocampus but not in the neocortex. Neocortical and hippocampal in-, but not out-degree scores, correlated with episodic performance. No significant associations were observed for out/in-degree scores in FLE.

### Conclusion

Our task-fMRI analysis reveals differential but disrupted episodic signal flow in both patient groups, providing novel insights into the episodic memory reorganization, which may underpin impairments in some patients but potentially serve as compensatory adaptations.

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## Neuroimaging

Abstract #6

### Artificial Intelligence and Machine Learning in Neuroimaging of Epilepsy: A Systematic Review and Meta-Analysis

Judy Chen[1], Ella Sahlas[2], Yigu Zhou[2], Natalie Chen[3], Sienna Armstrong[2], Farhan Wadia[2], Lorenzo Caciagli[4], Andrea Bernasconi[5], Neda Bernasconi[5], [6]Dewi Schrader, Boris Bernhardt[2]

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#### Rationale
Artificial intelligence (AI) and machine learning (ML) methods have been increasingly leveraged to analyze brain magnetic resonance imaging (MRI) data to aid with clinical decision-making, yet their accuracy and effectiveness remains unclear. Here, we assess the performance of current AI/ML models in four major clinical applications: diagnostic ability to identify epilepsy patients, lateralize the epileptic lesion, localize the seizure-onset zone, and predict post-surgical outcomes.

#### Methods
A systematic review utilizing MEDLINE and Embase databases yielded 2606 publications. Studies were included if they used any AI/ML model trained on MRI images to classify patients according to the four stated outcomes and reported any evaluation metric (sensitivity/specificity, AUC under ROC, or total accuracy score). Risk of bias of each study was assessed using the Prediction model Risk of Bias Assessment Tool (PROBAST) tool.

#### Results
200 studies were included. 171 studies that reported an accuracy score (diagnosis n= 87/95; localization n=17/35; lateralization n= 37/42; surgical outcome n=20/28) were used in the meta-analysis. Subsequent analyses show robust accuracy rates: diagnosis=91%, lateralization=90%, localization=80%, surgical outcome=84%. All estimates had significant heterogeneity between studies (I^2>99, p<0.01). There were no significant differences between using unimodal vs. multimodal MRI data. All studies reported an overall high risk of bias.

#### Conclusion
AI/ML in clinical applications show robust accuracy across various study designs and algorithm types. However, high risk of bias remains a challenging barrier to clinical translation. Future studies should

prospectively image participants prior to their diagnosis or surgery, verify patients' diagnoses histopathologically, and incorporate model validation using independent test cohorts.

## Neuroimaging

Abstract #7

# Towards Personalized Multimodal Lesion Mapping of Drug-Resistant Temporal Lobe Epilepsy: A Multisite Validation

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## Rationale

Many drug-resistant patients are diagnosed with temporal lobe epilepsy (TLE), yet diagnostic methods to lateralize their lesion for curative treatment remains a challenge. Here, we develop and leverage our in-house image processing and analysis tools to: 1) map the distribution of patient-specific alterations in neocortical and hippocampal subregions; 2) evaluate the efficacy of these features to lateralize patients using machine learning.

## Methods

388 individuals from 3 independent sites comprosing of 123 TLE patients (61F; mean±SD: 32.4±11.1 years) and 265 healthy individuals (94F; mean±SD age: 29.0±9.6 years) were included. All participants underwent 3T T1-weighted (T1w) and diffusion MRI. Participant imaging data were processed using micapipe_v0.2.0, hippunfold_v1.3.0, and z-brains (https://github.com/MICA-MNI/z-brains). |z|>1.96 were considered altered. Probability of altered cortical thickness (CT), fractional anisotropy (FA), and apparent diffusion coefficient (ADC) were mapped. Logistic regression (LR) and support vector machine (SVM) algorithms were trained using 10-fold cross validation to classify each patient's lateralization.

## Results

Temporal regions were most likely to be altered; over 40% patients had altered ADC. However, mean proportion of each region show that high neocortical variability remains even in the best performing feature (ADC). Hippocampal maps show moderate atrophy, and highly pronounced ADC signal with slight anterior-posterior gradient. Models trained on hippocampal data achieved higher accuracy in lateralizing patients. SVM trained on ADC and CT cortical and hippocampal data achieved the highest accuracy score (87.1%).

## Conclusion

Patient MRI are too variable to rely on single imaging techniques. Personalized lesion mapping techniques supplemented with machine learning is a promising avenue for lateralization diagnostic ability.

## Neuroimaging

Abstract #8

### Whole Brain Profile of Hub Disruption in Frontal Lobe and Mesial Temporal Lobe Epilepsy

Arielle Dascal[1], Édouard Delaire[2], Thaera Arafat[1], Judy Chen[1], Chifaou Abdallah[1], Ella Sahlas[1], Alexander Ngo[1], Hans Auer[1], Jessica Royer[1], Raul Rodriguez-Cruces[1], Christophe Grova[1,2]

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#### Rationale

Resting state functional magnetic resonance imaging (rs-fMRI) profiles functional networks, where disruptions have been shown in focal epilepsy (Royer et al., Epilepsia, 2022). Our team proposed SParsity-based Analysis of reliable k-hubness to identify connector hubs (Lee et al., NeuroImage, 2016), crucial for long-range and inter-network communication (Van Den Heuvel and Sporns, Trends in Cognitive Sciences, 2013). Our study mapped connector hub alterations in epilepsy patients.

#### Methods

16 temporal lobe epilepsy (TLE), 10 frontal lobe epilepsy (FLE) and 30 matched Healthy Controls underwent 3T rs-fMRI scans. Hemispheres were parcellated into 20 regions using the Automated Anatomical Labelling Atlas (Rolls et al., NeuroImage, 2020). The hub disruption index (HDI) was estimated (Lee et al., NeuroImage: Clinical, 2018), quantifying hub changes via linear regression, where negative slopes indicate hub disruption in patients. Bootstrap resampling was considered to generate a null HDI distribution.

#### Results

TLE showed significant hub disruption (loss of hubness) in the right mesial temporal lobe, bilateral hippocampi, and left mesial parietal and posterior cingulum ($p<0.05$). FLE demonstrated significant hub disruption in the bilateral mesial ($p<0.05$ right, $p<0.001$ left), bilateral lateral ($p<0.001$), right middle ($p<0.05$), and bilateral orbitofrontal ($p<0.001$) frontal regions.

#### Conclusion

We identified widespread functional network disruption in both cohorts, with hub disruption in default mode network regions and frontal lobes. TLE demonstrated localized disruption, involving mesial temporal structures. Future work will replicate findings in larger cohorts to assess robustness, and associations with structural alterations.

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## Neuroimaging

Abstract #9

### Thalamo-Cortical Functional Network Alterations in TLE

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### Rationale
The thalamus is a crucial bilateral grey matter structure that assists in whole-brain coordination through relaying information between cortical and subcortical regions. It plays a significant role in the diagnosis and treatment of epilepsy. Previous studies have explored the structural reorganization in thalamus, both in grey and white matter. Here, we aim to leverage resting-state fMRI to explore the functional reorganization of thalamus in temporal lobe epilepsy (TLE) via functional connectivity gradient in thalamus.

### Methods
A total of 70 unilateral TLE patients and 81 healthy controls (HC) were recruited from two independent sites. Rs-fMRI timeseries were used to calculate Pearson correlations between thalamic and cortical connections using voxel-wise and cortex vertex-wise timeseries. First, we used the group functional connectivity of HC to calculate the reference gradient, then we aligned individual gradients to the reference standard, calculated z-scored group-wise gradient differences, and categorized data into ipsilateral and contralateral regions.

### Results
We show that principal gradient (G1) in both the TLE and HC showed a lateral to medial pattern whereas G2 showed an anterior to posterior pattern. Compared with HC, the extremes of the histogram of G1 and G2 in TLE patients showed compression, GLM statistical analysis showed that G1 compression is mainly caused by decreased G1 of the lateral thalamic region.

### Conclusion
TLE patients showed a compression in the thalamus-cortical gradient, which may indicate a reduced functional differentiation in thalamus. This is suggestive of impaired thalamic processing and integrative functions in TLE patients.

## Neuroimaging

Abstract #10

# The Importance of Diffusion Tractography for Visual Field Preservation in Laser Interstitial Thermal Therapy for Refractory Epilepsy

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### Rationale

Laser interstitial thermal therapy (LITT) is a minimally invasive therapy that uses a thin laser fiber guided by real-time MRI to ablate brain tissue. LITT for medial temporal lobe epilepsy (mTLE) and peri-atrial nodular heterotopia-associated epilepsy (PANHE) is often complicated by visual field deficits (VFD) due to the proximity of the optic radiations (OR) to the seizure focus. The objective of our study is to assess the correlation between tractography-informed injury to the ORs and VFDs in seven patients having undergone LITT for refractory mTLE or PANHE.

### Methods

Seven patients having undergone LITT for mTLE or PANHE at the University of Montreal Hospital Center and Montreal Sainte-Justine Hospital were selected for this study. All seven patients had failed conventional antiseizure drug treatment. Diffusion tractography of the ORs was performed pre-operatively. A mask of the ablation area was delimited on the postoperative contrast-enhanced T1 MRI. This mask was then registered onto preoperative T1 images and overlaid to the tractography-reconstructed ORs. A formal ophthalmology evaluation was completed to assess postoperative VFDs. The damage to the ORs revealed by tractography was correlated with VFDs.

### Results

None of the seven patients exhibited VFDs, and there was either no overlay or minimal overlay between the ablation mask and the ORs.

### Conclusion

Tractography may accurately delineate ORs. Moreover, the magnitude of injury to the OR reconstructed by tractography seems to be related to VFDs. Hence, the use of this non-invasive technique during presurgical planning may help reduce VFDs in patients who undergo LITT for mTLE and PANHE.

## Neuroimaging

Abstract #11

### Imaging Blood-Brain Barrier Dysfunction in Drug-Resistant Epilepsy: A Multi-Center Feasibility Study

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#### Rationale
Dysfunction of the blood-brain barrier (BBBD) has been linked to various neurological disorders, including epilepsy. This study aims to utilize dynamic contrast-enhanced MRI (DCE-MRI) to identify and compare brain regions with BBBD in patients with epilepsy (PWE) and healthy individuals.

#### Methods
We scanned 50 drug-resistant epilepsy (DRE) patients and 58 control participants from four global specialized epilepsy centers using DCE-MRI. The presence and extent of BBBD were analyzed and compared between PWE and healthy controls.

#### Results
Both greater brain volume and higher number of brain regions with BBBD were significantly present in PWE compared to healthy controls ($p < 10\text{-}7$). No differences in total brain volume with BBBD were observed in patients diagnosed with either focal seizures or generalized epilepsy, despite variations in the affected regions. Overall brain volume with BBBD did not differ in PWE with MRI-visible lesions compared with non-lesional cases. BBBD was observed in brain regions suspected to be related to the onset of seizures in 82% of patients (n = 39) and was typically identified in, adjacent to, and/or in the same hemisphere as the suspected epileptogenic lesion (n = 10).

#### Conclusion
These findings are consistent with pre-clinical studies that highlight the role of BBBD in the development of DRE and identify microvascular stabilization as a potential therapeutic strategy.

## Neuroimaging

Abstract #12

### Imaging-Transcriptomic Mapping of Hippocampal Alterations in Temporal Lobe Epilepsy

Alexander Ngo[1], Sara Larivière[2], Jessica Royer[1], Jacob Vogel[3], Raúl Rodríguez-Cruces[1], Luis Concha[4], Zhiqiang Zhang[5], Raluca Pana[6], Neda Labdon-Bernasconi[1], Andrea Bernasconi[1], Ziv Gan-Or[1], Alan Evans[1], Jordan DeKraker[1], Boris Bernhardt[1]

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#### Rationale

Hippocampal sclerosis (HS) is the pathological hallmark of temporal lobe epilepsy (TLE). Despite extensive research revealing TLE-related genes, their downstream effects rendering the hippocampus more vulnerable to seizures remain unclear. Here, we mapped hippocampal structural alterations in TLE, and examined associations to TLE-specific risk gene expression.

#### Methods

We investigated T1-weighted and diffusion MRI data of 67 individuals with pharmaco-resistant unilateral TLE (mean [SD] age = 31.9 [12.0] years, 34 females, 32 left sided focus) and 92 age/sex-matched healthy controls (age = 31.7 [10.0] years, 51 females).

Using HippUnfold, an automated pipeline for hippocampal unfolding and novel surface-based registration, we sampled hippocampal thickness (HT), fractional anisotropy (FA), and (mean diffusivity (MD) across all participants. Surface-based linear models compared patients with TLE to healthy controls.

Based on genome-wide association studies, we derived HS-related gene expression (C3orf33, GJA1, KCNAB1, SCN1A, SLC33A1) from the Allen Human Brain Atlas. Spatial correlations examined correspondence between structural and transcriptomic maps. Assessing disease specificity, we repeated analyses with generalized epilepsy (GE) risk genes.

#### Results

We observed widespread HT decreases, FA decreases, and MD increases in patients relative to controls. Imaging-transcriptomic correlations revealed strong associations between structure and TLE risk genes: (i) HT correlated with GJA1 and KCNAB1, and (ii) FA and MD correlated with C3orf33, SLC33A1, and SCN1A. Little significant correlations were observed for risk genes associated with GE.

## Conclusion

Capitalizing on recent imaging-transcriptomic initiatives, widespread hippocampal alterations in morphology and microstructure were related to independent sets of risk genes specific to HS, pointing to parallel and disease-relevant pathways.

## Neuroimaging

Abstract #13

# Mapping the Intra-Insular Structural Connectivity Using High Resolution Tractography Techniques

Farbod Niazi[1], Salma Khriss[2], Albert Guillemette[1], François Rheault[3], Etienne St-Onge[4], Maxime Descoteaux[5], Arash Sarshoghi[2], Emna Guibene[2], Dang K. Nguyen[6], Alain Bouthillier[7], Obaid[7]

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## Rationale

There is limited evidence on intra-insular connectivity patterns. This study aimed to describe and quantify the structural connectivity between insular subregions of healthy subjects using robust, anatomically constrained, microstructure-informed tractography techniques.

## Methods

T1-weighted and diffusion-weighted imaging data from 142 healthy subjects in the Human Connectome Project (HCP) database were obtained and analyzed. Probabilistic tractography was performed using the surface-enhanced particle filtering tractography pipeline. To quantify the connectivity between six insular subregions derived from the Brainnetome and Glasser atlases, we ran the Convex Optimization Modeling for Microstructure Informed Tractography (COMMIT) algorithm to assign COMMIT weights, an accurate microstructure-reflecting marker of connectivity strength, to each bundle. Using the Test-Retest subgroup of the HCP, test-retest reliability was calculated using the intraclass correlation coefficient (ICC) between 44 participants with imaging acquired at two different timepoints. Mann-Whitney U tests were used to compare the connectivity of corresponding regions between the left and right insulae.

## Results

Insular COMMIT-weighted connectomes for all 142 subjects were computed. ICC revealed excellent or good to excellent test-retest reliability, confirming the reproducibility of our pipeline. Widespread connections were observed between all insular subregions. The middle insula demonstrated overall higher connectivity strength, acting as a connectivity hub linking the anterior and posterior insula. The right insula demonstrated stronger intra-insular connectivity strength.

## Conclusion

For the first time, we have described and quantified intra-insular structural connectivity in healthy human subjects. These findings could provide a better understanding of epileptic networks and seizure propagation patterns within the insula, facilitating the diagnosis and treatment of epileptic patients.

## Neuroimaging

Abstract #14

### Segmentation of Intracranial Electrode Contacts Using Convolutional Neural Networks

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### Rationale

Stereoelectroencephalography (SEEG) is a minimally invasive procedure for epilepsy that uses intracranial electrodes to determine the seizure onset zone. Each electrode contains 5-10 millimetric contacts that must be localized prior to analysis. This is done by visually reviewing post-operative images for contact artifacts. Various semi-automated toolboxes exist to expedite this process, but they require 1-2 hours of manual review. Our project leverages a dataset of over 200 SEEG cases to develop a deep-learning workflow for automatic contact localization.

### Methods

A 3-dimensional U-Net was trained on Computed Tomography (CT) scans of 121 randomly selected patients who underwent SEEG implantation from 2017 to 2024. The manually localized contact coordinate formed the ground-truth label. MONAI (a PyTorch-based framework for deep learning) (version 2.9.0) was used to implement this model. The model was evaluated on a separate dataset of 16 randomly selected patients (194 electrodes, 1940 contacts). Predictions were labelled using the electrode trajectory, defined by two points placed at the end and tip of the electrode.

### Results

The model achieved an accuracy of 97.6% on the validation (1893/1940 contacts), with a prediction time of ~40 seconds. The mean Euclidean error for predicted contacts compared to the manual placement was 0.45 ± 0.27 mm. In comparison, the semi-automated tool employed at our centre (SEEG Assistant) had an error of 1.40 ± 0.74 mm ($p < 0.001$).

### Conclusion

We present a method for automatic SEEG contact localization that compares favorably to current standards in terms of both processing time and accuracy.

## Neuroimaging

Abstract #15

# Superior Lesion Detection on 3D FSE T1WI with Magnetization Transfer and CHESS Preparation Pulses in Children with Focal Epilepsy

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### Rationale
In childhood drug-resistant focal epilepsy, identification of an MRI lesion significantly affects the management and prognosis, although it is often challenging. Herein we report the preliminary results of a modified MR sequence that improves lesion identification and visualization.

### Methods
Retrospective chart review of patients receiving the mentioned MRI sequence between January 1, 2020, to December 31, 2023. We identified four patients with positive results of the reported sequence. The patients were scanned with our institutional standard epilepsy brain MR protocol. A 64-channel head coil was used. The 3D FSE T1-weighted SPACE sequence with MT and CHESS preparation RF pulses were performed in a sagittal plane with a TR of 400 ms, TE of 9 ms, echo-train-length of 44, slice thickness of 1 mm, NEX of 1.4, and a total scan time of 2 minutes and 45 seconds. The source images were reformatted into orthogonal axial, coronal, and sagittal planes with a 3-mm slice thickness and 1-mm increment.

### Results
The new sequence can be run with a scan time less than 3 minutes. In all four patients, the cortical/subcortical lesions were visible on standard high-resolution FLAIR images, but the lesions are more conspicuous and appear larger on the 3D T1WI with MT and CHESS guiding SEEG insertion and resection planning.

### Conclusion
The new MR sequence of 3D FSE T1-weighed SPACE with added MT and CHESS preparation RF pulses is a promising sequence, although further studies with pathology correlation and larger sample sizes are required to further assess its impact on the diagnosis and management of children with epilepsy.

## Neuroimaging

Abstract #16

### Individualized and Multiscale Profiles of Cortical Dysfunction in Temporal Lobe Epilepsy

Ke Xie[1], Jessica Royer[1], Ella Sahlas[1], Alexander Ngo[1], Thaera Arafat[1], Judy Chen[1], Yigu Zhou[1], Zhiqiang Zhang[2], Luis Concha[3], Boris Bernhardt[1]

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#### Rationale
Temporal lobe epilepsy (TLE) is the most common pharmaco-resistant focal epilepsy in adults, affecting over 50 million people worldwide. Here, we employed multi-site rs-fMRI data and several analysis strategies to investigate functional imbalances in TLE patients at individual levels and across different scales.

#### Methods
We analyzed 223 unilateral TLE patients and 258 matched healthy controls collected from three sites. Three functional properties across different scales were calculated from rs-fMRI timeseries at the node level: temporal variability, regional homogeneity, and degree centrality. A W-score was calculated for each patient and brain region as follows: W-score = (raw - predicted)/RSD, indicating the extent to which each brain region for that individual is atypical relative to the norm. We used a cut-off score of 2 standard deviations to isolate regions with significant atypicality and established a prevalence map to show the percentage of patients with markedly atypical W-scores in each region.

#### Results
Across all brain regions, the median prevalence of atypical temporal variability, regional homogeneity, and degree centrality in TLE was 36.6%, 7.6%, and 6.3%, respectively. A systemic assessment of the three measures using Mahalanobis distance revealed diffuse atypicality in TLE, with a higher prevalence in the bilateral temporal lobes. Additionally, a higher prevalence of atypical W-scores was observed in patients with hippocampal atrophy and longer illness duration in the ipsilateral temporal cortex.

#### Conclusion
The highest prevalence of functional atypicality observed in medial and lateral temporal regions supports the notion of the temporal cortex as a disease epicenter and may inform individualized therapeutic targets.

