

2022 CNS Research Day

Tuesday, May 17, 2022

King's University College London, Ontario





WELCOME

On behalf of Department of Clinical Neurological Sciences and the CNS Research Committee, I am pleased to welcome you to the 2022 CNS Research Day on Tuesday, May 17th at King's University College in London Ontario.

Research Day was established in 2004 with the goal of promoting research, collaboration and continuing education within the Department, institution and beyond. Our event allows members of the Department to share their passion for research and present their current research. Attendees have the opportunity to learn about clinical and basic research advances that push forward topics in the neurosciences, specifically in neurology and neurosurgery.

This year, we have over 40 abstracts submitted by clinical fellows, post-graduate students, residents, medical students and other undergraduate students. We have planned an exciting and interactive day that exemplifies the great research within our Department. The event will include a blend of oral and poster presentations, Q&A periods and our Keynote Address by Dr. A. Jonathan Stoessl.

I would like to take a moment to highlight our industry sponsors; Roche and UCB for their generous contributions. We are very thankful of your continued support of our research initiatives and Department in general. We welcome some of our industry members here today and hope you have a great time.

Lastly, I would like to thank our Judges for their commitment, Amanda at King's University, Michelle at Aramark and Adam our AV Support. Thank you to our Research Committee for their design of this year's program, and to Alexandra Kylindris for her incredible planning of today's events.

I hope you have an enjoyable experience and I am looking forward to a great event.

Sincerely,

David A. Steven, MD, MPH, FRCSC, FACS

Professor of Neurosurgery Richard and Beryl Ivey Chair Department of Clinical Neurological Sciences London Health Sciences Centre and Schulich School of Medicine & Dentistry Western University

EVENT ITINERARY

Morning Sessions:

8:00 to 8:15 a.m.	Registration and Continental Breakfast	Garron/Spriet Lounge
8:20 to 8:30 a.m.	Opening Remarks Dr. David Steven	Kenny Theatre
8:35 to 9:30 a.m.	Oral Presentation Session #1 A series of 5-minute presentations. Each presenter will be allotted 3 minutes for questions. PLAT-1 to PLAT-6	Kenny Theatre
9:30 a.m.	Refreshment Break	Garron/Spriet Lounge
9:40 to 10:15 a.m.	Oral Parallel Poster Session #1 A series of 2-minute presentations. Q&A will commence during refreshment break. POST-1 to POST-17	Basement Classrooms KC 005 & KC 006
10:15 to 10:40 a.m.	Refreshment Break Poster presentation Q&A	Garron/Spriet Lounge
10:45 to 11:40 a.m.	Oral Presentation Session #2 A series of 5-minute presentations. Each presenter will be allotted 3 minutes for questions. PLAT-7 to PLAT-12	Kenny Theatre

Afternoon Sessions:

11:45 a.m. to 12:40 p.m.	Lunch	Garron/ Spriet Lounge
12:45 to 1:40 p.m.	Oral presentation Session #3 A series of 5-minute presentations. Each presenter will be allotted 3 minutes for questions.	Kenny Theatre
	PLAT-13 to PLAT-16	
1:50 to 2:20 p.m.	Oral Parallel Poster Session #2 A series of 2-minute presentations. Q&A will commence during refreshment break.	Basement Classrooms KC 005 & KC 006
	POST-18 to POST-29	
2:20 to 2:40 p.m.	Refreshment Break Poster presentation Q&A	Garron/ Spriet Lounge
2:45 to 3:40 p.m.	Keynote presentation "In the Mind's Eye" Molecular Imaging Insights into Parkinson's Disease" Dr. A. Jon Stoessl	Kenny Theatre
3:40 to 4:00 p.m.	Closing Remarks and Awards Dr. Elizabeth Finger	Kenny Theatre

KEYNOTE ADDRESS



A. Jon Stoessl

A. Jon Stoessl is Professor & Head of Neurology at UBC. He was previously Director of the Pacific Parkinson's Research Centre, Co-Director, then Director of the Djavad Mowafaghian Centre for Brain Health. He held a Tier 1 Canada Research Chair in Parkinson's and is Editor-in-Chief of Movement Disorders. He has served on numerous other editorial boards including Lancet Neurology and Annals of Neurology. He has previously chaired the Scientific Advisory Boards of Parkinson's Canada and the Parkinson's Foundation and is Past-President of the World Parkinson Coalition. He is a Member of the Order of Canada. Dr. Stoessl uses positron emission tomography to study Parkinson's, including imaging biomarkers, the basis for complications of treatment and mechanisms of the placebo effect. He has published more than 300 papers and book chapters and has been cited more than 25,000 times in the scientific literature.