## Neuroimaging

Abstract #17

### MRI Features of Microstructure and Hemodynamics Reflect Pathological High Frequency Oscillations on iEEG

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### Rationale

Epilepsy is a syndrome of neuronal dynamics accompanied by defects in structure and hemodynamics that support neuronal communication. Intracranial EEG (iEEG) provides direct access to aberrant high-frequency neuronal dynamics (ripples and fast ripples), while MRI provides robust estimates for cortical structure and hemodynamics. In this work, we integrate iEEG and MRI data from surgical candidates to investigate the structural and hemodynamic underpinnings of epileptogenicity.

### Methods

Interictal iEEG recordings from nine patients (29□8 years; 8 females; 2 TLE; 849 channels) underwent automated detection for calculating ripple and fast ripple rates (RR; FRR). Channels were labeled abnormal if exceeding 95th percentile of region-specific normative RR distributions. Measurements of microstructure (cellularity, differentiation and columnarity), diffusion (T1 map, diffusivity, anisotropy), and hemodynamics (variability, autocorrelation, entropy) in patients were standardized against 50 matched healthy controls then sampled from vertices within 5mm from individual channels. We investigated the effects of MRI measures on RR, FRR and electrophysiological abnormality using linear mixed models (LMM) inputting patients and brain regions as random effects.

### Results

Across channels (338 abnormal), RR and FRR were highly correlated (r=.67); otherwise, uncorrelated to MRI measures. Using LMM, we found that hemodynamic autocorrelation and entropy related to electrophysiological abnormality (slopes=-.16; -.68). Microstructural cellularity, differentiation and columnarity were also correlated to RR (slopes=-.07; -.00003; 1.5) while only columnarity related to FRR (slope=1.0).

### Conclusion

Combining optimal access to brain dynamics via iEEG with advanced whole-brain MRI, our data highlighted that microstructural disarray reflected ripple and fast ripple production, while electrophysiological abnormality was ultimately related to MRI hemodynamics.

## Clinical Epilepsy / EEG / Antiepileptics

Abstract #18

# The Association of Air Pollution with New-Onset Epilepsy

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### Rationale

Air pollution has been associated with certain neurological disorders, but its association with epilepsy has been insufficiently explored. Our objective was to estimate the association of long-term exposure to fine particulate matter (PM2.5), nitrogen dioxide (NO2), and ozone (O3) with new-onset epilepsy among adults in Ontario, Canada.

### Methods

We used a nested case-control study design and individually linked health administrative and environmental databases. We included Ontario residents aged 18 to 80 on January 1, 2010, excluding those with prior diagnoses of seizures or epilepsy. We identified as cases those who developed epilepsy within six years and matched each with up to five controls using risk-set sampling. We used conditional logistic regression models to estimate the risk of new-onset epilepsy for an interquartile range increase in the concentration of each pollutant individually and in a multi-pollutant model.

### Results

We included 24,761 cases and 118,692 controls. The median [IQR] pollutant concentrations were 7.9 [1.3] µg/m3 for PM2.5, 9.6 [9.2] ppb for NO2, and 42.7 [5.4] ppb for O3. In the individual pollutant models, we observed significant associations between epilepsy onset and PM2.5 (OR=1.055 95% CI: 1.034, 1.076), NO2 (OR=0.938, 95% CI: 0.903, 0.974), and O3 (OR=1.096, 95% CI: 1.074, 1.119). In the multi-pollutant model, NO2 (OR=0.928, 95% CI: 0.891, 0.965) and O3 (OR=1.090, 95% CI: 1.060, 1.121) remained statistically significant.

### Conclusion

The negative association observed between NO2 and epilepsy may be a result of residual confounding. Future research should continue to explore the associations between specific air pollutants and epilepsy onset.

## Clinical Epilepsy / EEG / Antiepileptics

Abstract #19

# Hippocampal Tau Deposition as a Key Indicator of Sleep and Memory Impairment in Drug-Resistant Focal Epilepsy

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### Rationale

Tau aggregates measured in positron emission tomography (PET) is a biomarker for neurodegenerative disorders, leading to seizures and subclinical epileptic activity (Lam et al.,2020). Sleep impairment is linked to cognitive decline in tauopathy and focal drug-resistant epilepsy (DRE) (Kim et al., 2024). Pathological tau has been detected in post-mortem and surgically resected tissue in DRE patients (Smith et al., 2019). We aim to investigate the relationship between sleep spindles and tau deposition in the hippocampus in focal DRE, hypothesizing a negative correlation between spindle-rates and hippocampal tau deposits.

### Methods

We included 20 focal DRE patients who underwent scalp EEG (29 channels) and F18-MK6240 PET with 3T MRI. Sleep spindles (10-16Hz, 0.5-3 seconds) were automatically detected. PET uptake was aligned with T1-weighted MRI, volume-corrected, normalized to the cerebellum to obtain a standardized uptake value ratio (SUVR) and was extracted from the hippocampus after segmentation (DeKraker et al., 2022). Correlations were computed between ipsilateral hippocampal tau, age and spindle-rates with age adjusting.

### Results

Spindle-rate per minute during N2 sleep was negatively correlated with SUVR of tau deposits in ipsilateral hippocampus (r: -0.45, p: 0.05). Age showed a negative correlation with spindle-rate (r: -0.66, p: 0.001) and a positive correlation with tau deposits (r: 0.46, p: 0.04). After adjusting for age, a moderate negative correlation between spindle rates and tau deposits remained (r: -0.26, p:0.35).

### Conclusion

There is a negative correlation between spindle-rates and tau deposits, potentially associated with cognitive dysfunction in TLE patients. However, a direct association between spindles and tau deposits, independent of the age effect, needs to be clarified in a larger population.

## Clinical Epilepsy / EEG / Antiepileptics

Abstract #20

*Withdrawn*

## Clinical Epilepsy / EEG / Antiepileptics

Abstract #21

### Physical Activity in Young People with Epilepsy: Co-Design and Development of a Web App

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### Rationale
Being physically active is beneficial to the health of young people with Epilepsy (YPE). Recent work has found that YPE are interested in physical activities aligned with their preferences but may need guidance on participation. With input from YPE, their parents, and healthcare providers, this knowledge translation project developed a web app to promote safe engagement in physical activities.

### Methods
The study followed the Toronto Translational Framework to frame the context, ideate the design and test the prototype. A total of 73 specialists and providers in Child Neurology/Epilepsy in Canada, USA, Israel, and Turkey completed a survey on their approaches to discuss physical activity with YPE. Content Analysis of the survey responses using the themes identified in previous work as codes informed the app prototype design.

### Results
Respondents indicated the need for accessible, easy-to-use online tools to discuss physical activity in YPE. They identified 23 activities YPE prefers and suggested the tools should provide safety and accommodation guidelines, enable social connection and support, assist with setting goals, and reinforce advice discussed in clinical visits. The tool features align with the insights from YPE and their parents, identified in the previous study. Conversely, other respondents noted that the lack of resources and time during clinical visits prevents discussions of physical activities, which the online tool can address.

### Conclusion
A web app accessible on phones and computers is under development. By creating a user-friendly tool addressing physical activity concerns, providers can support promoting an active lifestyle for YPE and their families.

Funder: Physicians' Services Incorporated Foundation

## Clinical Epilepsy / EEG / Antiepileptics

Abstract #22

# The Transition from Pediatric to Adult Medical Care for Adolescents with Epilepsy: A Qualitative Assessment of Patient and Family Caregivers Priorities

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## Rationale

The transition from pediatric to adult care is a pivotal time for adolescents with epilepsy and their family caregivers. It is often accompanied by stress and uncertainty. We organized focus groups to study the experiences of adolescents with epilepsy and their caregivers. Our overall aim was to identify possible pathways for improving care and support.

## Methods

Three 90-minute focus groups were held in person (November 2023), each comprising 5-6 participants. The first group included adolescents with epilepsy aged 14-21 years. Two subsequent groups were parents of adolescents with epilepsy. Three major topics were addressed: their transition experience, their opinion on the greatest challenges to a successful transition experience, and their opinion on the proposed University of Montreal transition program (TÉCUM). We used a grounded theory framework and carried out a thematic analysis, collating and contrasting the opinions expressed by participants.

## Results

For patients, the period between their last appointment in pediatrics and their first in the adult setting (lasting sometimes 6-12 months) is unsettling, not knowing who to contact in an emergency. Physically navigating the adult hospital is an additional challenge. For parents of adolescents with intellectual disability, personalized care plans and centralizing services are priorities. For parents of those without intellectual disability, good communication and a complete transfer of medical records are essential.

## Conclusion

This qualitative analysis highlights the needs of patients and their family caregivers as they transition to adulthood. This initiative will lead to a TÉCUM program that is best adapted to support their overall well-being.

Funding sources: TD Bank Ready Commitment program

## Clinical Epilepsy / EEG / Antiepileptics

Abstract #23

# Under-Recognized Neurocognitive Deficits in Adults and Adolescents with Tuberous Sclerosis Complex

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## Rationale

Tuberous sclerosis complex (TSC) is a genetic disease associated with multiple manifestations affecting the brain. Patient-reported neurocognitive deficits are identified using the TAND (Tuberous sclerosis Associated Neuropsychiatric Disorders) Checklist. Patients may under-recognize mild cognitive impairment. This study aims to: 1) determine the frequency of abnormal scores on 3 cognitive function tests in people with and without diagnosed intellectual disability 2) examine associations between test scores and self-reported symptoms on the TAND Checklist.

## Methods

A cross-sectional validation study, where people with TSC (PwTSC; N = 46) completed the TAND Checklist and were examined using the Symbol Digit Modalities Test, Montreal Cognitive Assessment test, and Trail Making Test - Parts A and B. We calculated Pearson's correlation coefficients (95% CI) to determine the strength of the association between cognitive test scores and the TAND Checklist. We plotted Receiver Operating Characteristics (ROC) curves to assess the screening accuracy of each measure in identifying physician-diagnosed intellectual disability.

## Results

We found minimal correlations between test scores and the TAND Checklist. Twenty percent of PwTSC reported having no cognitive issues on the TAND Checklist but had at least one abnormal cognitive test performance. The ROC curves demonstrated similar results, with an area under the curve of 0.93 (95% CI: 0.79-1.00) for the SDMT and 0.70 (95% CI: 0.45-0.95) for the TAND Checklist.

## Conclusion

Unrecognized neurocognitive deficits in PwTSC can be identified with objective tests of cognitive function. These deficits likely have multifactorial origins, including mild and undiagnosed intellectual disability and the impact of chronic epilepsy.

Funding sources: TD Bank "Ready Commitment" program

## Clinical Epilepsy / EEG / Antiepileptics

Abstract #24

*Withdrawn*

## Clinical Epilepsy / EEG / Antiepileptics

Abstract #25

# Sex and Gender Reporting in Epilepsy Clinical Trials for US Food and Drug Administration Approvals: 30 Years of Inadequate Reporting

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## Rationale

Sex and gender are related but distinct determinants of disease, treatment response, and research reproducibility. In 2016, the NIH mandated sex as an important biological variable to be considered in research design and reported appropriately. The state of sex and gender reporting amongst epilepsy-related trials used in US Food and Drug Administration (FDA) approvals remains unknown.

## Methods

The Drugs@FDA database of agents approved between 1990-2023 was screened by two independent reviewers to identify all epilepsy therapeutics. For each identified drug, data of all published trials cited in approval were extracted, including study characteristics, sex/gender-based analysis and terminology use.

## Results

Data were extracted from 55 trials describing 17 unique drugs. 85% of trials were industry-funded. 41% (23/55) of studies used sex- or gender-associated terms correctly, and 56% (31/55) either used sex and gender terms interchangeably or incorrectly. Statistical analyses reveal no association between year of publication and appropriate sex/gender, sex, or gender reporting of clinical trials ($p > 0.05$) but reveal a non-significant trend toward more appropriate sex/gender reporting pre- versus post-2016. Only 2 trials reported the gender distribution of their primary outcome; 8 reported the sex distribution of any outcome. None reported the gender distributions of any outcome. Two trials discussed gender disaggregation for any outcome.

## Conclusion

Despite the importance of sex and gender considerations in epilepsy therapeutics, reporting and analysis of sex/gender variables continues to be minimal among trials supporting FDA epilepsy drug approval. The development of a common standard and accountability for sex and gender reporting and analysis will be important to bridge these identified gaps.

## Clinical Epilepsy / EEG / Antiepileptics

Abstract #26

# Prevalence, Perceptions, Motivations, and Quality of Life Impact of Non-medical Cannabis Use Among People with Epilepsy

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### Rationale
Several surveys suggest that nearly half of people with epilepsy (PWE) use non-medical cannabis (NMC; i.e., without medical supervision), primarily based on its purported anti-seizure properties. This rationale is concerning as NMC, typically high in THC and low in CBD, has not proven to be an effective anti-seizure product and has been associated with deleterious health effects. Given the potentially harmful effects of cannabis on health, it is necessary to describe the profile of cannabis users and evaluate its impact on quality of life (QoL).

### Methods
A total of 100 PWE completed an online questionnaire regarding their cannabis use habits, perceptions, and motivations for use, as well as a QoL questionnaire.

### Results
In the past 12 months, 42% of men and 19% of women reported using cannabis, including recreational motivations (48%) and combined recreational/auto-medication motivations (38%). Among NMC users, 72% reported consuming cannabis that was exclusively high in THC, more in THC than CBD, or an equal amount of both. Overall, 53% of female and 37% of male respondents believed there is a health risk associated with NMC use. No significant difference in QoL between cannabis users and non-users was reported ($U = 1169$, $p = 0.29$). The respondents considered themselves to have few or no information on the benefits (72%) and risks (71%) related to NMC use.

### Conclusion
Men were more represented among NMC users. Most respondents lacked information on the risks of NMC, highlighting the need to inform PWE about the implications of NMC use in epilepsy.

## Clinical Epilepsy / EEG / Antiepileptics

Abstract #27

# 30 Years Experience of Stiripentol Shows Efficacy and Safety in Dravet Patients Under 2 Years of Age

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### Rationale
To evaluate the efficacy and safety of stiripentol in Dravet patients when initiated during infancy (<2y), a critical period for life-threatening status epilepticus.

### Methods
Four retrospective cohorts were included: Center for Rare Epilepsies cohorts (CREER-1 1991-2004 and CREER-2 2005-2021), Stiripentol temporary authorization for use (2003-2007), and Stiripentol post-marketing survey (2007-2012). We extracted the data on tonic-clonic seizures, frequency and duration, adverse events and antiseizure medications before Stiripentol initiation (3 month-baseline), at short-term (< 6 months on Stiripentol) and long-term (last visit on Stiripentol before age 7).

### Results
Population comprised 131 patients. Stiripentol was initiated at a median age of 13 months, at a median dose of 50mg/kg/day (range 35-74mg/kg/day), with valproate and clobazam in 93% of cases (median dose=24mg/kg/day and 0.5mg/kg/day respectively). At short-term (median age=16m) seizure frequency had significantly decreased (p<0.01), both for prolonged seizures (5-30min) and status epilepticus (>30min), with 55%;61% responders and 39%;55% seizure free. At long-term (median age=41m) long-lasting seizures continued to decline (p=0.03 vs short-term, down to 67%;71% responders and 62%;67% seizure free). Hospitalizations dropped from 91% to 43% and 12% at short- and long-term. Three patients discontinued stiripentol for adverse events while 55% reported at least one adverse event, loss of appetite/weight (21%), sleep disorders (11%), somnolence (11%), agitation/irritability (7%), and hypotonia (5%). 5 and 4 patients had asymptomatic neutropenia and thrombopenia. Three patients died from SUDEP, but none from status epilepticus.

### Conclusion
Initiating stiripentol in infants with Dravet syndrome is safe and beneficial, drastically decreasing recurrent status epilepticus and related-mortality, long-lasting seizures and hospitalizations.

## Clinical Epilepsy / EEG / Antiepileptics

Abstract #28

# Efficacy and Safety of Stiripentol in the Prevention and Cessation of Status Epilepticus: A Systematic Review

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## Rationale
Stiripentol is a structurally unique antiseizure medication (ASM) approved for the treatment of refractory generalized tonic-clonic seizures in Dravet syndrome. A systematic review was performed to evaluate the effectiveness and safety of stiripentol in reducing the incidence of status epilepticus (SE) in patients with Dravet syndrome or any epilepsy characterized by recurrent SE.

## Methods
PubMed and Cochrane databases were searched, and relevant conference proceedings were also analyzed. Systematic search results were screened by title and abstract, and studies with data on the effect of stiripentol on SE outcomes (e.g., cessation of episodes, reduction in the frequency or duration of SE) were included.

## Results
Sixty-six records were identified, of which 17 were eligible for inclusion: 2 animal studies, and 15 human studies including 474 patients aged 1 to 78 years. Results of retrospective or prospective observational studies showed that add-on stiripentol reduced the incidence of SE in patients with Dravet syndrome and other developmental and epileptic encephalopathies (DEEs). Forty-one to 100% of patients (mean 68%) had a ≥50% reduction in SE episodes after stiripentol initiation, and a mean of 77% of patients (range 26% to 100%) became SE-free. Moreover, stiripentol used for acute treatment was also shown to be effective for the termination of super-refractory SE (SRSE) in adults, although data are limited. Stiripentol was generally well tolerated.

## Conclusion
Stiripentol reduces the incidence of SE episodes in patients with Dravet syndrome, and it is potentially efficacious in other DEEs and SRSE.

## Clinical Epilepsy / EEG / Antiepileptics

Abstract #29

# Post-hoc Analysis of the Sticlo Clinical Trials and Open Label Data Confirm Stiripentol's Highly Significant Efficacy on Seizure Reduction as Well as Positive Impact on Patient's Quality of Life

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### Rationale
Stiripentol (STP) was the first anti-seizure medication approved for Dravet Syndrome based on two placebo-controlled randomized trials: STICLO-France and STICLO-Italy.

### Methods
After a 2-month-blind period patients could continue STP in open-label (OL) for 1-month without breaking the blind, where placebo (PBO) patients (OL-PBO) were switched to stiripentol. Both STICLO studies were pooled and percentage change from baseline in generalized tonic-clonic seizure frequency (GTCSF), responder rates (≥75% GTCSF reduction), and seizure freedom were calculated. Quality of life was assessed via the longest period of consecutive seizure-free days from patient dairies.

### Results
64 patients were included during the 2-month-blind (STP 33, PBO 31),. GTCSF significantly differed at the end of the 2 month-blind (-84.4% vs -5.8%, p<0.001, STP vs PBO), which was no longer the case at the end of the OL (-79.8% vs -81.4%, p=0.7, OL-STP vs OL-PBO). Similarly, ≥75% responder rates were 56.3% vs 3.4% (p<0.001, STP vs PBO) and 59.3% vs 68.8% (p=0.5, OL-STP vs OL-PBO) at the end of the 2m-blind and OL periods respectively. No PBO patients achieved seizure freedom, while 37.5% did in the STP group (p<0.001) at 2m-blind. The median consecutive seizure free days was 32.5 vs 8.0 days (p<0.001, STP vs PBO) at the end of the 2 month-blind period. The significant superiority of STP to reduce GTCSF was reached as soon as 4 days-treatment and maintained to the end of the trial.

### Conclusion
These post-hoc analyses shed new light on the efficacy of STP on GTCS in Dravet syndrome: it is remarkably strong, rapid and maintained.

## Clinical Epilepsy / EEG / Antiepileptics

Abstract #30

# Real-World Utilization of Stiripentol by United States Prescribers: An Update

Matthew Clark, Veanna Fong, Fabiola Garcia, Carla Schad, Gabrielle Stires

*Biocodex, Inc.*

### Rationale

In 2018, in the US, Stiripentol was approved for seizures associated with Dravet Syndrome for patients 6 months or older (weighing 15 lb or more) taking Clobazam. An analysis of real-world US prescribing practices has been conducted.

### Methods

A retrospective analysis was performed that evaluated US prescribing data for Stiripentol from a singular specialty pharmacy. Data was collected from April 2019 to September 2023. Data collected included age, weight, dosage, specific dosing titration schedules, discontinuations, dosage at time of discontinuation, as well as concomitant medications as reported by the caregiver.

### Results

Dosing data was analyzed in all US patients receiving at least one dose one dose of Stiripentol. The overall average dose was 33.98 mg/kg/day.

The median starting dose at initiation was 27.55 mg/kg/d. The median second dose was 29 mg/kg/d, and the median maintenance dose (or last dose prescribed) was 32.46 mg/kg/d. 45% of patients treated with Stiripentol were not on concomitant Clobazam. 36% of patients that were initiated on Stiripentol discontinued therapy. The median last dose at time of discontinuation was 34.67 mg/kg/d (12% of discontinuations restarted STP treatment). The most common Adverse Event was lack of efficacy.

### Conclusion

Real World dosing of Stiripentol was found to be lower than the US labelled recommended dose of 50 mg/kg/d; and nearly half of the patients were not taking concomitant Clobazam. This analysis supplements the current US label and provides more real-world guidance for dosing, utilization, and titration to US prescribers of Stiripentol.

## Clinical Epilepsy / EEG / Antiepileptics

Abstract #31

# Prevalence of Attentional Impairment and Its Relationship to Seizure-Related Factors in Temporal Lobe Epilepsy

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### Rationale
Although temporal lobe epilepsy is often associated with memory deficits, studies have shown that it can also negatively affect attention. However, attentional impairments have not been extensively studied in adult patients, particularly regarding the prevalence of attentional deficits and their association to seizure-related factors. Moreover, many assessments of attention in patients with epilepsy have predominantly utilized tests that do not specifically measure pure attentional functioning. Given the fundamental role of attention in other cognitive functions and that its assessment is often overlooked due to time constraints, identifying seizure-related predictors of attentional difficulties in these patients is crucial.

### Methods
Binary logistic regressions were used to measure the prevalence of below-average scores on attentional tests of the Test of Attentional Performance and the D2-r Test of Attention and to explore which seizure-related factors predict these outcomes.

### Results
The results revealed a high incidence of below-average scores on tonic and phasic alertness, divided attention, sustained attention and concentration in 90 adult patients with temporal lobe epilepsy. Below-average attentional performances were associated with disease duration, age of onset, seizure frequency, and history of neurosurgery.

### Conclusion
Patients with temporal lobe epilepsy are likely to have poor performance on attentional tests. Consequently, evaluating pure attentional performance should be a key component of their neuropsychological assessment. These findings can help in developing personalized intervention strategies and improving both pre- and post-neurosurgery evaluations by having a more comprehensive and accurate assessment of cognition in temporal lobe epilepsy.

## Clinical Epilepsy / EEG / Antiepileptics

Abstract #32

# Epilepsy Risk Associated with the Receipt of General Anesthesia Relative to Neuraxial Anesthesia

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### Rationale
Recent evidence suggests that the receipt of general anesthesia may be associated with an increased risk of epilepsy compared with neuraxial (spinal or epidural) anesthesia. Our objective was to estimate the risk of new-onset epilepsy associated with the receipt of general anesthesia relative to neuraxial anesthesia.

### Methods
We conducted a population-based retrospective cohort study using linked health administrative databases in Ontario, Canada. We included adults who had an eligible surgical procedure (gynecological, lower extremity, peripheral vascular, and urological) between April 1, 2007 and March 31, 2015 and received general or neuraxial anesthesia. Participants were followed for up to five years to identify new-onset epilepsy. We used inverse probability of treatment weighting to control for confounding between the general and neuraxial anesthesia cohorts, and a Fine-Gray subdistribution model to estimate the hazard ratio for epilepsy, accounting for the competing risk of death.

### Results
The sample included 100,547 patients who received general anesthesia and 76,644 patients who received neuraxial anesthesia. The hazard ratio for epilepsy associated with general anesthesia was 0.61 (95%CI: 0.34-1.07). However, the risk of epilepsy increased over the follow-up period (interaction HR=1.36, 95% CI: 1.12-1.64), resulting in an increased risk of epilepsy associated with general anesthesia after approximately three years.

### Conclusion
Our results suggest that general anesthesia may be associated with an increased risk of epilepsy after three years. Future research should explore whether there is effect modification between specific surgical procedures and control for the onset of epilepsy risk factors after anesthesia receipt.

## Clinical Epilepsy / EEG / Antiepileptics

Abstract #33

# Epileptic Seizure Forecasting in Epilepsy Monitoring Unit Patients with Wearable-Based Nocturnal Sleep Features

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### Rationale
Wearable devices offer practical and accessible solutions for seizure forecasting in individuals with epilepsy (PWE). The bidirectional relationship between sleep and epilepsy has prompted the investigation of sleep quality as a non-invasive biomarker for seizure susceptibility. This study assesses the feasibility of forecasting seizure days using nocturnal sleep recordings from a smart shirt.

### Methods
Seventy-eight PWE admitted to the CHUM epilepsy monitoring unit wore the Hexoskin smart shirt that continuously measured cardiac, respiratory, and accelerometry activity. Each night, the shirt's sleep algorithm automatically computed ten sleep features. A support vector machine classifier was trained for pseudo-prospective seizure-day forecasting with 16-hour and 24-hour horizons. Forecasting performance was evaluated using a nested leave-one-patient-out cross-validation approach. Feature importance was determined by removing individual features and comparing the resulting forecasting performances.

### Results
Improvement over chance (IoC) was achieved for 46% (mean IoC: 36.7%) and 40% (mean IoC: 34.2%) of patients using 16-hour and 24-hour forecasting horizons, respectively. Single feature contribution analysis results showed high variability of selected features between PWE, which may be due to the inter-patient variability of pre-seizure signatures.

### Conclusion
Smart shirt-based nocturnal sleep monitoring shows promise for non-invasive seizure-day forecasting in PWE. Further studies in residential settings with long-term recordings could facilitate the development of novel and practical patient-specific seizure advisory devices.

## Clinical Epilepsy / EEG / Antiepileptics

Abstract #34

### Natural History of CACNA1A-Related Epilepsy: A Patient Perspective Study

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### Rationale
The natural history and progression of CACNA1A-related epilepsy is poorly understood. Comprehensive natural history studies are thus required to better counsel patients.

### Methods
Patients with CACNA1A-related disorders and epilepsy were recruited through the CACNA1A Foundation's Natural History Study and a collaboration across Italy. Clinical and genetic data, including epilepsy characteristics, were collected via online surveys completed by families or with a translator's help.

### Results
The study included 68 patients (47 P/LP and 21 VUS), aged 1 to 63 years. The average epilepsy onset was at 7.44 months, with focal aware seizures being the most frequent (51%). Seizure frequency ranged from daily to sporadic episodes, decreasing with age and significantly lower in patients with variants of unclear significance (VUS) (p=0.007). Drug-resistant epilepsy (DRE) was reported in 35.3%, and 48.5% experienced at least one status epilepticus (SE). Patients with DRE more frequently had global developmental delay (p=0.013) and hypotonia (p=0.009). The subgroup with gain-of-function variants (n=12) exhibited high DRE (75%) and SE (91%) rates. The most frequently prescribed antiseizure medications were levetiracetam (59.6%), valproic acid (40.4%), lamotrigine (24.6%), topiramate (21%), and clobazam (19.3%). Efficacy analysis indicated a benefit in using valproic acid in 78%, clobazam in 75%, lamotrigine in 67%, levetiracetam in 58%, and topiramate in 50% of individuals.

### Conclusion
This case series, the largest focused on CACNA1A-related epilepsy, highlights its heterogeneous phenotype, high drug resistance rates, and significant neuropsychiatric comorbidities, underscoring the complexity and the urgent need for novel therapeutic approaches.

## Clinical Epilepsy / EEG / Antiepileptics

Abstract #35

### Wearable-Based Seizure Detection: A Patient Perspective

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### Rationale
Wearable-based seizure detection holds the potential to improve the quality of life of people with epilepsy (PWE) by providing timely alarms to optimize epilepsy management. While early investigations show promising performances, patients' perspectives must be explored to maximize the benefits of these technologies. This study aims to gather the needs and opinions of PWE regarding seizure detection devices (SDDs) in an epilepsy monitoring unit setting.

### Methods
A survey-based approach was used to collect data from PWE admitted at the CHUM between 2019 and 2023. The surveys were completed before and after the use of SDDs to assess patients' initial perspective and experience thereafter. Participants were asked to provide feedback on various aspects of usability, including comfort, reliability of alerts, and overall satisfaction with the device.

### Results
Responses from 138 patients were collected. Upon admission, 92,0% of respondents believed that seizure detection was important and expressed interest in using SDDs. Most would use them continuously (65,2%). Eighty-two percent of patients agreed that automated alarms should be included in such devices. Respondents were most concerned about comfort, and least preoccupied with confidentiality of recorded data and appearance. Patients believed SDDs would reduce their stress levels (65,9%) and improve seizure management (72,4%) and the adequacy of their treatment (76,1%). Results for the second survey (after use of SDDs) will be available at the time of the conference.

### Conclusion
By examining the usability of SDDs from the patient's perspective, this study seeks to enhance user experience, thereby improving seizure detection in the management of PWE.

## Clinical Epilepsy / EEG / Antiepileptics

Abstract #36

### Cenobamate for Drug-Resistant Epilepsy: Initial Experience from a Single Center

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#### Rationale
Cenobamate (CNB), a new anti-seizure medication (ASM), has shown efficacy in decreasing seizures in patients with drug-resistant epilepsy (DRE) in randomized controlled trials. Authorized by Health Canada in June 2023, CNB was initially available through Health Canada's special access program in December 2022 and more readily since December 2023. We report here our initial experience with CNB.

#### Methods
A retrospective chart review was performed for patients treated with CNB at the CHUM epilepsy clinic. We collected demographic and epilepsy-related data. Efficacy was assessed using follow-up percentage seizure reduction and responder rates. Safety and tolerability were evaluated based on adverse effects and treatment discontinuation.

#### Results
At submission, 96 patients had started CNB, 40 of which were followed for ≥3 months. At baseline, a mean of 7.4 (±4.7) ASM had been attempted, 28.6% had previous surgery, and median 30-day seizure frequency was 10 (IQR:4-43.5). At 3 months, median dose was 100mg (IQR:100-112.5). Median percentage seizure reduction was 50.8% (IQR:7.3%-89.6%, n=40). The ≥50% and ≥75% responder rates and seizure freedom rate were 57.5%, 40.0% and 17.5%, respectively. At 6 months, median dose was 150mg (IQR:150-187.5). Median percentage seizure reduction was 60.8% (IQR:-0.2%-85.1%, n=12). Both ≥50% and ≥75% responder rates were 50%. Seizure freedom rate was 8.3%. Notable adverse effects were somnolence (22.5%), dizziness (17.5%) and fatigue (12.5%). One patient discontinued CNB due to somnolence and headache.

#### Conclusion
Our real-life experience with CNB in a particularly drug-resistant cohort is promising as preliminary outcomes mirrored those reported in pivotal trials. Updated results will be provided at the conference.

## Clinical Epilepsy / EEG / Antiepileptics

Abstract #37

# Neurophysiological Correlates of Accelerated Long-Term Forgetting in the Context of Epilepsy: A Preliminary Study

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### Rationale
Accelerated long-term forgetting (ALF) is a phenomenon characterized by marked subsequent forgetfulness of material where learning and retention capacities were deemed normal during the initial administration of standard neuropsychological tests. So far, no study has used cognitive event-related potentials (ERPs) to identify which stage(s) of information processing is affected in individuals with ALF. This study aims to explore the neurophysiological correlates of ALF through ERPs recorded during memory tasks administered to individuals with epilepsy.

### Methods
In this preliminary study, two hospitalized epileptic patients, one with frontal lobe epilepsy and the other with temporal lobe epilepsy, engaged in novel and experimental recognition tasks at three different intervals (immediate, 30 minutes, and 48 hours) during long-term EEG recordings. The repetition effects on the amplitudes of the FN400 and P600 components, reflecting familiarity and recollection processes respectively, were examined based on the presentation interval. These results were then compared according to the presence or absence of ALF in neuropsychological tests.

### Results
No repetition effect of the FN400 was observed in the patients with epilepsy. The repetition effect of the P600 was observed under certain conditions for one patient, while in the other, this effect was not observed.

### Conclusion
Preliminary results suggest that individuals with epilepsy generate fewer familiarity signals. Moreover, the inverse pattern of the P600 repetition effect observed in one patient with poor behavioral performance, both in the task itself and in the neuropsychological tests, suggests it might be a correlate of ALF. The absence of both familiarity and recollection could indicate that ALF is a disorder of consolidation.

## Clinical Epilepsy / EEG / Antiepileptics

Abstract #38a

# The Perceived Benefits of Online Group Memory Strategy Training

David Gold[1], Mary Lou Smith[2], Elizabeth Kerr[2], Rosalee Smith[3], Susan Hayman-Abello[4], Sahil Patel[1], Mary Pat McAndrews[1]

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## Rationale

People with epilepsy may experience memory problems due to multiple factors. Evidence indicates the benefit of rehabilitation efforts that include education about medical and psychosocial factors that impact memory together with strategies that can be used in daily life. We aimed to develop a brief, group-based, distance-delivered program that could be readily implemented in multiple settings - STREAM (Strategies for Epilepsy and Memory).

## Methods

STREAM was delivered to adult individuals living with epilepsy with self-reported memory problems. There were four cycles of the program with 36 participants in total. It comprised eight weeks of online facilitated sessions and individual homework including brief instructional videos. At the beginning and end of the program, participants completed the Multifactorial Memory Questionnaire, a validated self-report measure with three subscales characterizing satisfaction with memory, perceived memory abilities/mistakes, and use of memory strategies in daily life. There was also a single rating for a global impression of memory on a four-point scale ranging from ‘very poor’ to ‘good’.

## Results

The majority of individuals participated in all eight sessions. Using criteria based on reliable change scores, significant improvements were seen on all three scales, ranging from 35% to 45% of respondents. As expected, participants with the poorest self-rated memory efficacy and strategy use at baseline showed the largest gains at the end of the program ($r2 = 0.35$).

## Conclusion

This proof-of-concept study indicates the feasibility and effectiveness of STREAM, a highly ‘portable’ program, to enhance self-evaluation of memory functioning in daily life for individuals with epilepsy.

## Clinical Epilepsy / EEG / Antiepileptics

Abstract #38b

### Participant Experience of an Online Group Memory Strategies Program

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### Rationale

STREAM (STrategies for Memory And Epilepsy) is an 8-week, distance-delivered group program developed to teach adults with epilepsy strategies for managing memory deficits. Hourly sessions provide information regarding brain systems underlying epilepsy and lifestyle factors influencing memory (nutrition, exercise, sleep, stress). Time is allocated for discussion, practice of strategies, and sharing of experiences in implementing taught strategies. STREAM differs from other memory programs by combining an online presentation (facilitating ease of participation) and a group format (providing social support). This study aimed to evaluate participant experience.

### Methods

Nineteen adults were interviewed about their views on the impact of STREAM within 6 weeks after completion of the program.

### Results

95% rated their ability to apply the strategies in everyday life as 'good' or 'excellent', and 84% believed that they managed their memory better. 75% spontaneously mentioned that they valued the group format.

Perceived benefits included learning the science of memory and the relationship of epilepsy and its treatment to memory impairments. Sharing with others with epilepsy who also experienced memory deficits had a powerful personal effect (not alone in dealing with challenges, attributing issues to medical factors not personal failures, legitimizing concerns). The strategies were recognized as practical, flexible, and helpful. Participants felt empowered and had greater confidence in managing the limitations imposed by their memory deficits.

### Conclusion

STREAM is a valued, time- and cost-effective, way of offering psychoeducation to people with epilepsy. Benefits extended to social support, improved understanding of the interrelationship between epilepsy and memory, and improved self-acceptance.

## Clinical Epilepsy / EEG / Antiepileptics

Abstract #39

### Computerized Cognitive Testing for People with Epilepsy and Survivors of Status Epilepticus

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*Western University*

### Rationale

Cognitive impairments are an essential comorbidity of epilepsy. Unfortunately, neuropsychological evaluations for people with epilepsy (PwE) are time-demanding and have long waitlists. Cognitive tests may be used to triage neuropsychology referrals, but their validity in PwE is understudied. Also, findings on clinical factors associated with worse cognition in PwE are inconsistent and several aspects of cognition, such as planning abilities, have yet to be thoroughly investigated. Even less is known about cognition in people that survived status epilepticus (SE). This study assessed the feasibility of a computerized cognitive testing battery called Creyos in PwE for comparison against SE survivors.

### Methods

Participants were recruited from the Epilepsy Monitoring Unit in London, Ontario and completed Creyos on an iPad. Creyos involves 12 tasks, each evaluating a different aspect of cognition. Participants' scores were compared to age- and sex-matched norms from the Creyos database of over 85,000 healthy individuals.

### Results

Participants (N=45; mean age = 39.2 years, SD = 15.5 years; 31 females) performed significantly worse than matched norms on 11 tasks ($p<.01$) and in the three domains that the 12 tasks map onto: short-term memory ($t = -5.19$), reasoning ($t = -3.17$), and verbal processing ($t = -7.53$). We did not find any relationships between Creyos performance and clinical factors (e.g., age of epilepsy onset, epilepsy duration). Longitudinal data collection for SE survivors is ongoing.

### Conclusion

The Creyos battery is feasible for PwE and identified widespread cognitive impairment among participants. These results from PwE will ultimately be compared to longitudinal performance in SE survivors.

## Clinical Epilepsy / EEG / Antiepileptics

Abstract #40

*Withdrawn*

## Clinical Epilepsy / EEG / Antiepileptics

Abstract #41

### Dynamics of Phase-Amplitude Coupling During Seizure

Eleanor Hill, Jeremy Moreau, Erica Minato, Marc Lalancette, Elisabeth Simard-Tremblay, Roy W.R. Dudley, Sylvain Baillet

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### Rationale

Intracranial electroencephalography (iEEG) studies have documented increased phase-amplitude coupling (PAC) between lower-frequency phases and higher-frequency amplitudes, indicating that slower frequencies alter local network excitability, within the epileptogenic zone (EZ) during seizures. However, non-invasive evidence is limited. To address this, we leveraged magnetoencephalography (MEG) ictal events, rarely captured, to explore the spatiotemporal PAC dynamics in pediatric drug-resistant epilepsy.

### Methods

We recorded seizures in 13 participants (9 female, 4-16 years old) during their MEG sessions, conducted in preparation for epilepsy surgery. We derived time-resolved PAC from MEG source time series in the surgically resected zone (RZ) and the contralateral homologous zone (CZ) in patients who achieved long-term (>1 year) seizure freedom (N=8). We analyzed inter-ictal and ictal segments, calculating PAC between lower frequency bands (delta/theta/alpha/beta) and higher frequency bands (gamma/ripple/fast-ripple).

### Results

Our preliminary results indicate that PAC is greater in the RZ compared to the CZ across delta to gamma/ripple/fast-ripple band ranges, observed in both pre-ictal and ictal stages. Notably, upon ictal onset, PAC increased in both regions of interest for all delta pairs except for the delta-fast-ripple range pair, which was exclusive to the RZ.

### Conclusion

These results align with previous iEEG-PAC studies, suggesting that non-invasive PAC measurement during inter-ictal and ictal states can potentially delineate the EZ. Future steps include whole-brain PAC mapping for all participants, which may enhance presurgical planning and improve surgical outcomes.

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## Clinical Epilepsy / EEG / Antiepileptics

Abstract #42

# Screening and Management of Symptoms of Generalized Anxiety Disorder in People with Epilepsy : A Quality Improvement Study

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### Rationale
Due to the high prevalence of generalized anxiety disorder (11.1%) in people with epilepsy (PWE), the ILAE Commission on the Neuropsychiatric Aspects of Epilepsy recommended implementing routine screening for anxiety symptoms. Thus, our epilepsy group decided in 2018 to administer to all clinic patients the Generalized Anxiety Disorder-7 (GAD-7) assessment. In this study, we sought to review our experience with this approach.

### Methods
We reviewed 1997 GAD-7 questionnaires from January 2018 to March 2020 and studied the actions taken by epileptologists in response to a positive screening for generalized anxiety symptoms.

### Results
Out of the total GAD-7 questionnaires assessed, 30.3% had a score above 7, indicating more severe anxiety, warranting further assessment. Among patients with positive screening, 40.9% received a management option, 52.2% did not, and 6.9% declined the epileptologist's recommendation. Among patients who received a management option, 31.5% had their antiseizure medication adjusted to reduce their symptoms, 7.7% of patients received another form of management option, and 60.8% were referred to a mental health professional. Most of them were referred to a neuropsychiatrist (48.3%), 5.9% were referred to a psychiatrist, and 22.6% were referred to a psychologist. Eleven percent (11.3%) of patients received referrals to both a psychologist and a neuropsychiatrist, and 11.9% were advised to seek further assistance from their family physician.