JUDGES

ANDREA ANDRADE, MD, CSCN-EEG



Dr. Andrea Andrade is a pediatric neurologist and epileptologist. She completed her medical degree and pediatric residency in Mexico City by the National University of Mexico. She subsequently completed a child neurology residency and epilepsy fellowship at University of Texas Southwestern in Dallas. Then moved to Canada where she completed further training in paediatric stroke and epilepsy surgery at University of Toronto, Sickkids Hospital.

Currently Dr. Andrade leads the paediatric epilepsy program at Western and she is heavily involved on the Ontario Epilepsy taskforce and Project ECHO: Epilepsy across the life span. She also leads the Paediatric Stroke Program at Children's/LHSC and she is a member of the International Pediatric Stroke Study (IPSS) and a founding member of the International Paediatric Stroke Organization (IPSO). Her research interests are in paediatric epilepsy surgery, pharmacoresistant epilepsies, paediatric stroke and implementation science areas where she has awarded multiple grants and published peer review articles and book chapters.

SACHIN K. PANDEY, MD, FRCPC



Dr. Sachin Pandey is an Associate Professor of Medical Imaging, at the University of Western Ontario, London, Ontario. He is the Division Head for Diagnostic and Interventional Neuroradiology, the Co-Director of Charles Drake fellowship in Cerebrovascular and Endovascular Neurosurgery, and has Cross-Appointments in the Department of Clinical Neurosciences and Otorhinolaryngology. He serves as the Ontario Medical Association Section Chair for Neuroradiology; and has just completed his term as the President of the Professional Staff Organization, London Health Sciences Center.

Dr. Pandey attended medical school at Boston University School of Medicine, in Boston, MA, graduating in 2007. He is a graduate of the Diagnostic Radiology Residency Program, Harvard University — Beth Israel Deaconess Medical Center; and continued on to a Fellowship in Interventional Neuroradiology, and Endovascular Neurosurgery at Harvard University, Brigham and Women's Hospital and Boston Children's Hospital.

He is deeply committed to education, and the training and mentoring of medical learners. He is the Director of Undergraduate Medical Education, in the Dept of Radiology; and the Education and Research director for the Diagnostic Neuroradiology Fellowship, University of Western Ontario Schulich School of Medicine. He serves as a Diagnostic Radiology Examiner, for the Royal College of Physicians and Surgeons (Canada). He has received multiple awards in recognition of

his excellence in teaching, including the Harvard University Humanism Award and the Harvard University's Andrew Berezin Award; as well as the Faculty Educator of the Year Award, and the Chair's Award of Inspiration – Department of Medical Imaging, at University of Western Ontario.

Dr. Pandey lives in London, Ontario, with his wife, Charmi, and three bright, beautiful and talented daughters.

A. JON STOESSL, CM, MD, FRCPC, FAAN, FCAHS



Dr. A. Jon Stoessl is Professor & Head of Neurology at UBC. He was previously Director of the Pacific Parkinson's Research Centre, Co-Director, then Director of the Djavad Mowafaghian Centre for Brain Health. He held a Tier 1 Canada Research Chair in Parkinson's and is Editor-in-Chief of Movement Disorders. He has served on numerous other editorial boards including Lancet Neurology and Annals of Neurology. He has previously chaired the Scientific Advisory Boards of Parkinson's Canada and the Parkinson's Foundation and is Past-President of the World Parkinson Coalition. He is a Member of the Order of Canada. Dr. Stoessl

uses positron emission tomography to study Parkinson's, including imaging biomarkers, the basis for complications of treatment and mechanisms of the placebo effect. He has published more than 300 papers and book chapters and has been cited more than 25,000 times in the scientific literature.

SHANNON VENANCE, MD, PhD, FRCPC



Dr. Shannon Venance earned her PhD from Queen's University in 1993 and her MD from the University of Ottawa in 1997. Neurology residency training was completed at the University of Ottawa, followed by a Neuromuscular Fellowship at London Health Sciences Centre and muscle fellowship at the University of Rochester, NY.

Dr. Venance joined the Department of Clinical Neurological Sciences, Schulich School of Medicine & Dentistry, Western University in 2004 and was promoted to Associate Professor in 2010. Her clinical expertise is in

disorders of muscle, and she collaborates with a diverse group of health professionals in the investigation and management of individuals with chronic muscle conditions.

Dr. Venance is a highly engaged clinician teacher, teaching and learning through the spectrum of undergraduate, postgraduate and continuing medical education. Most recently, she was appointed as the Vice Dean, Undergraduate Medical Education at the Schulich Medicine & Dentistry. She works collaboratively to effect change in medical education with a focus on generalism within competency-based medical education models.

EVENT SPONSORS

We would like to thank our event sponsors for their contribution to the 2022 CNS Research Day. We are appreciative of your continued support of this event and our Department. We look forward to future collaboration!