### Conclusion
In our epilepsy clinic, a third of GAD-7 questionnaires screened positive for more severe anxiety symptoms. This led to a change to an intervention in most cases. The next step will be to assess whether actions taken were beneficial.

## Clinical Epilepsy / EEG / Antiepileptics

Abstract #43

# AnxEMU–VR: Randomized Controlled Trial Evaluating the Impact of Virtual Reality Exposure Therapy on Epilepsy/Seizure-Specific Interictal Anxiety in People with Epilepsy

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## Rationale

Anxiety disorders are the most common psychiatric comorbidity in people with epilepsy (PwE). PwE often experience anxiety specifically related to their epilepsy or seizures. However, limited research concerning interventions for epilepsy-specific (ES) interictal anxiety has been conducted. Recently, a feasibility pilot study ("AnxEpi-VR") developed a virtual reality exposure therapy (VR-ET) program for PwE experiencing ES-interictal anxiety, showing promising results and forming the basis for this current study.

## Methods

AnxEMU-VR is a prospective, open-label, randomized control trial recruiting in-patients from the Epilepsy Monitoring Unit in Toronto Western Hospital. Control-arm participants (n=7) engage with a neutral VR environment, while experimental-arm participants (n=7) experience VR-ET with 360-degree videos targeting their specific epilepsy-related fears. Both groups complete 5-minute exposures twice daily for 7-10 days. Anxiety is measured pre- and post-intervention using self-report questionnaires, interviews, and physiologic measurements. A one-month follow-up post-discharge is used to assess participants' avoidance behaviours related to their anxiety-inducing scenarios.

## Results

Recruitment is ongoing. Three participants have completed the program (n=1 control, n=2 experimental). Both experimental participants reported decreases of two and five points in their Epilepsy Anxiety Survey Instrument scores pre- versus post-intervention; the control participant's score remained unchanged. Two participants missed exposures on specific days due to seizures and memory lapses, however, they completed the required protocol on subsequent days. Final results for all measures will be presented (expected n=14).

## Conclusion

The study, thus far, has provided valuable insights regarding the feasibility, usability, and potential of VR-ET.

## Clinical Epilepsy / EEG / Antiepileptics

Abstract #44

# A Study of Patient- and Physician-assessed Quality of Care in a Newly Launched Seizure Investigation Unit at a Comprehensive Epilepsy Centre

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### Rationale

The SIU or Epilepsy Monitoring Unit (EMU) is a specialized unit that provides continuous video EEG monitoring within the safety of a specialized unit staffed by an epileptologist, 24h nursing staff and EEG technologists. The indications for admission to SIU are pre-surgical evaluation of drug-resistant epilepsy; characterization of paroxysmal events; classification and quantification of seizures/seizure syndrome; and optimization of anti-seizure medications (ASMs). The objective of this quality improvement study, based on PDSA paradigm, is to explore the performance of SIU at RUH through patient interviews and by applying quality indicators for an EMU used by level 4 Epilepsy Centres.

### Methods

This will be an observational study of all patients aged 18 years or older who were admitted to SIU at Royal University hospital Saskatoon since it became operational in September 2023. There will be two arms of this study. One in which patients or their caregivers will be interviewed on their experiences during admission in SIU and the other in which a physician member of the Saskatchewan Epilepsy program will fill a form based on quality indicators of EMU. The patients will be interviewed using the Hospital-Consumer Assessment if Healthcare Providers and Systems (H-CAHPS) questionnaire. The results will be descriptive.

### Results

This study is at the stage of REB approval.

### Conclusion

This study will help improve the quality of care at SIU by exploring experiences of patients as well as evaluating the care based on EMU quality indicators.

## Clinical Epilepsy / EEG / Antiepileptics

Abstract #45

### Level 4 Seizure Monitoring Unit Admissions are Associated with Reduced Long-Term Health Care Costs

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### Rationale
To determine if admission to dedicated seizure monitoring units (SMUs) result in reduced health care use (HCU).

### Methods
This was a retrospective open cohort study covering years 2010-2018. Patients were required to have ≥3 years pre- and post-admission follow-up. The outcome was the change in trajectory of composite HCU (primary care, specialist outpatient visits, emergency department visits, and hospitalizations) for the 3-years pre- and post-SMU using the point of admission as the 'index date'. Secondary outcomes were HCU limited to specific settings. We used adjusted restricted maximum likelihood linear and non-linear effects models to determine trajectories expressed as Canadian dollars.

### Results
A total of 315 of 600 (53%) patients met eligibility criteria. Mean age was 40 years old (standard deviation [SD] 17.4), 176 (56%) were female, 220 (70%) had focal epilepsy, and 60 (19%) had functional seizures or physiologic seizure mimics without epilepsy as adjudicated by the attending physician at the point of discharge. Mean per person health care costs increased by C$341.28 (95% confidence interval [95%CI] -25.17 to 707.74) for each successive 6-month interval prior to SMU admission (p=0.07). Following admission, mean per person costs decreased by C$802.34 (95%CI 699.62 to 905.06; p<0.001) for each successive 6-month interval up to 3-years post-discharge. Similar trends were noted for primary and specialist care, emergency department, admitted care, and when non-linear models were applied.

### Conclusion
Admission to an SMU is associated with significant and enduring declines in HCU. Comprehensive epilepsy care not only reduces morbidity and mortality but also reduces cost.

## Clinical Epilepsy / EEG / Antiepileptics

Abstract #47

# Cardiac Conduction Delay for Sodium Channel Antagonist Antiseizure Medications: An Analysis of the Canadian Longitudinal Study on Aging (CLSA)

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## Rationale

People with epilepsy are at risk of arrhythmias. We investigated cardiac conduction delays (CCDs) odds on ECG in older people using sodium channel blockers (NAB) versus those not using NAB. We also determined the prevalence of CCD by individual NAB.

## Methods

We included 209 people with epilepsy and 29,868 without, aged 45-85 years at baseline, from the CLSA. We defined epilepsy as self-reported epilepsy and taking antiseizure medications. NABs were phenytoin, lamotrigine, carbamazepine, oxcarbazepine, or lacosamide. We assessed baseline ECGs for CCDs, particularly prolonged PQ (>200ms), QRS (>100ms), and QTc (>430ms for males; >450ms for females). We estimated, using logistic regression models, the association between CCD and age, sex, active epilepsy, and NAB, with and without Framingham score or heart rate-lowering medications (HRLRX). Missing data were handled using multiple imputations (200 iterations).

## Results

In total, 141 people with epilepsy used NAB, and 68 did not, with similar demographics between groups. People with epilepsy taking NAB were more likely to have prolonged QRS (odds ratio [OR] 2.85 [95% CI: 1.09-7.43]) and any CCD (OR 1.94 [1.03-3.63]). Our multivariable analyses showed that NAB was associated with prolonged QTc (OR 1.52 [1.06-2.18]) and any CCD (OR 1.78 [1.16-2.74]). The probability of any CCD was 36.1% [24.2-49.4%] for carbamazepine, 45.5% [31.7-58.5%] for phenytoin, and 54.7% [28.9-75.6%] for lamotrigine.

## Conclusion

People with epilepsy using NAB more frequently have CCD on ECG. This was most likely to occur with lamotrigine, carbamazepine, and phenytoin. A baseline ECG may be warranted for selected individuals with epilepsy.

## Clinical Epilepsy / EEG / Antiepileptics

Abstract #48

# The Diagnostic Accuracy of Tuberous Sclerosis Complex (TSC) Manifestations

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### Rationale

Up to 15% of people with TSC (PwTSC) do not carry an identifiable pathological genetic variant and are diagnosed clinically. In such situations, family members cannot be screened using genetic testing. We aimed to establish the diagnostic accuracy of TSC clinical features to better guide the screening process for the families of PwTSC.

### Methods

We used the TSC Natural History Database, a longitudinal database of PwTSC from 22 North American centres. We excluded people without a definite genetic TSC diagnosis. We estimated the sensitivity (95% CI) of "any TSC brain manifestation" (subependymal nodules, cortical tubers, or subependymal giant cell astrocytoma) as well as that of "any TSC skin manifestations" (fibrous cephalic plaque, facial angiofibromas, hypomelanotic macules, Shagreen patches, periungual fibroma, and confetti lesions). We estimated positive and negative predictive values (PPV and NPV) while assuming a specificity of 80% and a population prevalence of 5 to 50%.

### Results

Among 1300 PwTSC, 50.3% were female, and the mean age at diagnosis was 3.7 years. The sensitivity for any brain manifestation and any skin manifestation were 95.5% (95% CI: 94.2-96.5) and 92.9% (91.3-94.2), respectively. The sensitivity was 98.7% (98.0-99.2) when considering either a brain or skin manifestation. With this last combination, PPV and NPV were 83.2% (81.6-84.6) and 98.4% (97.8-98.8) at a 50% prevalence, respectively. At lower prevalences PPV decreased but NPV increased to near-100%.

### Conclusion

Screening for brain and skin manifestations in family members of genetics-negative PwTSC is sufficient, with excellent sensitivity and near-perfect NPVs.

## Clinical Epilepsy / EEG / Antiepileptics

Abstract #49

# Ictal Activity is Sustained by Estrogen Receptor B-Mediated Activity During the Estrous Cycle

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### Rationale
Catamenial epilepsy is defined as a periodicity of seizure exacerbation with the menstrual cycle that affects up to 70 % of epileptic women. These seizures are often non-responsive to medication and our understanding of the relation between the menstrual cycle and seizure generation (i.e. ictogenesis) remains limited.

### Methods
We used the in vitro 4-aminopyridine model of epileptiform synchronization to study with field potential recordings the changes in ictal discharges occurring during the estrous cycle in the entorhinal cortex of parvalbumin (PV)-ChR2 female mice (P60-P120). Optogenetic stimulation was used to activate PV-positive interneurons. Light pulses were delivered at 8 Hz for 5 seconds with a 30 second interval between stimulating blocks. 3 µM PHTPP was used to study the role of estrogen receptor β-mediated activity.

### Results
We found that (i) the duration of ictal discharges was significantly longer during estrus than during non-estrus; (ii) these ictal discharges displayed a specific pattern of onset characterised by the presence of chirps that are thought to mirror synchronous interneuron firing; (iii) blocking estrogen β-mediated receptor signaling reduced ictal discharge duration; (iv) 8Hz optogenetic stimulation of PV-positive interneurons triggered field responses with higher oscillation power during estrus compared to non-estrus.

### Conclusion
Our findings indicate that ictal discharges are modulated during the estrous cycle. They also suggest that the estrus phase, which corresponds to the human peri-ovulatory period, is presumably associated to increased interneuron excitability, favors seizure generation and maintenance due to increased estrogen β-mediated receptor signaling.

Funding sources: This work was supported by the Canadian Institutes of Health Research (PJT153310, PJT166178 and MOP130328; M.A.) and the Savoy Foundation

## Clinical Epilepsy / EEG / Antiepileptics

Abstract #50

# Acetazolamide Use for Myoclonus: Case Report of 2 Patients With Progressive Myoclonic Epilepsy and Literature Review

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## Rationale

Cortical myoclonus originates at cerebral cortex, predominantly occurring on voluntary movements, such as gait and is triggered by stimuli including touch.
Acetazolamide (ACZ) is an inhibitor of the carbonic anhydrase protein which ultimately results in a low intracellular pH, causing acidification.
Current evidence shows that a seizure focus tends to be alkaline, thus the change in pH induced by ACZ is postulated to explain some of the anti-seizure effects.
To date, very few cases have described the use of ACZ in myoclonus. In this work, we present 2 patients with progressive myoclonic epilepsy (PME) with an improvement in their myoclonus with ACZ, despite poor response to other antiseizure medications (ASMs).

## Methods

Chart review of 2 patients was performed. Literature review was conducted on myoclonus and ACZ using PubMed.

## Results

Case 1: 22-year-old female, diagnosed with PME secondary to a KCNC1 variant. Her symptoms started at 10 years of age with bilateral tonic clonic seizures (BTCS). She later developed progressive ataxia and myoclonus, involving face and limbs, which worsened with stimulus and menses. Perampanel, Clonazepam and Levetiracetam was started, however myoclonus was still limiting. At the age of 19, ACZ 250 mg BID was started for 2 weeks around her menses which led to significant improvement of myoclonus, resulting in better ambulation, balance and speech. These improvements were sustained 2.5 years later.
Case 2: 67-year-old male, previous history of diabetes, sleep apnea and hypothyroidism presented with BTCS at the age of 53 along with cortical myoclonus, dementia and ataxia, leading to diagnosis of PME with an IRF2BPL variant. His myoclonus would worsen in the morning or with anxiety, ranging from 4 to 10 per hour, compromising his ability to perform independent activities of daily living and requiring a walker on a regular basis. Improvement of myoclonus occurred with ACZ 250 mg BID biweekly which was sustained after 2 years, although balance and cognition continued to deteriorate as part of his condition.

## Conclusion

Previous literature outlines 4 cases of action myoclonus that responded to ACZ. Our study adds 2 patients to the current literature. Hence, we conclude that the use of ACZ should be considered in the treatment of myoclonus, especially in cases with cortical involvement and hormonal fluctuations.

## Clinical Epilepsy / EEG / Antiepileptics

Abstract #51

# Tuberous Sclerosis Associated Neuropsychiatric Disorder: Survey Results Identify Opportunities for Care Advances in Ontario

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## Rationale

Tuberous Sclerosis Complex (TSC) is a genetic condition associated with pathogenic variants in the TSC1 or TSC2 genes, resulting in multisystem complications and prominent neurologic involvement, particularly in children. Common neurologic manifestations include epilepsy in up to 80% of individuals and Tuberous Sclerosis Associated Neuropsychiatric Disorder (TAND) in 90% of individuals with TSC. TAND is currently under-recognized and under-treated but is being increasingly appreciated for its contribution to overall disease burden in TSC.

## Methods

We performed a survey of practitioners at tertiary care centers across Ontario who provide treatment for patients with TSC to identify current gaps in care regarding the identification and treatment of TAND. A thematic analysis was performed on the survey results.

## Results

Nine participants, representing their respective multidisciplinary centers, responded to the survey. Two were adult providers and seven were pediatric providers. Participants were from Toronto, Ottawa, Hamilton and London. Wait times for psychiatric services was identified as the most consistent barrier to management of TAND-associated symptoms across both pediatric and adult centers. Access to mental health services and knowledge of TAND were the other most significant themes identified.

## Conclusion

Although awareness of the impact of TAND is increasing, significant barriers exist within Ontario in accessing care for patients with symptoms of TAND. The results of this survey will be used to inform initiatives of the Ontario TSC Network to advance care for patients with Tuberous Sclerosis Complex.

## Clinical Epilepsy / EEG / Antiepileptics

Abstract #52

*Withdrawn*

## Clinical Epilepsy / EEG / Antiepileptics

Abstract #53

*Withdrawn*

## Clinical Epilepsy / EEG / Antiepileptics

Abstract #54

# Caregiver-Reported Non-Seizure Outcomes Following Use of Cannabidiol in Patients with Tuberous Sclerosis Complex (TSC): Interim Results from the BECOME-TSC Survey

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## Rationale

To report preliminary non-seizure findings from the ongoing cross-sectional BECOME-TSC caregiver survey designed to quantify the real-world impact of cannabidiol (CBD) on seizure and non-seizure outcomes in patients with TSC.

## Methods

Caregivers of patients with TSC receiving plant-derived highly purified CBD (Epidiolex®, 100 mg/mL oral solution) for ≥6 months completed an online survey, based on the TSC-associated neuropsychiatric disorders (TAND) questionnaire, other validated measures, and previous caregiver reports. CBD-associated adverse events were not assessed.

## Results

At time of analysis, 12 caregivers had completed the survey. Mean (SD) patient age was 16 (8) years; 58% were female. Mean (SD) age at seizure onset was 17 (33) months; 50% had a history of infantile spasms. Median CBD dose was 17 mg/kg/day. Most common concomitant antiseizure medications were everolimus (42%) and clonazepam (33%). Co-occurring symptoms included developmental delay (92%), autism spectrum disorder (83%), anxiety disorder (42%), attention deficit hyperactivity disorder (33%), and obsessive-compulsive disorder (33%). Severe-profound intellectual disability (ID) was reported in 75% of patients and mild-moderate ID in 17%; 8% had fluent verbal language. Compared with the pre-CBD initiation period, most respondents reported definite improvements in a patient's ability to be happy (67%), shake head for yes/no answers (63%), accomplish visuospatial tasks (63%), and recall past events (60%). Definite worsening was reported by ≤2 respondents in domains including using repetitive words/phrases, repetitive behaviours, impulsivity, and overactivity/hyperactivity.

## Conclusion

These preliminary results show that a substantial proportion of caregivers of people with TSC reported improvement in TAND-related outcomes since initiating CBD.

Funding source: Jazz Pharmaceuticals, Inc.

## Clinical Epilepsy / EEG / Antiepileptics

Abstract #55

# Clinically Meaningful Reduction in Drop Seizures in Patients with Lennox-Gastaut Syndrome Treated with Cannabidiol

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### Rationale
Evaluate the threshold for a clinically meaningful reduction in drop seizures in patients with Lennox-Gastaut syndrome (LGS) receiving cannabidiol (CBD) associated with Caregiver Global Impression of Change (CGIC) scores of "slightly improved" or better, or "much improved" or better.

### Methods
Post-hoc analysis of randomized clinical trials (NCT02224560; NCT02224690) in patients with LGS receiving 10 or 20 mg/kg/day plant-derived highly purified CBD (Epidiolex®[US]/Epidyolex®[EU]; 100 mg/mL oral solution) for 14 weeks. Drop seizure frequency reduction from baseline and CGIC scores at end of treatment were analyzed to quantify thresholds for a clinically important response (CIR) and minimal clinically important difference (MCID) in seizure reduction. Thresholds were anchored to CGIC ratings of "slightly improved" or better, or "much improved" or better.

### Results
Among 215 patients, 129 (60%) reported "slightly improved" or better and 67 (31%) "much improved" or better. Best fit thresholds for CIR in drop seizure reduction were −30.6% for CGIC "slightly improved" or better (accuracy: 72%) and −49.6% for "much improved" or better (accuracy: 69%); MCIDs were −21.0% and −18.4%, respectively. Based on best fit CIR thresholds, 124/215 (58%) patients responded to CBD with "slightly improved" or better and 87/215 (40%) "much improved" or better.

### Conclusion
For a CGIC of "slightly improved" or better, the best fit threshold for CIR in seizure reduction analyzed herein was approximately −30%, with smallest detectable change (MCID) approximately −20%. Anchoring between drop seizure change and CGIC may be appropriate (correlation >0.30) for defining clinically meaningful thresholds and warrants further research.
Funding source: Jazz Pharmaceuticals, Inc.

## Clinical Epilepsy / EEG / Antiepileptics

Abstract #56

# Patient Characteristics and Treatment Patterns in Patients with Lennox-Gastaut Syndrome: Real-World Evidence from a Cross-sectional Survey of Physicians in Europe

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## Rationale
To describe clinical characteristics and treatment patterns of patients with Lennox-Gastaut syndrome (LGS) using real-world data from the Adelphi LGS Disease-Specific Programme™.

## Methods
Eighty-eight physicians (70 neurologists; 18 pediatricians) reported data for patients diagnosed with LGS in France, Germany, Italy, Spain, and UK (June 2022–August 2023). Descriptive statistics were performed for pediatric (0–17 years) and adult (≥18 years) patients.

## Results
The study included 276 patients with LGS: 201 (72.8%) were pediatric (male 67.7%); 75 (27.2%) were adult (male 69.3%). Median (IQR) age at first seizure and LGS diagnosis in pediatric patients was 4.0 (2.0–5.5) and 4.5 (2.8–6.1) years, respectively (adult: 3.5 [2.0–5.0] and 5.4 [3.1–7.3]). 53.7% of pediatric patients were diagnosed with another seizure disorder before LGS (adult 81.3%). At first consultation, most frequently reported seizure types were tonic (pediatric 66.5%, adult 53.3%) and atypical absence (55.0%, 61.3%). The most frequent non-seizure symptom was learning/intellectual impairment (pediatric 53.5%, adult 66.7%). Valproate was the most frequently reported initial monotherapy treatment (pediatric 46.5%, adult 48.1%). 83.2% of pediatric (adult 82.7%) patients received ≥2 medications at subsequent treatment. Physicians cited treatment effectiveness as the top reason for adding a medication (pediatric 99.1%, adult 100.0%); lack of treatment effectiveness (pediatric 97.6%, adult 84.6%) or poor tolerability (pediatric 29.3%, adult 23.1%) were top reasons for removing a medication.

## Conclusion
Initial inaccurate diagnoses were common, and patients experienced the burden of multiple medications. Findings suggest the necessity for improving LGS diagnosis and treatment, including accounting for managing non-seizure outcomes.
Funding source: Jazz Pharmaceuticals, Inc.

## Clinical Epilepsy / EEG / Antiepileptics

Abstract #57

*Withdrawn*

## Clinical Epilepsy / EEG / Antiepileptics

Abstract #58

# Beyond Seizure Control: A Longitudinal Study of Cenobamate's Effect on Cognition in Patients with Drug-Resistant Epilepsy

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### Rationale

Preserving cognitive function amidst the treatment of drug-resistant epilepsy (DRE) poses a formidable challenge. Cenobamate (CNB) is approved as an adjunct treatment for DRE in Canada. Studies have shown that treatment with CNB results in lower rates of cognitive adverse events. Our study seeks to elucidate effect of CNB on cognition in a larger sample of patients with DRE during one-year follow-up period. We hypothesize that patients with DRE who are treated with CNB will have stable or improved cognitive function at one year.

### Methods

In this prospective observational study, we will enroll 60 patients aged 18-60 with DRE of focal onset. Patients will be enrolled through the epilepsy clinics run by the Saskatchewan Epilepsy program. The following variables will be collected: patient demographics, age at epilepsy onset, etiology of epilepsy, baseline seizure frequency, episodes of status epilepticus, dose of CNB, concomitant ASMs and their doses, other medications that might affect cognition, rate of reduction in seizure frequency by 50% and seizure freedom. Utilizing the EpiTrack scale, a validated cognitive assessment tool for attention and executive functioning in epilepsy, we will conduct cognitive evaluations at baseline ($T_0$) and subsequently at 6-month (T1), and 1-year (T2) intervals. The primary outcome will be change in cognition during follow-up, as assessed by EpiTrack score.

### Results

This is an ongoing project awaiting REB approval.

### Conclusion

This study represents one of the pioneering investigations in Canada, aiming to delve into and elucidate the cognitive effects of Cenobamate in individuals with DRE.

## Clinical Epilepsy / EEG / Antiepileptics

Abstract #59

### Adult Phenotype of CHD2-Associated Disorders

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### Rationale

Pathogenic CHD2 variants are associated with neurodevelopmental disorders (NDDs) and developmental and epileptic encephalopathy (DEE). While pediatric CHD2 phenotypes have been readily explored, adult phenotypes are not well understood. We aimed to investigate the phenotypic spectrum of adult patients with CHD2 variants.

### Methods

Patients 18 years or older with likely pathogenic or pathogenic (LP/P) CHD2 variants were included. We used standardized tools to evaluate current seizures, medication use, sleep, gastrointestinal symptoms, pain response, gait, social communication disorder and adaptive behavioural skills of patients.

### Results

Fourteen unrelated adult patients (age range: 18-45 years, median: 21 years) with LP/P CHD2 variants were described. Eleven novel variants were identified. No genotype-phenotype correlations were identified. Seventy-nine percent of adults still have ongoing seizures. Photosensitivity was present in 64% of adult patients. Autism spectrum disorder (ASD) was diagnosed in 71% of patients. Only 29% were able to read and understand material at a sixth-grade level or higher. Behavioural issues were reported in 100% of adult patients and 71% had internalizing features, such as anxiety. Self-injurious behaviors were present in 50%. Only 43% could ambulate independently. Additional characteristics included reflux (36%), constipation (71%), and abnormal nociception (43%). One patient presented with non-epileptic breath

holding spells leading to cyanosis. No patient could perform basic activities of daily living independently. Higher seizure severity was associated with worse non-seizure outcomes (p=0.04).

## Conclusion

Most adults with CHD2 continue to have seizures, and seizure severity is associated with worse comorbidities such as maladaptive behaviours, gait, gastrointestinal, sleep, and nociception problems. Longevity has not been systematically studied in this group of patients, but to the best of our knowledge, the oldest patient living with a CHD2 variant is described here, at the age of 45 years. These data may provide prognostic insights for families of pediatric patients, as well as help identify key points to be addressed in future precision trials for patients with CHD2 variants.

## Clinical Epilepsy / EEG / Antiepileptics

Abstract #60

# Variants in ATP6V0C Causes a Dravet-Like Developmental and Epileptic Encephalopathy

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## Rationale

Dravet Syndrome (DS) is a developmental and epileptic encephalopathy (DEE).
Diagnosis is clinical, but approximately 90% of patients have pathogenic variants in SCN1A.
The ATP6V0C protein is highly expressed in the brain across the whole lifespan, and plays a key role in proton gradient generation and pH regulation.
ATP6V0C has recently been proposed as a novel candidate gene for epilepsy, with or without developmental delay.
Only 4 four adults (i.e., adults over 18 years of age) with ATP6V0C variants have been described in the literature thus far. Here, we describe 2 adult patients with a clinical diagnosis of DS caused by ATP6V0C variants.

## Methods

Patients with DEEs were evaluated by physicians with expertise in managing DS, and their clinical diagnosis was correlated with genetic findings. A subgroup of those patients with DS, but without known genetic causes, were evaluated through gene panels, whole exome sequencing and chromosome microarray. Phenotype was determined by pediatric and adult chart reviews as well as interviews and physical examinations.

## Results

Out of 753 patients with DS, two unrelated individuals with classic DS features during childhood and adulthood were identified with heterozygous de novo missense variants in ATP6V0C (c.319G>C, p.Gly107Arg) and (c.284C>T, p.Ala95Val), respectively. Both variants were absent in the general population and computational prediction algorithms suggested deleterious effects on protein structure and/or function (Table 1). No disease-causing variants in other genes previously associated with DS were found.

## Conclusion

Here we describe two adult patients with Dravet-like syndrome and pathogenic/likely-pathogenic variants in ATP6V0C. We propose that abnormal ATP6V0C function can, at the severe end of the clinical spectrum, be associated with Dravet-like phenotype. This is relevant as these patients would not qualify for disease modifying anti-sense oligonucleotides (ASOs) or gene therapies targeting SCN1A.

## Clinical Epilepsy / EEG / Antiepileptics

Abstract #61

# Unspoken Monogenic Etiologies for Landau-Kleffner Syndrome (LKS) and Continuous Spike-and-Wave During Sleep (CSWS): A series of Cases and Literature Review

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## Rationale

Continuous spike-and-wave during sleep (CSWS) is an electrographic epileptic abnormality that can lead to significant morbidity. The EEG shows near-continuous interictal epileptiform discharges during non-REM sleep. (Specchio et al. (2022). . Epilepsia, 63(6), 1398-1442. ) Patients can have seizures, but often, the main complaints initially are lack of attention and language deterioration. Neurocognitive development is interrupted. Patients will fail to attain new skills or can have a regression, losing skills previously mastered. CSWS can happen in previously normotypical people or in people with previous neurocognitive delay. The causes are unclear, but in some patients, a genetic abnormality has been shown. (Posar, A., & Visconti, P. (2024). Children, 11(2), 169. ) Here we set up to look for genetic causes of CSWS.

## Methods

A retrospective chart review was conducted with patients followed at the Adult Genetic Epilepsy Clinic in Toronto, Canada. A literature review was conducted on EE-SWAS and CSWS using PubMed. This included “Genes” and “Genetic” with "SWAS” (Spike-and-wave activation in sleep); “CSWS”, “LKS” (Landau Kleffner Syndrome) and “ESES” (Electrical Status Epilepticus in Sleep).

## Results

Out of 699 patients who had genetic testing, seven were identified with a genetic cause for their epilepsy and had CSWS at some point in their lives. Presenting with different degrees of Autism Spectrum Disorder, Intellectual Disability and seizures, we describe two siblings with a deletion involving the SHANK3 gene (Phelan-McDermid Syndrome), one individual with a KMT5B de novo missense variant and another one with an SCN8A missense variant. Finally, polysomnography indicated CSWS in a patient with a CHD2 truncating variant. The last two patients have fallen into the phenotype of Landau Kleffner Syndrome (LKS),
one with a missense known mutation in the GRIN2A gene and the other with a novel mutation as etiology: a duplication involving the KCNC2 gene.

## Conclusion

Here, we share four novel monogenic epilepsies associated with CSWS: SHANK3, KMT5B, SCN8A mutations and KCNC2 (fulfilling criteria for LKS). Current literature indicates a growing diversity in genetic

etiologies for this complex framework of conditions. (Lesca et al. (2020) Epileptic Disorders, 21, S41-S47. ). As the decision for treatment is challenging and time-sensitive, early recognition of potential conditions related to this finding can prompt increased surveillance and timely intervention if deemed appropriate. The recent broadening from a language-restricted phenotype such as LKS to EE-SWAS is an important advancement. Such understanding will help elaborate on the nature of the cognitive impairment of individuals, which could be everted or at least minimized. This can also lead to further understanding of potential pathways in which this condition leads to pervasive and long-lasting cognitive and behavioural abnormalities.

## Clinical Epilepsy / EEG / Antiepileptics

Abstract #62

# Reduced Widespread Coupling of Spindles and Slow Waves in Patients with Temporal Lobe Epilepsy: A Potential Mechanism for Neurocognitive Deficits?

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### Rationale

Neurocognitive deficits are common in temporal lobe epilepsy (TLE) (1). Recent studies in healthy subjects showed a positive correlation between sleep spindles coupled to sleep slow waves and cognitive functioning (2, 3). We aimed to determine local and global differences in coupling in TLE patients compared to healthy controls using combined high-density electroencephalography (HD-EEG) and polysomnography.

### Methods

Twenty patients (12 female; 36.5 ± 9.9y) with unilateral drug-resistant TLE (10 left) and 20 age- and sex-matched healthy controls were included. Spindles (10-16Hz; 0.5-2s) and slow waves (0.5-4Hz) were automatically detected during all N2 and N3 epochs using validated detectors. Coupling of spindles and slow waves was defined as any overlap of both detections.

### Results

Coupled spindle-slow waves (rate per minute) were globally reduced in patients with TLE compared to healthy controls (median [range]: 0.18 [0.01; 0.65] vs. 0.35 [0.09; 0.98], non-parametric p=0.009, Cliff's d=0.48). This reduction was also found in coupled fast spindles (12-16Hz)-slow waves (0.06 [0.001; 0.35] vs. 0.18 [0.02; 0.46], p=0.006, d=0.46) and slow spindles (10-12Hz)-slow waves (0.11 [0.01; 0.38] vs. 0.19 [0.04; 0.55], p=0.023, d=0.42). Within TLE patients, there was no local difference between the coupling rates in the lobe with the epileptic focus compared to the contralateral side (0.08 [0.01; 0.29] vs. 0.05 [0.001; 0.18], p=0.135, d=0.065).

### Conclusion

Despite a focal epileptic generator, patients with TLE showed a widespread reduction of coupled spindle-slow wave rates. As coupling was found to be associated with neuropsychological performances, this widespread reduction may contribute to mechanisms of poor cognitive functions in patients with TLE.

Funding: This study was supported by project grants of the Canadian Institutes of Health Research to BF (PJT-175056) and JG (FDN-143208). KS was funded by a postdoctoral fellowship by the German Research Foundation (507037359).

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## Clinical Epilepsy / EEG / Antiepileptics

Abstract #63

# Paroxysmal Slowing Linked to Drug-Resistant Epilepsy: Analysis of a Large Open-Source Database

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## Rationale

Paroxysmal slow wave events (PSWEs) are EEG segments where the median power frequency falls below 6Hz for ≥5 consecutive seconds. A recent study suggested that PSWEs predict epilepsy in patients with a first seizure. Our study aimed to assess the prevalence of PSWEs in independent EEG datasets, exploring their potential as biomarkers for drug-resistant epilepsy (DRE).

## Methods

An exploratory analysis used natural language processing (NLP) to extract clinical data from 5090 outpatient records from the Temple University Hospital (TUH) EEG corpus. Additionally, clinician reports from a random sample of 500 TUH subjects were manually reviewed to compare patients with confirmed epilepsy diagnoses against those with seizure-mimics with normal EEGs. A validation analysis used a well-defined cohort of 95 patients with either drug-responsive or drug-resistant epilepsy from Bonn University.

## Results

In the exploratory arm, the proportion of time PSWEs were detected was higher in both the manually validated epilepsy group (n=188) and the NLP-detected epilepsy group (n=715) compared with non-epileptic subjects (n=161, P=0.003 and P<0.0001, respectively). Patients with DRE showed a prolonged time in PSWEs (P=0.005), corresponding with an increased risk of refractoriness (OR=1.9, 95% CI 1.2-2.9). The validation analysis showed prolonged time in PSWEs (P<0.0001, AUC=0.740) and increased mean PSWEs duration (P<0.0001, AUC=0.829) in DRE (n=44) compared with drug-responsive patients (n=51), indicating fair-to-good DRE classification. In patients with poor surgical outcomes (Engel IB-IV, n=13), pre-surgical EEGs showed prolonged time in PSWEs compared with Engel IA patients (n=24, P=0.038).

## Conclusion

Analysis of 1159 EEGs from two independent cohorts confirmed that PSWEs are more prevalent and prolonged in patients with epilepsy and may indicate a lack of therapeutic response.

## Clinical Epilepsy / EEG / Antiepileptics

Abstract #64

*Withdrawn*

## Clinical Epilepsy / EEG / Antiepileptics

Abstract #65

# The ILAE Classification of Epilepsy Syndromes Should Incorporate Multilobar Epilepsies Such as Temporal Plus Epilepsy

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## Rationale

Multilobar involvement in epilepsy with the epileptogenic zone (EZ) extending beyond one lobe, can be an important cause of pharmacoresistant epilepsy. Temporal plus epilepsy (TPE), the best-described of the multilobar epilepsies, was first characterized in 2001. Clinical and scalp electrographic features of TPE may be indistinguishable from those of mesial temporal lobe epilepsy (MTLE), and hippocampal sclerosis (HS) may be associated with TPE. Hence, MTLE-HS may not be as specific a focal epilepsy syndrome as implied in the 2022 ILAE classification.

## Methods

We summarize evidence to support the inclusion of multilobar epilepsies, with TPE as a subtype, in the ILAE classification of epilepsy syndromes.

## Results

TPE is an epileptic entity in which the EZ involves the temporal lobe and anatomically and functionally connected regions that extend beyond its limits. Three TPE subgroups have been described: temporo-frontal, temporo-perisylvian (includes insula), and temporo-parietal-occipital; however, their EZs and therefore their electro-clinical features may overlap, as may the seizure semiology in TPE and TLE. Intracranial electroencephalography is often needed to distinguish TPE from MTLE.

## Conclusion

The recognition of multilobar epilepsies as distinct syndromes, and in particular of TPE as a subtype, should facilitate their earlier detection and hence improve medical and surgical treatment. Since the temporal lobe is always involved in the EZ of TPE, it is not surprising that TPE can mimic TLE, explaining why pre-operatively unrecognized TPE is an important cause of TLE surgery failures.

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## Clinical Epilepsy / EEG / Antiepileptics

Abstract #66

# Transforming Transition Care for Young People with Epilepsy

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## Rationale
The transition period to adult care is critical for adolescents with epilepsy and their families. The TÉCUM program (University of Montréal transition program) aims to establish a new model of care for adolescents with epilepsy.

## Methods
This initiative is aimed at all young people with epilepsy, as well as their caregivers. Particular attention is paid to people who are drug-resistant, those with comorbid intellectual disability, and those with a genetic disease. TÉCUM is based on four main pillars: 1) a biopsychosocial approach, 2) knowledge dissemination, 3) the promotion of patient autonomy, and 4) accessibility.

## Results
To address these 4 main pillars, the TÉCUM program has implemented: 1) the TÉCUM symposia series, in-person and online, presented by experts in their field, to allow for knowledge dissemination on patient-centered topics (e.g. reproductive health and autonomy development), 2) The TÉCUM website acting as a hub for patient-oriented resources (virtual tour of adult health centres, video recordings of each symposium, available social resources in the community), and 3) an online questionnaire used to measure overall patient well-being and transition readiness, to allow for more personalized patient care and to monitor the impact of the TÉCUM program (using the Triple Aim Framework).

## Conclusion
We anticipate that the TÉCUM program will have important positive results for adolescents with epilepsy and their families living through the transition period to adult care. There are participating centres in 3 cities across Quebec. Plans are underway to extend our impact across Canada.

Funding: TD Bank Ready Commitment program

## Pediatric Epilepsy

Abstract #67

### From Alpha Thalassemia Trait to NPRL3-Related Epilepsy: A Genomic Diagnostic Odyssey

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### Rationale

A neurotypical 2-year-old boy began experiencing night-time episodes of sweet taste in his throat, followed by intense fear, choking and repetitive swallowing, while he remained aware but unable to articulate. Medical history included microcytic anemia, thought to be alpha thalassemia trait present in his family, but alpha-globin gene testing was negative.

### Methods

He was treated for gastroesophageal reflux disease for several years, until his first bilateral tonic-clonic seizure at age 7. His gastrointestinal events were then understood to be seizures originating from temporal/insular regions. Ictal electroencephalogram localized left temporo-occipital seizures. An epilepsy multigene panel revealed full gene deletion of NPRL3, a gene in the mTOR pathway. Pathogenic NPRL3 variants cause autosomal dominant familial focal epilepsy with variable penetrance. Approximately 22% have malformations of cortical development, with mostly favorable surgical outcomes and mTOR inhibitors are also used in some. To further investigate his deletion, chromosomal microarray was performed and revealed a maternally inherited 106 kb deletion on chromosome 16p13.3, including the whole NPRL3 gene, as well as a regulatory region for the alpha globin gene cluster (not the cluster itself). Regulatory region mutations are a more recently identified cause of human genetic disease that can escape traditional testing methods.

### Results

Further postprocessing of his brain imaging showed left hippocampal sclerosis and mid-posterior para-hippocampal focal cortical dysplasia, confirming the presence of cortical malformations. The patient is now being considered in the surgical pathway.

### Conclusion

Genetic assessment in childhood conditions, along with awareness of phenotypic overlap can prevent prolonged odysseys and enable personalized treatments.

## Pediatric Epilepsy

Abstract #68

*Withdrawn*

## Pediatric Epilepsy

Abstract #69

### Factors Influencing Long-Term Outcome of Infantile Epileptic Spasms Syndrome Due to Genetic Etiology

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### Rationale
To assess electro-clinical, neuroimaging, response to treatment, long-term outcome, and mortality in individuals with Infantile Epileptic spasms syndrome (IESS) due to a genetic etiology.

### Methods
Retrospective review of a cohort of individuals with IESS diagnosed at BC Children's Hospital (BCCH) between January 1, 1990, and December 31, 2022 and a minimum of one year follow-up.

### Results
139 (34.75%) patients with a genetic etiology of IESS were identified from a cohort of 400 patients with IESS over a 32-year period.
Mean age of onset of spasms was 6.5 months (2 weeks to 20 months), 49 had normal development and 35(26%) had seizures prior to the onset of spasms.
Etiologies were Tuberous Sclerosis complex (TSC) (22.85%), Trisomy 21 (14.28%) and neurometabolic in 10%. STXBP1, IDIC(15), CDKL5, ARX, DEPDC5, LIS1 and TUB1 were also implicated genes.
Mean interval from spasm onset to treatment was 24 days. Vigabatrin was first line in 121 (93%), of whom 40 (33%) responded, mainly in TSC. Mean number of ASMS used was 5.5 (1-17).
Mean follow up was 11.9 years (15m- 32 y). 18 patients died at a mean age of 11.35 years. 9% had normal development, 9 patients evolved to Lennox Gastaut syndrome. 27.4 % had autism spectrum disorder and 44.2% cerebral palsy.

### Conclusion
TSC and Trisomy 21 were the most common genetic causes of IESS. One third responded to Vigabatrin. 76.3% had moderate to severe intellectual disability. Single gene abnormalities were likely underestimated due to lack of availability of whole exome sequencing or gene panels.

## Pediatric Epilepsy

Abstract #70

### Comparing QoL in Transition-Aged Adolescents with Epilepsy: Pre- and Post- the Covid-19 Global Emergency

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### Rationale
Research completed during the Covid-19 global emergency showed that young people reported significantly decreased QoL as well as lowered mental health. Although the pandemic remains ongoing, the World Health Organization has declared the end to Covid-19 as a global health emergency and almost all restrictions were lifted in 2023. Therefore, life returned to a sort of normalcy. However, emerging research suggests that individual's QoL has not returned to pre-covid-19 pandemic levels. Given that adolescents with epilepsy already have lower QoL than the general population, we set out to compare pre-and post-global emergency QoL scores in transition-aged adolescents to determine if adjustments should be made to the information given during our transition clinic.