ORAL PRESENTATIONS

PLAT-1

Association between acute myocardial infarction and death in 386 patients with a thrombus straddling a patent foramen ovale

P. Shah, A. Jiménez-Ruiz, A. Gibson, JC. Vargas-González JC, M. Bres-Bullrich, R. Bagur, LA. Sposato

Importance: Right atrial thrombi are rarely found straddling a patent foramen ovale (PFO). A thrombus straddling a PFO (TSPFO), also known as impending paradoxical embolism, is a medical emergency associated with up to 11.5% risk of death within 24 hours of being diagnosed.

Objectives: To determine if acute myocardial infarction (MI) and ischemic stroke (IS) diagnosed upon the admission of patients with a thrombus straddling a PFO (TSPFO) are associated with increased risk of death. We also investigated if specific acute therapies are associated with reduced in-hospital mortality.

Design and Participants: We performed a systematic search including case reports and series of adult patients with TSPFO published from 1950 to October 30, 2020. We gathered patient-level data and we applied a logistic regression model to evaluate on the risk of in-hospital death. We performed timetrends and several sensitivity analyses.

Results: We included 386 cases with a TSPFO comprised in 359 publications. The median age was 61 years and 51.2% were females. Fifty (13.0%) patients died during hospital stay, 82 (21.2%) had an acute IS, and 18 (4.6%) had an acute MI diagnosed upon admission. Acute MI (OR 7.83, 95%CI 2.70-22.7; P &It; 0.0001), but not IS, was associated with increased risk of death. Right atrial thrombectomy was associated with a 65% decreased in-hospital mortality (OR 0.35, 95%CI 0.18-0.70, P = 0.003). Results remained unchanged on sensitivity analyses.

Conclusion: In this systematic review of 386 cases of TSPFO, acute MI but not IS was associated with 8-fold increased risk of death, while surgical thrombectomy was associated with a significant 65% reduction of in-hospital mortality.

Multi-Electrode Intracranial Electric Field Treatment for Brain Tumors: Planning System and Robot-Assisted Electrode Implantation

E. Iredale, B. Voigt, A. Rankin, K. Kim, J. Chen, S. Schmid, M. Hebb, T. Peters, E. Wong

Importance: The control of malignant brain tumors using low intensity electric fields applied using multiple implanted electrodes, termed Intratumoral Modulation Therapy (IMT), has been explored and validated for efficacy in-vitro and in-vivo. For expansion into the clinical setting, a multi-electrode treatment planning system is required for non-parallel electrode trajectory and programming optimization to cover a patient tumor with the prescription electric field.

Objectives: To develop a treatment planning system for IMT, with implementation of the pipeline on a brain phantom with robot-assisted electrode implantation and voltage measurements for validation.

Design and Participants: The IMT planning system was developed as a custom application in 3D Slicer, where patient image segmentation and smoothing, electrode trajectory planning, optimization of electrode tip coordinates, stimulation voltage and phase shift, and results visualization were incorporated. The planning and optimization pipeline was implemented on a brain phantom, where multiple electrodes were robotically implanted into the brain at planned trajectories. The voltage and phase shift of delivered waveforms were measured and post-operative parameter re-optimization was evaluated for accommodation of electrode placement uncertainty.

Results: The IMT planning system enables users to select the entry points and initial electrode trajectories based on the patient image, where the trajectories and stimulation programming are simultaneously optimized to cover the tumor with the prescription electric field. Robot-assisted electrode implantation of four stimulating and two measurement electrodes resulted in geometrical offsets of 1.1 ± 0.6 mm tip separation and $1.2 \pm 0.6^\circ$ in the angle between electrode pairs. Uncertainty in the implant electrode geometry and the delivered phase shift from voltage measurements impacted the electric field by under 2.6% and 0.4% respectively, mitigated through post-implantation voltage and phase shift re-optimization.

Conclusions and Relevance: In this study, a semi-automatic treatment planning system for multielectrode IMT was established for patient specific non-parallel electrode trajectory planning and electric field optimization. Validation of the planning system on a brain phantom with robot-assisted electrode implantation, post-implant stimulation parameter re-optimization and voltage measurements lay the groundwork for future IMT clinical trials.

Presence of apathy as a major predictor of disease progression in cognitively normal and cognitively impaired subjects: an Alzheimer's disease neuroimaging initiative study

R. Malik, S. Pasternak, J. Wells, M. Borrie, Garcia, R.R., E. Finger, and the ADNI Investigators

Importance: Identifying early neuropsychiatric predictors of Alzheimer's Disease (AD) will help inform future clinical treatment of individuals who are at risk for development of AD.

Objective: To investigate the link between apathy and rate of diagnostic conversion from cognitively normal (CN) to mild cognitive impairment (MCI) and MCI to Alzheimer's Disease.