### Methods
Baseline QoL data were compared in 148 adolescents with epilepsy (M= 16.14 years, 81 females) enrolled in a transition clinic before and after the COVID-19 global emergency

### Results
Reported Total QoL scores were lower in participants enrolled in the clinic post-global emergency, compared to those enrolled prior to the pandemic. When looking at the different QoL subscales, results showed that "Attitudes towards Epilepsy" scores were significantly lower in participants enrolled post-global emergency ($t(59.65)=6.96$, $p=0.11$)) and "Social Support" scores were nearly significantly lower ($t(43.29)=3.44$,$p=.070$).

### Conclusion
Results suggest that the QoL profile differs in adolescents recruited prior to and post Covid-19 global emergency. As a result, it may be important to make changes to the information taught to adolescents now entering the transition clinic; such as additional education to help alter stigmatized beliefs and attitudes and additional encouragement to develop and maintain personal relationships.

## Pediatric Epilepsy

Abstract #71

# Standardizing Language Mapping Using Intracranial Stimulation in Pediatric Hospitals: A Multi-Center Analysis

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### Rationale

Language mapping using intracranial stimulation is an important procedure in the evaluation of patients with pharmacoresistant epilepsy. In recent years, intracranial language mapping in children has gained popularity as a technique for identifying critical language areas in the brain, therefore maximizing surgical resection while minimizing post-operative language deficits. However, language mapping procedures in children vary considerably across centers. This inconsistency may impact candidate selection, patient outcomes, research contributions, and overall care coordination. As such, standardized approaches to language mapping using intracranial stimulation are needed. This study aims to analyze current language mapping practices across Canadian pediatric hospitals with the ultimate goal of developing national guidelines.

### Methods

This multi-center cross-sectional study will assess language mapping protocols at Canadian pediatric hospitals. Using a questionnaire, we will survey the techniques employed (e.g., intraoperative direct stimulation, stereotactic electroencephalography, subdural grids), patient considerations, implicated professionals, administration procedures (e.g., language task(s), stimulation technique), and perceived benefits and barriers. The questionnaire will be completed by pediatric neurologists/epileptologists, neurosurgeons, neuropsychologists, speech-language pathologists, and EEG technologists. Our analysis will identify challenges and areas of inconsistency in clinical settings.

### Results

A questionnaire has been developed and is being distributed to pediatric tertiary care centers across Canada.

### Conclusion

These data will provide insight regarding the range of practice across Canada for intracranial language mapping in pediatric patients. We plan to use the data in the development of evidence-based guidelines for language mapping using intracranial stimulation in pediatric settings. This standardization should facilitate surgical decision-making and improve patient outcomes.

## Pediatric Epilepsy

Abstract #72

# Cost Reduction for Families and Healthcare System with the Implementation of a Paediatric Comprehensive Epilepsy Clinic

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### Rationale
Epilepsy is considered by the WHO as the most common serious neurological condition affecting children. 30% will develop drug resistant epilepsy (DRE) who require comprehensive care and represent a significant financial burden for the health care system and the families. In London, Ontario, the Comprehensive Epilepsy Clinic (CEC) is a specialized multi-disciplinary clinic model that provides advanced therapies and facilitates access to health disciplines and resources. A focused cost-benefit analysis was conducted to determine if this clinic model impacts the economic burden for the healthcare system and families.

### Methods
We collected data identifying 70 new consults to the CEC in the year 2020. We looked at epilepsy related hospital utilization 365 days +/- the CEC consult date for each. This included emergency room (ER) visits, inpatient and critical care admissions and telephone encounters with the epilepsy nurse.

### Results
ER visits pre-CEC consult went from 198 to 87 post with a 56% cost reduction (CR), inpatient admissions went from 48 to 39 with a 19% CR, critical care admissions went from 7 to 4 with a 43% CR and telephone calls with a nurse for education went from 38 to 161, which has no associated cost to the system or to families.

### Conclusion
A CEC model appears to reduce the financial burden to both the healthcare system and families of children living with DRE. This model could be replicated and beneficial in underserviced and low-income countries to provide epilepsy care in an efficient way.

## Pediatric Epilepsy

Abstract #73

### Increasing Epilepsy-Related Diagnostic Yield from Short-Read Genome Sequencing

Jimmy Nguyen[1], Ted Higginbotham[1], Katrina Bell[2], Natalie J. Chandler[3], Lyn S. Chitty[3], John Coleman[2], Matthew Coleman[2], J. Helen Cross[3], Anna Griffiths[2], Britt Hanson[3], Maria Lachgar-Ruiz[3], Patrick Lombard[3], Cristina Magro[3], Christian R. Marshall[1], Ben Paternoster[3], Ashley Pritchard[3], Ingrid E. Scheffer[2], Wanqing Shao[4], Jashanpreet Sidhu[1], Sarah Stephenson[2], Brett Trost[1], Gene-STEPS Study Group, Vann Chau[1], Katherine B. Howell[2], Amy McTague[3], Annapurna Poduri[4], Zornitza Stark[2], Gregory Costain[1], Alissa M. D'Gama[4]

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#### Rationale
Gene-STEPS is a multi-centre study of the diagnostic yield and clinical utility of rapid genome sequencing (GS) in infants with unexplained seizures. We have reported a clinical diagnostic yield of 43 % for the first 100 infants. However, clinical laboratories' bioinformatics pipelines have limited ability to detect some variant types, including non-coding, mosaic, and structural variants . Here, we describe initial results of advanced analysis strategies that further increase diagnostic yield.

#### Methods
For Gene-STEPS participants without genetic diagnoses after clinical GS (n=170), we conducted the following analyses: 1) re-evaluation of variants of uncertain significance, 2) review for a second variant in cases with a single pathogenic variant in an autosomal recessive gene, 3) reanalysis of all coding SNVs and indels, including in a consensus epilepsy gene list (n=1,045), 4) assessment of additional variant types, such as mosaic and structural variants, and 5) targeted RNA-sequencing.

#### Results
We established (likely) diagnoses for 15 infants, including candidate variants in both known disease-causing genes and genes not previously associated with disease like ATP6V0B and HECTD1. Further investigations are ongoing to establish associations between these candidate genes and epilepsy. The remaining diagnoses included a complex structural variant (2.3 Mb inversion disrupting KMT2A) and a mosaic SNV (PIK3R2 present in 8.5% of reads).

#### Conclusion
Reanalysis of short-read GS increases the diagnostic yield for infants with unexplained seizures, with considerable anticipated impact on clinical management. Continuing improvements in bioinformatics analysis strategies, updates to variant interpretation guidelines, and discovery of new epilepsy-associated genes emphasize the importance of ongoing reanalysis of GS data.
Funding Sources: The Hospital for Sick Children is supported by the following funders: Canadian Institutes of Health Research; Epilepsy Canada; Feiga Bresver Academic Foundation; Ontario Brain Institute.

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Ormond Street Hospital. The Boston Children's Hospital (BCH) site is supported by the BCH Children's Rare Disease Cohorts Initiative and the One8 Foundation.

## Pediatric Epilepsy

Abstract #74

### Genotype-Phenotype Correlation in CLCN4-Related Developmental and Epileptic Encephalopathy

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### Rationale

CLCN4-related disorder is a rare X-linked neurodevelopmental condition with a pathogenic mechanism yet to be elucidated. CLCN4 encodes the vesicular 2Cl-/H+ exchanger ClC-4, which is hypothesized to play a role in the ion homeostasis of endosomes and intracellular trafficking. ClC-4 relies on its formation of heterodimers with ClC-3, which possesses signals for target organelles.

### Methods

Case-series. Then, we examined the functional properties of our patients' ClC-4 variants in mammalian cells using patch-clamp electrophysiology, protein biochemistry, and confocal fluorescence microscopy.

### Results

Three male patients with developmental-and-epileptic-encephalopathy were identified. Patients #1 and #2 had normal growth parameters with no dysmorphic features and normal-appearing brains on MRI. Patient #3 had microcephaly, microsomia, bilateral talipes equinovarus, complete agenesis of the corpus callosum, and cerebellar and brainstem hypoplasia. Patient #1 had recurrent status epilepticus separated by months of seizure freedom, while Patient #2 and #3 had brief, daily seizures. The p.(Gly342Arg) variant of Patient #1 significantly impaired ClC-4's heterodimerization capability with ClC-3 and suppressed anion currents. The p.(Ile549Leu) variant of Patient #2 and p.(Asp89Asn) variant of Patient #3 both shifted the voltage dependency of transport activation by 20 mV to more hyperpolarizing potentials, relative to the wild-type, with p.(Asp89Asn) favouring higher transport activity.

### Conclusion

We extend the phenotypic spectrum of CLCN4 variants and demonstrate the pathological functional-consequences of three previously unclassified variants. The p.(Gly342Arg) and p.(Ile549Leu) variants impaired ClC-4 transport function, while the p.(Asp89Asn) variant resulted in a gain-of-transport function. Targeted animal or induced pluripotent stem-cell models are needed to further understand epileptogenic mechanisms of CLCN4 variants.

## Pediatric Epilepsy

Abstract #75

*Withdrawn*

## Pediatric Epilepsy

Abstract #76

### Infantile Onset Epilepsia Partialis Continua: Institutional Experience at Alberta Children's Hospital

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*Alberta Children's Hospital*

### Rationale

Epilepsia partialis continua (EPC) represents a rare type of epilepsy with diverse underlying etiology. Infantile EPC onset (<12 months of age) is rare and exhibit unique features of diagnostic and management considerations. We retrospectively reviewed cases of infantile onset EPC evaluated at Alberta Children's Hospital (ACH) to provide insight regarding diagnostic strategies and management.

### Methods

Cases of infantile onset (< 12 months of age) with clinical findings and electroencephalogram finds consistent with EPC that were evaluated at ACH between 2016 and 2023 were reviewed. Underlying etiologies were confirmed, and treatment strategies and outcomes were assessed.

### Results

Two patients with infantile onset EPC were identified. Both patients had unremarkable medical history and development prior to presentation. Both patients were found to have mitochondrial disease, one with POLG-related disease and one with RMND1 pathogenic variant. Patient with POLG-related disease passed away in infancy and patient with RMND1 pathogenic variant remains seizure free and progressing with development.

### Conclusion

Infantile onset EPC are commonly associated with underlying metabolic disease, in particular mitochondrial disease. While POLG-related disease has been known to cause EPC, RMND1 related disease has not been reported to the best of our knowledge and further illustrates that mitochondrial diseases in general are an important etiology in this patient population. Early genetics and metabolic consultation is warranted in these patients and due to multisystemic involvements, patients require multidisciplinary care, including palliative care.

## Pediatric Epilepsy

Abstract #77

### Social Competence and Peer Relations in Adolescents with Epilepsy

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### Rationale
Adolescence is a sensitive period for social development and peer relations, which predicts mental well-being. This study evaluated social functioning among adolescents with epilepsy using parent- and adolescent-reported measures.

### Methods
Adolescents with (n=100) and without (n=56) epilepsy were recruited from the Hospital for Sick Children, Canadian Epilepsy Support Centers and the community. Youth and their parents both completed the Self-Perception Profile for Adolescents to evaluate adolescents' knowledge of how to make friends (Social Competence scale) and adolescents' abilities to form close friendships (Close Friendship scale), and the Strength and Difficulties Questionnaire (Peer Problem subscale) to assess adolescents' peer difficulties. Multiple linear regressions evaluated group differences while controlling for adolescents' sex, age, and household income.

### Results
Based on parent reports, youth with epilepsy had poorer social competence (b=-1.23, p=0.03), poorer abilities to make friends (b=-1.57, p=0.03), and greater peer problems (b=0.67, p=0.03), relative to youth without epilepsy. Seizures within the past 12 months was associated with poorer social competence (b= -2.17, p=0.003) and forming fewer close friendships (b=2.73, p=0.003). Youth with epilepsy rated their own social competence and relations similarly as controls. Furthermore, rating agreements between adolescents and parents were low (Epilepsy: Intraclass Correlation=0.3; Controls: Intraclass Correlation =0.2).

### Conclusion
The results underscore the importance of incorporating both adolescent and parent ratings in clinical and research assessments. Future research should evaluate how epilepsy affects social behaviours but also how social challenges adolescents with epilepsy face might, in turn, influence the development of social behaviours.

Funding: SickKids Foundation

## Status Epileptics / Critical Care

Abstract #78

# Comparative Analysis of New-Onset Refractory Status Epilepticus (NORSE) in Adult and Pediatric Patients: Immunotherapy Timing and Functional Outcomes

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### Rationale

Immunotherapy timing is hypothesized to play a crucial role in modulating the inflammatory response associated with NORSE, potentially improving patient outcomes. This study investigated the impact of immunotherapy timing on intensive care unit (ICU) stay duration and functional outcomes in adults and children with NORSE.

### Methods

We reviewed all patients with a diagnosis of NORSE admitted at McGill University Health Centre between January 2013 and July 2023. We evaluated demographics, diagnostics, treatments, ICU stay length, long-term anti-seizure medication use, and modified Rankin Scale (mRS) scores at discharge, defining good outcomes as mRS 0-2 and poor outcomes as mRS 3-6. Comparisons were made between adult and pediatric patients.

### Results

15 NORSE patients were identified (10 adult, 5 pediatric) with median ages of 34 and 4 years, respectively. Early initiation of first-line immunotherapies correlated with shorter adult ICU stays ($r = 0.748$, $p = 0.021$), however not in children. Delayed chronic immunosuppression escalation was associated with shorter ICU stays in children ($r = -0.995$, $p = 0.005$); no significant association was seen in adults, however ICU stays tended to be longer ($r = 0.689$, $p = 0.130$). Better functional outcomes at discharge were observed among children that had earlier escalation of chronic immunosuppression ($r = 0.943$, $p = 0.057$), contrasting with adults who, likely due to more severe disease, did not exhibit similar outcomes.

### Conclusion

Tailoring immunotherapy timing for NORSE patients across age groups should account for disparities in disease severity between pediatric and adult cohorts. Further investigation into age-specific factors may guide more targeted therapeutic approaches.

## Status Epileptics / Critical Care

Abstract #79

# Outcome of Emergency Neurosurgery in Patients with Refractory and Super-Refractory Status Epilepticus: A Systematic Review and Individual Participant Data Meta-Analysis

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## Rationale

efractory (RSE) and super-refractory status epilepticus (SRSE) are serious neurological emergencies requiring aggressive management. Current management lacks comprehensive evidence beyond anesthetic agents. This systematic review and individual participant data meta-analysis (IPDMA) seeks to evaluate the currently available surgical techniques for the acute treatment of RSE and SRSE.

## Methods

An IPDMA was performed according to PRISMA guidelines, including only patients who underwent surgery while in RSE and SRSE. Multivariable logistic regression models were constructed to identify predictors of status epilepticus (SE) cessation, long-term overall seizure freedom, and favorable functional outcome at last follow-up.

## Results

87 studies including 161 participants were included. Resective surgery showed higher SE cessation rate (93.9%) compared to non-resective techniques (83.9%), though not reaching significance (p=0.071). Resective techniques were also more likely to achieve seizure freedom (69.1% vs. 34.4%, p=<0.0001). Older age at SE (OR=1.384[1.046–1.832], p=0.023) was associated with increased likelihood of SE cessation, while longer duration of SE (OR=0.603[0.362–1.003], p=0.051) and new-onset seizures (OR=0.244[0.069–0.860], p=0.028) were associated with lower likelihood of SE cessation, though SE duration was not significant. Only shorter duration of SE prior to surgery (OR = 1.675[1.168–2.404], p = 0.0060) and immediate termination of SE (OR=3.736 [1.323–10.548], p=0.014) were independently associated with long-term seizure status.

## Conclusion

Our findings suggest that emergency neurosurgery may be a safe and effective alternative in patients with RSE/SRSE and may be considered earlier during the disease course.

## Basic Science / Engineering

Abstract #80

### Structural Subnetwork Associated with Specific Domains of Cognitive Function in TLE

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### Rationale

There is no clear association between brain connectivity and neuropsychological function in temporal lobe epilepsy (TLE). The present study aims to relate cognitive and sensorimotor dysfunction detected by robotic assessment to altered structural connectivity in participants with TLE.

### Methods

A sample of 33 patients with TLE and 24 controls were included. All participants performed twelve tasks using Kinarm robot to evaluate several domains. A principal component analysis (PCA) of the performance on these tasks was conducted. Structural connectivity matrices were obtained from multi-shell DWI using Micapipe for processing. Statistical analysis was conducted using a network-based statistical approach combined with the features of machine learning.

### Results

The PCA yielded three orthogonal components accounting for 68% of the variance. A structural subnetwork of 38 nodes and 41 edges was significant associated only with the second component ($R = 0.6$, p-value $< 0.01$). This subnetwork includes connections between regions of the temporal lobe, occipitotemporal cortex, basal ganglia nucleus, frontal lobe, parietal lobe, lateral fissure, insula and cerebellum. The circular sulcus of the insula was the node with highest degree. Notably, this second component contains tests that are more associated with executive function as well as tests of attention.

### Conclusion

The results provide evidence that the insular cortex plays a hub role in executive dysfunction in TLE. This study extends our understanding of the cognitive, behavioural and neural network changes associated with TLE by describing the structural substrate underlying the executive-attention dysfunction identified by robotic assessment. Future investigations can explore which specific aspects of attention and executive function are crucial for cognitive-behavioural interventions.

## Basic Science / Engineering

Abstract #81

# Investigating Cell Types Responsible for Increased Seizure Generation in a Model of Neurofibromatosis Type 1

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### Rationale

Neurofibromatosis type 1 (NF1) is a neurocutaneous disorder caused by a heterogeneous mutation in the Nf1 tumor suppressor gene resulting in decreased levels of the protein neurofibromin. Individuals with NF1 have an increased prevalence of seizures and epilepsy in comparison to the general population. We previously showed increased seizure susceptibility and epileptogenesis in a mouse model of NF1, but the cell types behind this are unknown. Understanding the mechanism of seizures in NF1 is crucial for targeted therapy development for this population, as patients are often medically refractory.

### Methods

We generated mice with cell specific deletions of the Nf1 gene in either excitatory neurons or inhibitory interneurons using the Cre/loxP system. Mice were implanted with intracranial electrodes and underwent continuous video-EEG monitoring to detect spontaneous epileptiform abnormalities and seizures, followed by challenge with kainic acid to determine differences in seizure susceptibility.

### Results

Mice with a heterozygous knockout of Nf1 in vGlut+ neurons have increased susceptibility to kainic acid induced seizures, as evidenced by an increase in total seizure duration ($p<0.05$) compared to control groups and mice with cell specific knockout of Nf1 in PV+ neurons. Data on spontaneous epileptiform abnormalities continues to be analyzed.

### Conclusion

Results to date indicate the increased seizure susceptibility in a mouse model of NF1 appears to be driven by vGlut+ excitatory neurons. These results provide the first evidence for the contributing mechanism of increased seizures in NF1 and could provide rationale for the development of alternative treatments for this population.

Funding Sources: U.S. Department of Defense, Canadian Institute of Health Research, University of Toronto

## Basic Science / Engineering

Abstract #82

# ASIC1a: A Novel Gatekeeper of the Anti-seizure Effects of the Ketogenic Diet in a Model of Infantile Spasms

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### Rationale

Infantile Spasms (IS) represent a devastating form of epilepsy with limited treatment options. Ketogenic Diet (KD), a high-fat diet, shows promise, yet its mechanism remains unclear. Recent breakthroughs in our research link KD's seizure control to low brain pH. Since Acid Sensing Ion Channel (ASIC) 1a governs all relevant low pH-evoked currents, we hypothesize that low pH-induced activation of ASIC1a controls KD's anti-seizure properties.

### Methods

Using the triple-hit IS model, we assessed spasm frequency in ASIC1a knockout (KO) rats fed either KD or control milk (CM) using video-EEG recordings. We investigated the effect of low pH (pH=6.8; activating ASIC1a) and Ammonium Chloride (8mM; ASIC1a agonist) on epileptiform brain activity using the zero-magnesium brain slice seizure model. Western blot was used to examine ASIC1a protein.

### Results

ASIC1a-KO pups exhibited an 83% increase in spasm frequency compared to wildtype (WT) (n=8, $p<0.001$). The spasm-suppressing effects of KD were nullified in ASIC1a-KO pups, highlighting ASIC1a's crucial role in mediating KD's therapeutic benefits. In CM-fed WT pups, zero magnesium-induced epileptiform activity decreased by 72.6% with the low pH challenge, and this reduction was further enhanced by KD supplementation (n=7, $p<0.001$). However, ASIC1a-KO animals showed no response to pH changes, regardless of their diet (n=6). Ammonium chloride reduced epileptiform activity by 98.6% in WT rats (n=2). Western Blot analysis confirmed the absence of ASIC1a protein bands in KO pups (n=3).

### Conclusion

Our study reveals a critical link between ASIC1a and low pH in KD's seizure control in IS, promising the development of novel therapies.

## Basic Science / Engineering

Abstract #83

### Reducing Hyperoxia in the Hippocampus in a Neonatal Rat Model of Febrile Seizures

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### Rationale

Febrile seizures in neonatal rat models result in a hyperoxic response in the hippocampus. Febrile seizures have been shown to cause long-term recognition memory impairments in female adult rats that are ameliorated with a transient receptor potential vanilloid 1 (TRPV1) inhibitor by decreasing hyperoxia. Hyperoxia is also decreased by a cyclooxygenase 1 (COX1) inhibitor and a cannabinoid 1 (CB1) inhibitor when injected prior to the seizure. Treatment of tThis study examined the effects of TRPV1 inhibitor, COX1 inhibitor, and CB1 inhibitor on hyperoxia when given after the termination of a behavioural febrile seizure.

### Methods

Pups received surgical implantation of an electrode and an optode into the dorsal hippocampus at postnatal day 8. Pups then received four days of a daily injection of lipopolysaccharide and were exposed to exogenous heat on day 12 until they had a seizure. Pups also received AMG9810 (a TRPV1 inhibitor at 200 mg/kg, i.p.), SC560 (a COX1 inhibitor at 20 mg/kg, i/p.), AM251 (a CB1 inhibitor at 2 mg/kg, i.p.) or a vehicle either before or directly after the febrile seizure. Oxygen in the dorsal hippocampus was measured for 2 hours after the start of external heat.

### Results

Preliminary results show a reduction in hyperoxia in all treatment groups compared to seizure groups.

### Conclusion

TRPV1, COX1, and CB1 are active in the expression and continuity of hyperoxia in the dorsal hippocampus of neonatal rats after a febrile seizure.

## Basic Science / Engineering

Abstract #84

### Microvascular Pathology as a Target for the Treatment of Epilepsy

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*Dalhousie*

### Rationale

About 30% of patients are considered “drug resistance” as they continue to experience recurrent seizures despite treatment. Dysfunction of the blood-brain barrier (BBB) has been shown to play a key role in epileptogenesis via activation of transforming growth factor betta (TGFB) signaling. BBB pathology has also been described in chronic epilepsy in both experimental animals and in tissue resected from patients with drug-resistant epilepsy. The FDA-approved anti-hypertensive angiotensin receptor II antagonist, losartan, has been shown to block TGFB signaling, reduce BBB permeability and prevent status-epilepticus induced epileptogenesis. However, the effect of losartan treatment on established epilepsy is not known. The goal of the present study was to the potential of losartan treatment in reducing BBB leakage and seizure frequency in a rat model of temporal lobe epilepsy.

### Methods

We used the well-established paraoxon-induced status epilepticus (SE) model of epilepsy. Seizures were monitored using continuous video-electrocorticographic (ECoG) telemetric recordings from implanted epidural electrodes. Following 2-weeks baseline recordings, animals were treated with losartan (i.p. 30mg/Kg/day) for two weeks followed by two weeks wash-out. BBB integrity was assessed using Evans blue. Interictal ECoG features and seizures were analyzed blindly and automatically.

### Results

We report a significant decrease in the frequency of seizures in losartan-treated animals and a trend in the decrease of epilepsy-related interictal features. Losartan-treated animals showed a more intact BBB compared with non-treated epilepsy controls.

### Conclusion

Our study supports the use of losartan to target BBB pathology in epilepsy.

## Basic Science / Engineering

Abstract #85

### Deep Learning to Detect Epilepsy on Routine EEG

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### Rationale
Epilepsy has a high misdiagnosis rate of ~20%. While interictal epileptiform discharges (IEDs) can sometimes support the diagnosis, the EEG remains limited by poor sensitivity and a risk of overinterpretation. We aimed to leverage Deep Learning (DL) to detect epilepsy on EEG.

### Methods
We selected a retrospective cohort of consecutive patients undergoing an EEG at the CHUM (train/validation set: Jan 2018–July 2019; testing set: July–Sep 2019, no overlap of patients) and reviewed their record for the diagnosis of epilepsy. Seven DL models were implemented based on the Vision Transformer [ViT] and ResNet architectures and were trained to classify 30s EEG segments according to the diagnosis of epilepsy. The predictions were aggregated at the EEG level (median of the segments). We compared the DL models to previous methods: the ShallowConvNet and extraction of linear and nonlinear features. We used the train/validation set to select hyperparameters (80/20% random split) and the testing set to evaluate performances.

### Results
The train/validation set contained 820 EEGs from 728 patients. The testing set had 128 EEGs from 118 patients (72 with epilepsy [61%]; median follow-up of 89 weeks [IQR: 48–121]). All DL models exceeded previous methods. The larger ViT model had the highest performance, with a testing AUROC of 0.75 (95% CI: 0.68–0.83). In patients with no IEDs on EEG (n = 110), performances were similar (AUROC: 0.76 [0.66–0.84]).

### Conclusion
This work suggests that DL could be used to uncover biomarkers of epilepsy on EEG without relying on IEDs, increasing its diagnostic yield.

## Basic Science / Engineering

Abstract #86

# Optogenetic Activation of Parvalbumin-Positive Interneurons in the Medial Septum Has Seizure-Suppressing Effects That Are Frequency-Dependent in a Model of Mesial Temporal Lobe Epilepsy

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### Rationale

Electrical or optogenetic stimulation of the medial septum exerts anti-ictogenic effects in animal models of mesial temporal lobe epilepsy (MTLE). Here, we compared the effects exerted by open-loop optogenetic stimulation of medial septum parvalbumin (PV)-positive interneurons at 0.5 and 8 Hz on interictal spikes, high-frequency oscillations (HFOs) and seizures in the pilocarpine animal model of MTLE.

### Methods

Pilocarpine-treated PV-ChR2 male mice (P60-P100) were implanted with an electrode in the CA3 region of the hippocampus and an optic fiber in the medial septum. Light pulses were delivered at 0.5 (n = 8) or 8 Hz (n = 6) for 5 min with a 10 min interval between stimulating blocks from day 8 to day 12 after SE.

### Results

No effects were observed on interictal spikes and interictal HFOs but optogenetic stimulation induced significant seizure-suppressing effects that were frequency-dependent. While the 0.5 Hz protocol induced anti-ictogenic effects up to 16 days after SE ($p < 0.05$), the 8 Hz protocol could instead trigger seizures ($p < 0.05$). In the 0.5 Hz group, seizures occurring during the ON condition were associated with lower rates of ictal fast ripples (250-500 Hz) compared to seizures occurring during the OFF condition ($p < 0.05$).

### Conclusion

Stimulation of PV-positive interneurons in the medial septum at 0.5 Hz is efficient in blocking ictogenesis and pathological HFOs when compared to 8 Hz stimulation, suggesting that optogenetic stimulation at this frequency induces changes in neuronal plasticity that prevent ictogenesis.

Funding sources: This work was supported by the Canadian Institutes of Health Research (PJT153310, PJT166178 and MOP130328; M.A.) and the Savoy Foundation (M.A.).

## Basic Science / Engineering

Abstract #87

# Using Artificial Rearing to Test Dietary Therapy in a Model of Infantile Epileptic Spasms Syndrome

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### Rationale

Infantile epileptic spasms syndrome (IESS) is a devastating infantile onset epileptic encephalopathy, with an incidence of 30 per 100,000 live births. Clinically, it is characterized by epileptic spasms, hypsarrhythmia, and development stagnation and regression. Despite the use of first line medications, the prognosis is poor in over 50% of cases. Thus, there is a need to identify novel therapies for IESS. Although ketogenic diet has been used successfully in some cases of drug-resistant epilepsies, it is unclear whether ketogenic diet is beneficial for IESS.

### Methods

The betamethasone-NMDA model of IESS was adapted by the Velisek's group. Sprague-Dawley pregnant dams were treated with betamethasone on G15. On P11, pups were subjected to cheek cannulation on P11 under anesthesia. After recovery, artificial rearing using control milk or the ketogenic diet was started as per the pup-in-a-cup protocol. Intraperitoneal NMDA was administered on P12, P13, and P15. Weights and blood ketones were measured. The number of sustained flexion spasms (emprostotonus) were scored.

### Results

Rats reared on both control milk and the ketogenic diet gained weight appropriately. Blood ketones were elevated as early as 24 hours after initiation of ketogenic diet. There was substantial variability in the number of NMDA-triggered emprostotonus.

### Conclusion

We have successfully artificially reared rats using the pup-in-a-cup method in the betamethasone-NMDA model of IESS. This should allow us to determine the preclinical efficacy and underlying mechanisms of ketogenic diet in IESS, its effect in developmental outcomes.

## Basic Science / Engineering

Abstract #88

### Assessment of the Hexoskin Wearable Biometric Shirt in Measuring Body Position During Sleep

Emmanuelle Nguyen[1], Manon Robert[2], Tian Yue Ding[2,3], Oumayma Gharbi[2,3], Amirhossein Jahani[2,3], Jérôme St-Jean[2,3], Claudia Rodriguez[2], Isabel Sarzo Wabi[2,3], Daniel Alejandro Galindo Lazo[2,3], Dang Khoa Nguyen[2,3], Elie Bou Assi[2,3]

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### Rationale
Patients with uncontrolled epilepsy are at increased risk of sudden unexpected death in epilepsy (SUDEP). There is some evidence suggesting that sleeping in a prone position and being in a prone position postictally increase the risk of SUDEP. Some commercially-available wearable devices have the potential to track sleeping habits. If so, these could eventually be used to screen patients with epilepsy with a tendency to sleep in a prone position (allowing interventions such as sleep training strategies to influence ideal sleep position) or to continuously monitor body positioning (allowing responsive alarms and/or interventions). In this study, we assessed the accuracy of the Hexoskin biometric shirt, which incorporates a sleep position classification algorithm, in identifying sleep body positions.

### Methods
Patients were recruited at the University of Montreal Health Center (CHUM) epilepsy monitoring unit and were asked to wear the Hexoskin biometric shirt. A built-in algorithm identified sitting/standing, left, right, supine, or prone body positions using an accelerometer. Sleeping positions predicted by the algorithm were compared to "true" values collected via independent blind video analysis to generate multiclass confusion matrices.

### Results
Across 5 patients and 174 hours of sleep analyzed, 73% of prone, 72% of supine, 93% of right lateral decubitus, 65% of left lateral decubitus, and 65% of sitting/standing positions were correctly classified by the Hexoskin algorithm. Balanced accuracy was 0.73 and weighted F1-score was 0.79.

### Conclusion
Our preliminary results show promise in the use of the Hexoskin shirt for detecting sleep positions.

## Basic Science / Engineering

Abstract #89

# Excitation/Inhibition Balance Relates to Cognitive Function and Gene Expression in Temporal Lobe Epilepsy: An Hdeeg Assessment with Aperiodic Exponent

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## Rationale

Patients with epilepsy are characterized by a dysregulation of excitation-inhibition balance (E/I). The assessment of E/I may inform clinicians during the diagnosis and therapy management, even though it is rarely performed. An accessible measure of the E/I of the brain represents a clinically relevant feature. Here we exploited the exponent of the aperiodic component of the power spectrum of EEG signal as a noninvasive and cost-effective proxy of the E/I balance.

## Methods

We recorded resting-state activity with high-density EEG from 67 patients with temporal lobe epilepsy (TLE) and 35 controls. We extracted the exponent of the aperiodic fit of the power spectrum from source-reconstructed EEG and tested differences between TLE and controls. Spearman's correlation was performed between the exponent and
clinical variables (age of onset, epilepsy duration and neuropsychology) and cortical expression of epilepsy-related genes derived from Human Allen Brain Atlas.

## Results

Patients with TLE showed a significantly larger exponent, corresponding to an inhibition directed E/I balance, in bilateral frontal and temporal regions. Lower E/I in the left entorhinal, and bilateral dorsolateral prefrontal cortices corresponded to a lower performance of short term verbal memory. Limited to TLE, we detected a significant correlation between the exponent and the cortical expression of GABRA1, GRIN2A, GABRD, GABRG2, KCNA2and PDYN.

## Conclusion

EEG aperiodic exponent maps the E/I balance non-invasively in patients with epilepsy and reveals a tight relationship between altered E/I patterns, cognition and genetics.

## Basic Science / Engineering

Abstract #90

### Detection of Focal Impaired Awareness Seizures Using a Smart Shirt and Machine Learning Classifiers

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#### Rationale
In recent years, seizure detection using wearable technology has gained significant attention in research. Most studies, however, have focused on detecting generalized or focal to bilateral tonic-clonic seizures. This study explores the potential of a smart shirt to detect focal impaired awareness seizures (FIAS) by monitoring respiratory, electrocardiography, and accelerometry signals.

#### Methods
Patients with epilepsy were recruited at the CHUM epilepsy monitoring unit and seizures were annotated by epileptologists based on simultaneous video-EEG recordings, blindly to the shirt data. Features were extracted from the respiratory, accelerometry and electrocardiography signals using varying window sizes and overlaps. An XGBoost classifier was trained and tested using a nested leave-one-subject-out cross-validation. Post-processing included a firing power regularization method to reduce false alarms.

#### Results
We recorded 113 FIAS from 27 patients who wore the shirt continuously for over 5000 hours. After post-processing, we detected 71 seizures, resulting in a sensitivity of 63%, a 15% time in warning and a false alarm rate (FAR) of 30 per 24 hours. By optimizing the threshold to reduce false alarms, we achieved 8% time in warning, a FAR of 21 per 24 hours, but a lower sensitivity of 54%. Performances varied across patients. Some patients experienced high sensitivity and low FAR, while others had lower sensitivity and higher FAR, indicating variability in algorithm effectiveness across patients.

#### Conclusion
Our results demonstrate that detecting FIAS seizures with a connected shirt could be feasible for certain patients, although the rate of false alarms remains considerable. Adopting a personalized algorithm approach and selecting patients who exhibit significant physiological changes during seizures could make wearable-based FIAS detection viable in the near future.

## Basic Science / Engineering

Abstract #91

# Activation of Hippocampal CA3 Principal Neurons Triggers Hypersynchronous-Onset Seizures in Kainic Acid-Treated Mice

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### Rationale

Mesial temporal lobe epilepsy (MTLE) is the most common form of focal epilepsy and is characterized by spontaneous recurrent seizures that are often refractory to medications. Seizures in MTLE mostly originate from the hippocampus and the seizure onset patterns can be categorized into hypersynchronous (HYP) and low-voltage fast (LVF) onset, which are believed to be mainly dependent on excitatory principal neurons and inhibitory interneurons, respectively. In the current study, we aimed to test the hypothesis that HYP onset seizures are mainly dependent on the activity of principal neurons.

### Methods

Unilateral open-loop optogenetic stimulations were implemented on kainic acid (KA)- treated CaMKII-ChR2 mice. Optogenetic stimulation cycles (1Hz, 180 s ON, 220 S OFF) were implemented for 15 days after the status epilepticus induced by KA.

### Results

We found that only HYP seizures occurred during the optogenetic activation of principal neurons in CaMKII-ChR2 mice (n=5) and that these HYP seizures followed a circadian pattern. In contrast, both HYP and LVF seizures were observed in non-stimulated CaMKII-ChR2 mice (n=6) and stimulated CaMKII-Cre mice (n=5). During optogenetic activation of principal neurons, we also found higher rates of fast ripples (250-500 Hz) than in non-stimulated mice.

### Conclusion

These findings provide firm evidence that different seizure onset patterns in MTLE result from the involvement of different neuronal populations. Moreover, principal neurons are the main contributors to fast ripple generation.

## Basic Science / Engineering

Abstract #92

### Pharmaco-Resistant Temporal Lobe Epilepsy Gradually Perturbs the Cortex-Wide Excitation-Inhibition Balance

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### Rationale
Excitation-inhibition (E/I) imbalance is proposed as a fundamental pathophysiological mechanism in temporal lobe epilepsy (TLE). This study aims to non-invasively elucidate the cortical pattern of E/I imbalance in TLE patients and explore its associations with disease severity and cognitive impairment.

### Methods
We studied 40 pharmaco-resistant TLE patients and 40 matched healthy controls who underwent 3T MRI and comprehensive cognitive testing. Node-wise Hurst exponent score was estimated from rs-fMRI and used as a proxy for the overall E/I ratio within each region. Surface-wide between-group differences in Hurst exponent were assessed, with P-values adjusted for false discovery rate (FDR). We also examined associations with clinical and cognitive measures at baseline and a 2-year follow-up.

### Results
Surface-based analysis revealed marked reductions in local Hurst exponent values in bilateral temporal, prefrontal, and occipital cortices in TLE compared to healthy controls, indicating an elevated E/I ratio ($P_{FDR} < 0.05$). In TLE patients, lower Hurst exponent scores were associated with longer disease duration ($t = -1.76$, $P = 0.021$) and poorer MoCA performance ($t = 2.93$, $P = 0.001$). Moreover, Hurst exponent scores declined at a 2-year follow-up in TLE ($d = -0.77$, $P < 0.001$) and correlated with the progressive decline in MoCA scores ($t = 2.05$, $P = 0.015$).

### Conclusion
In TLE, our finding of reduced Hurst exponent scores likely indicates widespread cortical E/I changes, tilting the balance towards increased. These changes were found to increase with ongoing disease progression and cognitive impairment, highlighting the potential of the Hurst exponent as a neuroimaging biomarker for TLE-related dysfunction.

## Basic Science / Engineering

Abstract #93

# Assessing the Performance of Open-Source Large Language Models in Epilepsy

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### Rationale
Large language models (LLMs) have shown promising capabilities in diverse tasks, including answering epilepsy-related questions. Critical flaws such as lack of recent knowledge and incorrect information generation limit their use in clinical practice. We hypothesize that a domain-specific LLM could overcome these challenges and outperform larger LLMs.

### Methods
To develop a specialized LLM, we systematically assessed nine open-source models' knowledge in epilepsy to select the best base model. They were tested using 224 unique questions from the American Epilepsy Society (AES) self-assessments (2021 to 2023). Each model was prompted to ensure optimal performance. Accuracy was our primary evaluation criterion. OpenAI's closed-source GPT models were tested for comparison, and a qualitative review of answers was performed.

### Results
Best accuracies obtained were: Llama-3 8B at 49.1%, Mistral 7B at 40.6%, Gemma 7B at 37.5%, Qwen2 7B at 34.4%, Meditron 7B at 31.3%, Llama-2 7B and Qwen2 1.5B at 27.7%, Gemma 2B at 23.21%, and Falcon 7B at 20.98%. Using similar techniques, we achieved 54% accuracy with GPT-3.5 and 79% with GPT-4, surpassing previously published data.

### Conclusion
Among open-source models, Llama-3 8B showed superior knowledge in epilepsy, outperforming Meditron, an LLM trained specifically on clinical data. Llama-3 reached nearly 50% accuracy on board practice questions, results comparable to GPT-3.5 despite being 22 times smaller. It still fared poorly compared to GPT-4, which exhibited expert-level knowledge with our specialized prompting. We aim to match this performance by further training Llama-3 on domain-specific data while ensuring patient privacy and transparency.

## Epilepsy Surgery

Abstract #94

*Withdrawn*

## Epilepsy Surgery

Abstract #95

# Evaluating Cenobamate Effectiveness in Medically Refractory Epilepsy Patients Using Clinical and RNS Biomarkers

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### Rationale

The Responsive Neurostimulation System (RNS) offers a method to objectively monitor seizures, potentially enhancing the accuracy of seizure tracking1. The efficacy of combining RNS with cenobamate is unknown.

### Methods

This study aims to assess the impact of cenobamate on seizure frequency and RNS biomarkers. We gathered clinical and device data from patients with RNS prescribed cenobamate. Clinical responses were assessed through patient reports, while electrographic responses using RNS data, including long episodes (patterns sustained beyond a patient-specific threshold, often correlating with seizures). These biomarkers were compared across response groups: super-responders (≥90% improvement), intermediate responders (≥50% improvement), and non-responders(<50% improvement).