Design and Participants: Participants from the Alzheimer's Disease Neuroimaging Initiative (ADNI) were included in this study. ADNI is a longitudinal multicenter study that enrolls adults, ages 55-90 years old, with MCI, AD, and cognitively normal controls. Of the 3,364 participants enrolled in ADNI, eligible candidates for the current study included those with an available apathy score from the informant-based Neuropsychiatric Inventory (NPI or NPI-Q), who completed at least three ADNI visits. Cox proportional-hazards survival analyses were used to examine the links between apathy and rate of diagnostic conversion (CN to MCI and MCI to AD). The primary covariate of interest was apathy endorsement. The Alzheimer's Disease Assessment Scale-Cognitive subscale (ADAS-cog), a revised Geriatric Depression Scale (GDS-12), the Clinical Dementia Rating scale (CDR), age, sex, and years of education were included as covariates in the analyses. The contributions of covariates to the Cox proportional-hazards survival models were assessed using omnibus likelihood ratio tests (LRT).

Results: 1441 participants (mean age: 73.3 years) were eligible for the current study. Approximately 53% of participants were male. Results of the Cox proportional-hazards model in the CN to MCI cohort (LRT: $\lambda(7) = 80.69$, p<0.001) revealed a 76% increase in risk of conversion in participants who endorsed apathy (HR=1.76, p<0.001). A higher ADAS-Cog score increased risk of conversion from CN to MCI by 9% (HR=1.09, p<0.001). In the MCI to AD cohort, results of the Cox proportional-hazards model (LRT: $\lambda(7) = 42.35$, p<0.001) revealed a 57% increase in conversion risk in MCI participants who endorsed apathy (HR=1.57, p<0.001). A higher ADAS-Cog score was found to increase risk of conversion from MCI to AD by 2% (HR=1.02, p<0.001).

Conclusion and Relevance: The presence of apathy is implicated in progression to cognitive impairment in healthy controls and to Alzheimer's Disease in cognitively impaired adults. This finding can help inform future diagnosis and treatment of adults, with and without cognitive impairment, who present with symptoms of apathy.

Functional near-infrared spectroscopy as a tool to assess residual and covert consciousness in the intensive care unit

A. Abdalmalak and K. Kazazian (co-first authors), L. Norton, S. L. Novi, R. Moulavi-Ardakani, M. Kolisnyk, T. E. Gofton, R. C. Mesquita, A. M. Owen, D. B. Debicki

Importance: We demonstrate that functional Near-Infrared Spectroscopy (fNIRS) can be used to detect covert cognition in a clinically unresponsive patient in the intensive care unit (ICU).

Objective: To establish the feasibility of using fNIRS to detect the neural correlates of conscious processing in critically ill brain-injured patients and healthy control participants.

Design and participants: A series of validated paradigms were employed to assess somatosensory perception, auditory processing, covert command following, and resting-state connectivity in an unresponsive patient in the ICU following an ischemic pontine infarct. The patient's neural response to these paradigms was compared to a convenience sample of 16 healthy volunteers. At the time of imaging (post-admission day 24), the patient was behaviourally unresponsive (GCS 6T) with no evidence of command following and no evidence of responses suggestive of a clinical diagnosis of locked-in syndrome. An fNIRS system with 129 channels providing full head coverage was used. For all task related paradigms, a channel was considered activated if there was a significant increase in oxyhemoglobin and a concurrent decrease in deoxyhemoglobin (p<0.05) during the task period.

Results: Consistent and reliable hemodynamic changes were detected in predicted cortical areas for all paradigms in healthy volunteers (mean age = 25, 10 males, 6 females) and the patient (68 years old, male). This includes significant activation of the post-central and supramarginal gyrus (HbO=2.81±0.11, HbR=-2.99±0.22) for the somatosensory perception task; the superior temporal gyrus (HbO=2.45±0.16, HbR=-2.33±0.16) for the auditory processing task; and preserved functional networks (r=0.45) for the resting state paradigm. When asked to imagine playing tennis or moving around their home, changes were detected over the premotor and parietal areas, respectively (HbO=2.96±0.19, HbR=-2.88±0.20 and HbO=2.60±0.89, HbR=-2.61±0.71).

Conclusion and Relevance: In this work, we show that fNIRS can reliably detect covert cognitive processing in a clinically unresponsive patient and with 16 healthy participants. Importantly, we report a level of conscious awareness that was inconsistent with the patient's clinical diagnosis. Future work will explore the clinical utility of using fNIRS to assess residual cognitive function and covert awareness in the ICU and establish whether these measures can supplement diagnosis and prognostication.

Using quantitative susceptibility mapping to identify midbrain and striatal structural features of early-stage Parkinson's disease

E. Alushaj, D. Hemachandra, N. Handfield-Jones, A. Kuurstra, R.S. Menon, A.M. Owen, A.R. Khan, P.A. MacDonald

Importance: Currently, there are no validated imaging diagnostic biomarkers of Parkinson's disease (PD), but MRI has great potential for their discovery.

Objective: To identify an imaging diagnostic biomarker of PD for use in clinics by applying structural magnetic resonance imaging (MRI) techniques: quantitative susceptibility mapping (QSM) and diffusion MRI.

Methods: In a case-control study, early-stage PD patients and age-matched healthy controls were scanned using 3T MRI. T1-weighted anatomicals coupled with diffusion MRI were used for segmenting the midbrain nuclei and striatum subregions based on the CIT168 probabilistic subcortical atlas (2018). Probabilistic tractography was conducted to parcellate the striatum into seven subregions using the segmentation proposed by Tziortzi and colleagues (2014). Subsequently, we measured average susceptibility using QSM in each hemisphere in midbrain nuclei and striatum subregions.

Results: Repeated measures analysis of variance of average susceptibility values from QSM revealed significantly higher SNc values in early-stage PD patients (n=25) compared to healthy controls (n=25), indicating higher iron content. No significant group differences in average susceptibility were found in the SNr, VTA, or total striatum measures (i.e., caudate, putamen, nucleus accumbens). We found significant group differences in the caudal motor subregion of the striatum. SNc and caudal motor striatum average susceptibility were combined using a binary logistic regression model. Receiver operating characteristic curve analysis with repeated 5-fold cross validation of this model revealed an excellent diagnostic accuracy of 0.90.

Conclusions: These findings suggest that QSM in the SNc combined with the caudal motor subregion can function as a diagnostic biomarker of PD, following validation, given its excellent diagnostic accuracy at the single-subject level.

Postoperative Ventricle Volume and Whole-Brain Tractography in Pediatric Hydrocephalus

R.M., Ragguett, R. Eagleson, S. de Ribaupierre

Importance: Treatment of pediatric hydrocephalus (PH) is one of the most common procedures performed by pediatric neurosurgeons. Despite this, little is known about impact of postoperative ventricle volume on white matter (WM) integrity.

Objective: To determine if postoperative lateral ventricle volume (LVV) can predict postoperative WM integrity using whole-brain tractography.

Design and Participants: This cross-sectional study assessed children with shunt-treated hydrocephalus and healthy controls who were recruited through the Pediatric Neurosurgery clinic, and the OurBrainsCAN Research Registry. Participants were not eligible for the study if they had any MRI contraindications. All participants underwent an imaging and behavioral protocol. Probabilistic tractography was used to generate region-to-region WM streamline counts. Using network-based statistics, structural connectivity differences between patients and controls were assessed. Further, regression models were used in those with PH to assess the impact of age at assessment and postoperative LVV on streamline counts.

Results: Eight patients with PH (age M = 8.75 years) and 36 healthy controls (age M = 9.53 years) completed the study. Four networks were identified as differing between patients with PH and controls. One composed of 56 nodes (p = .003) had more connections in those with PH relative to controls. Three networks composed of two nodes each were found to have more connections in controls relative to patients (all p &It; .05). Regression models revealed the number of connections between various regions including the dorsal raphe nucleus and hippocampus, as well as the intralaminar thalamic nucleus and hippocampus in the 56-node network could be positively predicted by LVV in patients (p &It; .005).

Conclusions and Relevance: This study has shown there are differences in structural connectivity between PH patients and controls, and LVV correlates with WM structural connectivity metrics. Similarly to previous studies, in PH, LVV was a predictor of WM integrity measures. Contrary to previous studies, this study suggests smaller LVV predicts WM organization more closely resembling healthy controls, as opposed to larger LVV. While this study contributes to further understanding the impact of postoperative LVV on WM integrity, a larger sample size is needed to further elucidate the results.

Comparison of fixed cell-based assay to radioimmunoprecipitation assay for acetylcholine receptor antibody detection in myasthenia gravis

A. Mirian, M. W. Nicolle, P. Edmond, A. Budhram

Importance: Radioimmunoprecipitation assay (RIPA) is the historical gold standard test for acetylcholine receptor antibody (anti-AChR) detection in myasthenia gravis (MG), but may miss low-affinity anti-AChR that are detected by live cell-based assay (L-CBA). Unfortunately, widespread use of L-CBA is limited by its costly and time-consuming nature. A commercial fixed cell-based assay (F-CBA) for anti-AChR is available that can more easily be implemented in many clinical laboratories, but its diagnostic utility requires investigation.

Objective: To compare specificity and sensitivity of a commercially available fixed cell-based assay (F-CBA) to radioimmunoprecipitation assay (RIPA) for acetylcholine receptor antibody (anti-AChR) detection in myasthenia gravis (MG).