### Results

We identified 22 medically refractory patients seen November 2019 to February 2024, who had RNS and were prescribed cenobamate. Four patients were excluded: three for prior cenobamate use and one for early discontinuation. Reported cenobamate benefit was noted in 11/18 patients (7 super-responders; 5 intermediate responders). A significant reduction in total detections ($p<0.05$) after reaching steady dose of cenobamate was seen in 6/7 super-responders, 4/5 intermediate responders, and 1/6 non-responders. Similarly, significant reduction in long episodes was seen in 4/7 super-responders, 2/5 intermediate responders, and 0/6 non-responders. Reduction in either biomarker was associated with clinical response ($p= 0.0128$).

### Conclusion

More than half of our cohort experienced ≥50% reduction in clinical seizures with cenobamate, and over half of these were super responders with ≥90% reduction. The clinical reports were supported by changes in objective RNS biomarkers. This high responder rate among medically refractory patients raises the possibility of potential synergy between cenobamate and RNS.

## Epilepsy Surgery

Abstract #96

# Determinant Factors of Epilepsy Surgical Outcome after Stereo-Electroencephalography Investigation Using Bayesian Causal Inference

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## Rationale

Epilepsy surgery outperforms medical treatment for seizure-control and quality of life. However, the factors determining success after stereo-electroencephalography (SEEG), the gold-standard for identifying surgical targets in patients with complex epilepsy, are uncertain. We investigated the effect of clinical, imaging, histopathological, and electrophysiological variables on surgical outcome after SEEG investigation.

## Methods

This study included consecutive patients with drug-resistant epilepsy who underwent SEEG guided resective surgery at three centers. We applied directed-acyclic-graph to investigate the causal relationship between good surgical outcome (Engel-I) and variables such as epilepsy type, implantation laterality, seizure-onset zone [SOZ] focality, phase I-II concordance, histopathology, SOZ-resected fraction, and non-SOZ fraction of the surgical cavity.

## Results

We included 200 consecutive patients (43% temporal lobe epilepsy [TLE], 56% good outcome). The SOZ-resected fraction had the strongest positive impact on good outcome, while the non-SOZ fraction of the cavity had no effect. Among categorical variables, complete concordance between phase I-II had the most positive impact, followed by posterior [PE], operculo-insular, and frontal lobe epilepsy [FLE]. Focal and regional SOZ as well as focal-cortical-dysplasia II, also positively impacted good outcome. Widespread SOZ had the most negative impact followed by multifocal SOZ, PE+, TLE+, FLE+, PE+. Gliosis/scar, bilateral SEEG implantation, eloquent cortex in the SOZ, and partial phase I-II concordance also negatively impacted good outcome.

## Conclusion

The extent of SOZ resection is crucial for SEEG-guided epilepsy surgery outcome. Resecting beyond the SOZ does not improve success. This study emphasizes targeting the SOZ and challenges the belief that more extensive resection leads to better results.

## Epilepsy Surgery

Abstract #97

# The Effect of High Frequency Cortical Stimulation on SEEG-Recorded Interictal Epileptiform Discharges

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## Rationale

More than 15 million patients with epilepsy suffer from drug-resistant epilepsy (DRE). In these cases, a successful surgical outcome entails the removal of the Seizure Onset Zone (SOZ), the brain region(s) responsible for seizure initiation. In this regard, finding robust biomarkers of epileptogenicity will help clinicians to accurately localize the SOZ. In focal epilepsies, Interictal Epileptiform Discharges (IEDs) are paroxysmal events observed in both epileptogenic and non-epileptogenic zones.
To identify the SOZ, extraoperative Cortical Stimulation (CS) is used during phase II of presurgical investigation. We evaluated the impact of CS on IEDs to find biomarkers of epileptogenicity to accurately find SOZ.

## Methods

In this study, intracranial signals were recorded from thirty DRE patients implanted with depth electrodes (stereo-electroencephalography) for presurgical evaluation. Bipolar and high frequency (50 Hz) CS was performed with a pulse width of 300 µs and current spanning around 1–6 mA. Following preprocessing, IEDs were automatically detected pre- and post-stimulation, and their normalized absolute changes were compared between SOZ and non-SOZ.

## Results

Our findings reveal a significant increase in IED numbers following SOZ stimulation compared to non-SOZ stimulation (Mann-Whitney U test, $p < 0.001$). Furthermore, this increase extended beyond the stimulated site, indicating a broader effect of stimulation on the SOZ.

## Conclusion

These results feature the potential of tracking post-stimulation changes in IEDs' characteristics as a quantitative method for SOZ identification, enhancing localizing the SOZ with greater precision.

## Epilepsy Surgery

Abstract #98

### Involvement of the Posterior Cingulate Gyrus in Temporal Lobe Epilepsy: A Study Using Stereo-EEG

Miguel Arevalo-Astrada[1], Ana Suller-Marti[2], Richard McLachlan[2], Elma Paredes-Aragon[3], Michelle-Lee Jones[2], Andrew Parrent[2], Seyed Mirsattari[4], Jonathan Lau[2], David Steven[2], Jorge Burneo[2]

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#### Rationale
To analyze the involvement of the posterior cingulate gyrus (PCG) during mesial temporal lobe seizures (MTLS).

#### Methods
We retrospectively reviewed the stereo-EEG (SEEG) recordings of patients with MTLS performed in our institution from February 2013 to December 2020. Only patients who had electrode implantation in the PCG were included. Patients with lesions that could potentially alter the seizure spread pathways were excluded. We assessed the propagation patterns of MTLS with respect to the different structures sampled.

#### Results
Nine of 97 patients who had at least one seizure originating in the mesial temporal region met the inclusion criteria. A total of 174 seizures were analyzed. The PCG was the first site of propagation in most of the cases (8/9 patients and 77.5% of seizures, and 7/8 patients and 65.6% of seizures after excluding an outlier patient). The fastest propagation times were towards the contralateral mesial temporal region and ipsilateral PCG. Seven patients underwent standard anterior temporal lobectomy and, of these, all but one were Engel 1 at last follow up.

#### Conclusion
We found the PCG to be the first propagation site of MTLS in this group of patients. These results outline the relevance of the PCG in SEEG planning strategies. Further investigations are needed to corroborate whether fast propagation to the PCG predicts a good surgical outcome.

## Epilepsy Surgery

Abstract #99

# Surgical Outcome of Epileptic Spasms: A Systematic Review of the Literature and Individual Patient Data Meta-Analysis

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## Rationale

There is limited literature regarding outcomes of surgical interventions for infantile epileptic spasms syndromes (IESS) and prognostic factors guiding decision-making (1-3). This study aimed to evaluate surgical outcomes for IESS and identify prognostic factors.

## Methods

A systematic review and individual participant data (IPD) meta-analysis of 32 studies (825 participants; IPD for 358) reporting surgical outcomes for patients with IESS was performed.

## Results

The median ages at epileptic spasms (ES) onset and surgery were 6.0 (IQR = 3.0-15.6) and 37.0 (IQR = 17.2-76.8) months, respectively. Most patients (74.1%) exhibited other seizure types in addition to ES (226/305 with available data). A total of 136 patients (35.8%) underwent corpus callosotomy (CC), with 125 (91.9%) undergoing complete callosotomy and 11 (8.1%) undergoing partial callosotomy. A total of 222 patients (58.4%) underwent resective surgery. At a median follow-up of 36.0 months (IQR = 21.0-60.0), 213 (56.1%) patients were ES-free overall with 38.2% ES-free after CC and 67.1% ES-free after resection. Repeat surgery was performed in 41.7% of patients (118/283 with available data). Among resective surgery, hemispherectomy was associated with a lower likelihood (HR = 0.46; 95% CI = 0.23-

0.91) of ES recurrence compared with more limited resective surgeries. Additionally, patients with a lesional MRI (221/315 patients) were less prone (HR = 0.53; 95% CI = 0.31-0.93) to ES recurrence. Developmental improvement was seen in 65.7% of patients (44/67 with available data) after ES surgery.

## Conclusion

Surgical treatment of ES is effective, particularly in the resective cohort where hemispherectomy shows promise in lowering the likelihood of recurrence.

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## Epilepsy Surgery

Abstract #100

# Interim European Outcomes for Patients Enrolled in the CORE-VNS Registry

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### Rationale
The Comprehensive Outcomes Registry in Subjects with Epilepsy Treated with Vagus Nerve Stimulation (VNS) Therapy (CORE-VNS) is an ongoing prospective study in patients with drug-resistant epilepsy (DRE) in a real-world setting.

### Methods
DRE patients receiving implantable VNS (new or replacement) were eligible for participation in the CORE-VNS. Seizure frequency (SF), maximum SF free periods, seizure severity, post-ictal severity, changes in quality of life and sleep, anti-epileptic drug and rescue drug use, and seizure-related hospital, and emergency department visits were evaluated at baseline, 3, 6, and 12, 24 and 36 months. 24-month interim results are presented.

### Results
Across Europe, a total of 341 subjects signed informed consent with 327 included in the modified safety population and 226 implanted (implant naive) across 7 different countries. The mean age at consent was 24.9 years and epilepsy types included combined (31%), focal (54%), and generalized (14%). 67% of subjects were naïve to VNS Therapy (43.4% < 18 years of age and 53.1% female). The responder rate (percent of subjects with>50% reduction in seizures) at 24 months was 52.4% (all seizures) compared with 48.1% at 12 months. At 24 months, the median percent reduction in SF was 51.6% (all seizures) compared to 42.9% at 12 months.

### Conclusion
At 24 months, the median percent seizure reduction and response to VNS continued to be robust, with further improvement noted since 12 months.

## Epilepsy Surgery

Abstract #101

# Dynamic Spectral Imaging (DSI) of Cognitive Functions in Drug-Resistant Focal Epilepsy Explored by Stereo-ElectroEncephaloGraphy (SEEG)

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## Rationale

Epilepsy affects 50 million people globally, with 60% having focal epilepsy, where seizures originate from a specific brain area. Despite advances in pharmacology, 30% of cases remain drug resistant. For these patients, surgery can be effective if the epileptogenic zone is precisely identified. Stereo-electroencephalography (SEEG) uses depth electrodes to define epileptogenic areas. In the present study we investigated the activity of the seizure onset zone (SOZ) during various cognitive tasks with the objective to predict post-surgery neuropsychological outcomes.

## Methods

Since 2021, CHU de Québec's epilepsy surgery program has used SEEG to guide surgical decisions. We record LFPs that are good forecasting measures of epileptic discharges and are appropriate predictors of task related brain activity (in the gamma > 30Hz range). We asked 14 patients to perform cognitive tasks (reading, perception, attention, memory, motor production...). We then extracted task-related gamma activity (Dynamic Spectral Imaging, DSI) in the SOZ for each patient.

## Results

To date only 4 patients had a surgery following post SEEG evaluation, and the SOZ was not recruited in any of the cognitive tasks. For the remaining patients, task-related gamma activity has been observed in the SOZ, but the surgery has not been proposed (or is in discussion, decision independent of the present study).

## Conclusion

While recordings of more patients are need, we are confident that this research will offer new avenues for the prediction post-surgery neuropsychological outcomes.

Funding : NSERC Discovery Grant to P.A.

## Epilepsy Surgery

Abstract #102

### Factors Impacting Application Accuracy in Stereoelectroencephalography: An Integration of Qualitative and Computational Methods

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*Western University*

#### Rationale
Stereoelectroencephalography (SEEG) is a neurosurgical procedure involving implantation of diagnostic electrodes to determine the epileptogenic zone in patients with drug-resistant epilepsy. We aim to provide a detailed characterization of the factors that can impact application accuracy in SEEG.

#### Methods
We evaluated 237 consecutive SEEG procedures performed at our centre (205 robot; 31 frame). Baseline demographics, procedural details (robot versus frame-based), and electrode trajectory coordinates were collected. Computational methods were employed for calculating different forms of error (Euclidean and radial; target and entry) as well as for automated skull thickness and trajectory angle calculations. Information about additional treatments was collected, if available.

#### Results
For robot-based (2456 electrodes), mean target and entry point Euclidean errors were 2.27 ± 1.19 mm and 1.37 ± 0.99 mm respectively. Mean target and entry point radial errors were 1.58 ± 1.03 mm and 1.21 ± 0.84 mm respectively. For frame-based (302 electrodes), mean target and entry point Euclidean errors were 2.30 ± 1.71 mm and 3.08 ± 1.73 mm respectively. Mean target and entry point radial errors were 1.99 ± 1.48 mm and 2.26 ± 1.57 mm respectively. Reliability was good between automated and manual CT skull segmentation with an ICC of 0.88 and agreement bias of 1.673 mm.

#### Conclusion
SEEG electrodes can be placed with millimetric accuracy with statistically significant improvements using the robot versus frame. Targeting accuracy varied based on a number of factors with evidence of clusters of trajectories having similar patterns of predictable error. Current directions include building predictive models of expected error.

## Epilepsy Surgery

Abstract #103

# Comparison of Effective and Functional Connectivity Measures for the Identification of the Epileptogenic Zone

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## Rationale

The success of epilepsy surgery depends on the accurate localization of the epileptogenic zone (EZ) which can frequently require intracranial electroencephalography recordings (iEEG). Recent research suggests that connectivity approaches can improve the EZ localization by complementing visual interpretation of iEEG. This study evaluates the feasibility of identifying the EZ based on effective and functional connectivity measures.

## Methods

1) Simulated data: A nine-channel simulated connectivity pattern was generated based on autoregressive multivariate models to which random white Gaussian noise was added (0, -4dB, -8dB, and -12dB); 2) Patients' database: iEEG from 12 patients (mean age=36; 5 females) who underwent epilepsy surgery at the CHUM (Engel score I/II) were analyzed. Seizure onset and offset and resected zones were annotated by an expert epileptologist. Phase slope index (PSI) and directed transfer function (DTF) were computed. Surrogate data testing validated the significance of connections. An electrode was identified as part of the EZ if its outflow exceeded 80% of the maximum outflow in at least 50% of 4-second ictal segments.

## Results

Simulation analyses revealed that the average specificity of PSI and DTF across four SNR values was 90.62% and 93.75%, respectively. Results on 68 seizures showed that while none of the measures tested could alone detect all the electrodes in the EZ for all patients, specificity of the algorithm was high reaching 92.46% and 91.10% for PSI and DTF, respectively.

## Conclusion

Our preliminary findings suggest that although no single connectivity method works accurately for all patients and seizures, combining different measures may enhance the algorithm's sensitivity.

## Epilepsy Surgery

Abstract #104

# Disrupting the Epileptogenic Network with Stereoelectroencephalography-Guided Radiofrequency Thermocoagulation

Hellen Kreinter[1], Poul Espino[1], Sonia Mejía[2], Khalid Alorabi[1], Greydon Gilmore[1], Jorge Burneo[1], David Steven[1], Michelle-Lee Jones[1], Giovanni Pellegrino[1], Jonathan Lau[1], Ana Suller-Marti[1]

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## Rationale

Stereoelectroencephalography-guided radiofrequency thermocoagulation (SEEG-guided RF-TC) is a treatment option for focal drug-resistant epilepsy. In previous studies, this technique has shown seizure reduction by ≥50% in 50% of patients at one year. However, the relationship between the location of the ablation within the epileptogenic network and clinical outcomes remains poorly understood.

## Methods

Seizure outcomes were analyzed for patients who underwent SEEG-guided RF-TC and across subgroups depending on the location of the ablation within the epileptogenic network, defined as SEEG sites involved in seizure generation and spread.

## Results

Eighteen patients who had SEEG-guided RF-TC were included. SEEG-guided seizure onset zone ablation (SEEG-guided SOZA) was performed in 12 patients, and SEEG-guided partial seizure onset zone ablation (SEEG-guided P-SOZA) in six patients. The early spread was ablated in three SEEG-guided SOZA patients. Five patients had ablation of a lesion. The seizure freedom and responders rates in the cohort ranged between 22-50% and 67-85%, respectively. SEEG-guided SOZA demonstrated superior results for both outcomes compared to SEEG-guided P-SOZA at six months, with seizure freedom rates of 3/9 for SOZA and 0/4 for P-SOZA (p=0.294) and responder rates of 9/9 for SOZA and 1/4 for P-SOZA (p=0.014). Adding the early spread ablation to SEEG-guided SOZA did not increase seizure freedom rates but exhibited comparable effectiveness regarding responder rates.

## Conclusion

The ablation of all contacts involved in the seizure onset zone led to higher seizure freedom and responder rates. Ablating the early spread improved the responder rate but not the seizure freedom rate, indicating a potential network disruption.

## Epilepsy Surgery

Abstract #105

# Assessment of Material-Specific Memory Impairments with Two Novel Analogous Tasks after Temporal Lobe Epilepsy Surgery

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### Rationale
Episodic memory tasks employing verbal material are generally sensitive to material-specific memory impairments in individuals with left temporal lobe epilepsy (LTLE), whereas visuospatial memory tasks are less consistently failed by individuals with right temporal lobe epilepsy (RTLE).

### Methods
This study examines material-specific memory impairments among individuals who have undergone surgery in the left (n = 16) or right (n = 12) temporal lobe, using two novel analogous memory tests. The tasks consist of a learning phase in three trials of stimulus presentation (verbal: pseudowords; non-verbal: landscapes depicting mountains, trees, and lakes) followed by immediate recognition procedures, at 30 minutes, and 2 weeks.

### Results
The RTLE group showed significantly poorer performance on the non-verbal than on the verbal memory test on all trials. The LTLE group showed significantly poorer performance on the verbal than on the non-verbal memory test at the 30-minute and 2-week delay trials. Only the verbal memory test showed significantly poorer performances on all trials for the LTLE when compared to the RTLE.

### Conclusion
These results suggest that our novel tasks are sensitive to material-specific memory impairments in both LTLE and RTLE. LTLE seem to have more difficulties retaining verbal information in long-term memory, whereas people with RTLE show difficulties learning and retaining visuospatial material. These new tasks could constitute valid tools for objectifying specific memory impairments related to the material in individuals with temporal epilepsy and have the advantage of not relying on motor responses and allowing remote testing.

## Epilepsy Surgery

Abstract #106

### Seizure Outcomes Generalized Epilepsy Following VNS Therapy: CORE-VNS 2-Year Follow-Up

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#### Rationale
The Comprehensive Outcomes Registry in Subjects with Epilepsy Treated with Vagus Nerve Stimulation (VNS) Therapy (CORE-VNS) is an ongoing prospective study in patients with drug-resistant epilepsy (DRE) in a real-world setting.

#### Methods
Patients were enrolled into a prospective, multicenter observational registry called CORE-VNS (NCT03529045). Patients with primary GTCS were included. Those with focal seizures at baseline or GTCS in the context of Lennox-Gastaut Syndrome were excluded. Patients completed a 3-month retrospective baseline period, where seizure information and other patient-reported outcome measures were collected. After VNS implantation, participants were followed for up to 36 months. A subpopulation of patients implanted within 5 years of original epilepsy diagnosis as compared to those implanted greater than 5 years from diagnosis.

#### Results
Fifty-nine patients met the criteria and received an initial VNS implant. Twelve subjects were implanted within less than 5 years of their initial epilepsy diagnosis, and 47 were implanted later than 5 years. Patients implanted earlier tended to be younger (9.7 vs 25.9 years old, median) and nearly all were pediatric (11/12 participants). Participants had failed several previous ASMs (6 median, range 2 to 20). For the entire cohort, the responder rate (≥50% reduction from baseline) for GTCS at 24 months, the responder rate for GTCS was 65.4% (95% CI: 53.1% to 76.3%) and the median seizure frequency change was -69.0% (95% CI: -100% to -50.0%). Patients with GTCS implanted earlier were slightly less likely to be responders at 12 months (55.6% vs 60.5%) and had a lower median seizure frequency change (-50% vs -73.3%), but these trends were non-significant. The most frequent side effects associated with VNS stimulation were dysphonia (11.9%,n=7), dyspnea (5.1%, n=3), cough (3.4%, n=2), and implant site pain (3.4%,n=2).

#### Conclusion
VNS was well tolerated and effective in reducing the frequency of GTCS. There were no relevant differences in seizure outcomes between GTCS response in patients implanted less than 5 years versus greater than 5 years from initial epilepsy diagnosis.

Epilepsy Surgery

Abstract #107

*Withdrawn*