Design and Participants: In this retrospective diagnostic cohort study we reviewed the clinical information of suspected MG patients evaluated at the London Health Sciences Centre MG clinic who had anti-AChR RIPA and then F-CBA performed, in order to classify them as MG or non-MG. Classification of each patient as anti-AChR F-CBA- negative/positive, RIPA-negative/positive, and MG/non-MG permitted specificity and sensitivity calculations for each assay.

Results: Six-hundred-eighteen patients were included in study analysis. The median patient age at time of sample collection was 45.8 years (range: 7.5–87.5 years) and 312/618 (50.5%) were female. Of 618 patients, 395 (63.9%) were classified as MG. Specificity of both F-CBA and RIPA was excellent (99.6% vs. 100%, P > 0.99). One F-CBA-positive patient was classified as non-MG, although in retrospect ocular MG with functional overlay was challenging to exclude. Sensitivity of F-CBA was significantly higher than RIPA (76.7% vs. 72.7%, P = 0.002). Overall, 20/97 (21%) otherwise seronegative MG (SNMG) patients after RIPA evaluation had anti-AChR detected by F-CBA.

Conclusions and Relevance: In our study anti-AChR F-CBA and RIPA both had excellent specificity, while F-CBA had 4% higher sensitivity for MG and detected anti-AChR in 21% of SNMG patients. Our findings indicate that F-CBA is a viable alternative to RIPA for anti-AChR detection. Prospective studies comparing F-CBA, RIPA and L-CBA are needed to determine optimal anti-AChR testing algorithms in MG.

Dopaminergic modulation of a fast visuomotor pathway in Parkinson's disease

M. Gilchrist, R. Kozak, M. Prenger, P. MacDonald, B. Corneil

Importance: This study elucidates the effect of Parkinson's disease (PD) on fast visuomotor responses. Although it is well-known that voluntary movement is impaired in PD, this study demonstrates that fast visuomotor responses are preserved. Further, PD patients are hyper-reflexive and have difficulty modulating fast visuomotor responses compared to healthy controls (HC).

Objective: The objectives of this study are to determine the effect of PD, dopamine (DA) medication, and instruction time on the contextual modulation of express arm responses.

Design: This cross-sectional study includes 10 patients with PD recruited from the Movement Disorder Database at London Health Science Centre (5 males, 5 females, mean age = 67), and 5 healthy age and sex-matched controls recruited from a volunteer database (3 males, 2 females, mean age = 67). The study consisted of one ON session (i.e. PD patients took DA medication as prescribed and HC took single dose of levodopa) and one OFF session (i.e. PD patients refrained from taking DA medication and HC took placebo). Express arm responses, which drive the arm towards a visual target at extremely short latencies (<100ms), were measured with surface electrodes during a reaching task consisting of randomly assorted pro-reach (i.e. reach towards) and anti-reach (i.e. reach away) trials. Contextual modulation of express arm responses was quantified by comparing the magnitude of the response on anti-reach trials to that on pro-reach trials. The trial type (i.e. pro/anti-reach) was indicated by an instructional cue either 500ms or 1000ms before target onset.

Results: PD patients and HC produced express arm responses of equal magnitude (<100ms after target onset), demonstrating the preservation of fast visuomotor response well into disease progression (PD: M = 39.2, SD = 17.5; HC: M = 41.9, SD = 20.3; p = .748). Further, PD patients demonstrated significantly less modulation of express arm responses on anti-reach trials, especially with only 500ms of instruction time, indicating a deficit in suppressing automatic responses in favour of the contextually appropriate response (PD: M = .601, SD = .235; HC: M = .888, SD = .059; p <.001).

Conclusions: Unlike voluntary muscle recruitment, which is delayed and dampened in PD, this study clearly demonstrates fast visuomotor responses are spared by the disease. Additionally, PD patients exhibit hyper-reflexivity in the modulation of express arm responses and cannot modulate the response according to task instruction to the same degree as HC. This study helps us to better understand the effect of PD on different types of movement.

Creation of an Advanced 3D printed Vertebral Model For In Vitro Biomechanical Testing

Johnston, R.B., Jarzem, P.

Importance: Age related changes decrease bone strength. This is particularly striking in osteoporosis, where bone quality and density are significantly degraded. This can affect the biomechanical performance of constructs utilized in spinal instrumentation.

Objective: The purpose of this study is to use 3D printing to create a high-fidelity vertebral model to represent osteoporotic specific mechanical models for benchtop testing of spinal instrumentation.

Design: In order to achieve the aim of a 3D printed high fidelity vertebral model, a generalizable methodology has been developed for creating targeted biomechanical properties. This is applied to model the properties of an osteoporotic L3 vertebra. Firstly, target parameters for biomechanical response are explicitly defined. Subsequently the material properties and performance of the 3D printer are thoroughly explored and an admissible design domain for the fabrication of a micro-architecture lattice structure is determined. Representative points are selected for further investigation throughout the design domain. The mechanical behaviour of the micro-architecture lattice is characterized throughout the design space and is used to create a response surface. The response surface can then be tailored to achieve the targeted biomechanical properties of a high-fidelity biomechanical model.

Results: The methodology was applied to target the biomechanical behaviour of an osteoporotic lumbar vertebra with cortical stiffness of 11 GPa, cortical thickness of 200 microns, and 120 MPa cancellous bone stiffness. Based on the printer characterization, the admissible design domain for a tetrahedron unit cell is determined, and subsequently tested at porosities ranging from 42% to 96% porosity. The elastic modulus is fitted to the relative density with a power law, with an exponent of 1.77 fitting within the expected theoretical bounds for lattice materials. The results of the mechanical characterization are then used to develop a 3D printed vertebral body with equivalent biomechanical properties with a resulting morphology of 459 micron cortical thickness, 72% porosity, and 1000 micron pore size.

Conclusion: This work demonstrates a systematic methodology for creating a targeted high-fidelity 3D printed vertebral body. This model can be used as a basis to understand biomechanical performance and in vitro safety of spinal instrumentation in pathologically osteoporotic vertebra.

Changes in Connectivity after a Single Unprovoked Seizure: an fMRI resting state and movie-driven data study

E. Paredes-Aragon, M Mofrad, A Busch, A Kahn, I Johnsrude, L Muller & S Mirsattari

Importance: A single unprovoked seizure occurs in up to 10% of patients, but does not necessarily develop into epilepsy. It is unclear what determines the susceptibility to develop epilepsy. Although brain network changes have been ascertained in people with epilepsy, this field has not been studied in single seizure patients.

Objectives: In this study, we aimed to explore differences in functional connectivity using resting state fMRI, DTI and movie-driven data to explore potential differences between patients with a single seizure and age and sex matched healthy controls.

Design and Participants: Using 7T resting-state fMRI scanning, and co-registration watching a movie for naturalistic analysis of functional connectivity. Whole brain and limbic, default mode and salience network connectivity were analyzed with graph theory. To identify regions of Interest (ROIs), we implemented an image processing pipeline using shen268 atlas.(6) Whole brain, functional network connectivity (7) and Brodmann cortical areas were analyzed using phase similarity measures and graph theory across the extracted 268 ROIs. The phase similarity measure is computed across pairs of healthy participants (HH) and pairs of patients with a single seizure and healthy participants (HZ). We then used a Wilcoxon signed-rank test to identify functional networks or areas which show significant differences across single seizure and healthy participants.

Results: Ten patients that presented with a single unprovoked seizure and fourteen age- and sexmatched healthy controls were recruited. Baseline characteristics were similar between groups, connectivity at baseline had no differences between groups. Despite the fact that movie-driven analysis did not show a significant difference overall regions, there were significant differences in default mode and Visual I areas as well as Dorsal posterior cingulate cortex (Dorsal PCC). Results of this analysis is explained in Figure 1. Please see attached Figure 2 for image correlation of areas, initially developed by Shen et.al.(7)

Conclusions and Relevance: Functional connectivity is altered in patients with a single unprovoked seizure when compared to controls in the default mode, visual areas and dorsal posterior cingulate region. Changes in these areas may represent key elements involved in a possible increased seizure tendencies to develop epilepsy in the future.

Archetypes of Incomplete Stories in Chronic Illness Health Encounters

W. Koopman, K.LaDonna, S.Venance, C. Watling

Importance: During clinical encounters, patients and practitioners engage in conversations to address health concerns. Because these interactions are time-pressured events, any story exchanged during these encounters will be incomplete in some way, potentially jeopardizing how quality and safe care is delivered.

Objective: In this study, we explored how and why incomplete stories might arise in chronic illness interactions. The research question that guided this study is: How do interactions between patients and health practitioners shape the stories told during clinical encounters?

Design and Participants: A constructivist grounded theory methodology was used to explore how patients and practitioners approach their interactions during encounters. In this two-phase study, we interviewed patients (n=21, 13 neurological diagnoses) and then health practitioners (n=12, 3 neurologists) using a semi structured interview guide. We used constant comparative analysis to identify recurring themes and to develop a conceptual understanding of the process by which stories were rendered incomplete.

Results: We identified three distinct archetypes of incomplete storytelling - the hidden story, the interpreted story, and the tailored story. Hidden stories were guided by a patient's desire for autonomy or impartiality in what treatments may be offered, and practitioners were cued to an incomplete story when data and story were divergent. Interpreted stories were influenced by triadic conversations when family members were present, or synopses were generated by learners to facilitate discussions with colleagues or supervisors. Tailored stories were formed due to perceived time limitations, focusing on sharing or gathering information that was relevant, credible and appropriate.

Conclusion and Relevance: The realities of current health care structures and practices foster incomplete stories. By considering the typologies of hidden, interpreted and tailored stories as red flags for unspoken storylines we may mitigate threats to safe and quality care. But this work challenges us to think about how to strengthen patient-centered communication emphasizing the need to be aware of what goes unsaid in encounters from both sides of the conversation.

Spatiotemporal Dynamics of Neuronal Ensembles in the Primate Prefrontal Cortex during Virtual Reality Navigation Tasks

M. Abbass, R Johnston, B Corrigan, R Gulli, A Sachs, J Lau, J Martinez-Trujillo

Importance: The mechanisms underlying the function of the prefrontal cortex (PFC) at the single neuron level remain to be elucidated. Understanding the spatiotemporal dynamics of information encoded in the PFC has important implications regarding surgical planning, patient counselling and target selection in brain-machine interface research.

Objectives: We recorded from individual neurons in the primate PFC during a virtual reality cognitive task. We sought to determine which task-specific features could be decoded from neural activity in the primate PFC, along with spatiotemporal dynamics this information.

Design and Participants: Two male rhesus macaques (macaca mulatta) were trained to navigate a virtual reality environment using a joystick while learning a context-target association rule. Each session associated a context (steel/wood walls) to a specific colour. We implanted each monkey with two 96-channel Utah arrays (Blackrock Microsystems) in the lateral PFC (areas 9/46 and 8a) to simultaneously record from multiple single neurons. Neuron selectivity was evaluated using a linear regression (alpha = 0.05), and population decoding was performed using a linear support-vector machine with five-fold cross-validation. Mean decoding accuracy with standard error across sessions is presented.

Results: We recorded from 813 single neurons, with 299 (36.8%), 271 (33.3%) and 496 (57.7%) of neurons demonstrating significant selectivity to context, target configuration and chosen side respectively. These features were decoded with a maximum of $73.0 \pm 2.3\%$ (context), $82.0 \pm 2.0\%$ (configuration) and $94.5 \pm 0.7\%$ (chosen side) accuracy. This information was decoded in a sequential manner as the primates made their decision, with context information appearing first, followed by configuration, and then chosen side.

Conclusions and Relevance: We found that different neuronal ensembles encode the elements needed for implementing a cognitive task, and that such ensembles are activated sequentially when required. Regional specificity for different task features needs to be further studied and validated in human subjects. Further characterizing a functional map of the PFC can have implications regarding surgical planning and patient counselling. Additionally, brain-machine-interface systems may benefit by integrating neural data from the PFC, providing salient goal-related information including the content of a goal and its spatial location.

Resting State BOLD Variability in Pediatric Epilepsy: A Marker of Neuroplastic changes?

D. Pur, R. Eagleson, S. de Ribaupierre

Importance: Greater variability of neuronal signalling, measured as the standard deviation of the blood oxygen dependent signal (BOLDSD), relates to information processing capacity. Conversely, aberrant BOLDSD may underlie certain neurodevelopmental disorders.

Objective: Resting-state functional magnetic resonance imaging (rs-fMRI) was used to determine differences in BOLDSD between children with and without epilepsy. We hypothesized that changes in neural processing due to epilepsy lead to measurable variations in BOLDSD patterns, and that these could serve as biomarkers of regional functional integrity.

Design and Participants: We studied 24 controls (12 females, mean age 8.52 ± 1.35 years) and 18 patients (10 females, mean age 11.5 ± 3.4 years) with medically refractory epilepsy that underwent imaging for preoperative planning. Patients were included if they were able to cooperate with the scanning protocol. In addition to T1-weighted scans, rs-fMRIs were acquired while the children were watching a 5-minute animated movie. Standard preprocessing steps (FSL v6.0, FMRIB) were followed (motion correction, normalization, etc.). For each subject, the functional data was divided in 8 blocks, and the standard deviation of the normalized mean of the blocks was used to obtain BOLDSD values for each brain region (n = 90) as defined by AAL atlas. Whole-brain two sample t-tests were used for group comparisons and significance was set at p <0.05 FDR-corrected.

Results: Children with epilepsy showed significantly lower BOLDSD in left inferior and middle temporal gyri (p < 0.001), right caudate nucleus (p < 0.01), cuneus (p < 0.001), and fusiform gyrus (p < 0.001), and significantly increased BOLDSD bilaterally in inferior occipital gyri (p < 0.0001). There were no significant differences when comparing whole-brain BOLDSD values.

Conclusions: Neuroplastic changes in epilepsy may depend on an optimal amount of internal neural variability driven by the identified key regions. Certain temporal and occipital regions may underlie neural processing differences in children with epilepsy. Further studies may correlate these findings with behavioral testing.

Incidence of Intracranial Hemorrhage in Patients with Severe COVID-19 Infections on Extracorporeal Membrane Oxygenation (ECMO): Systematic Review and Meta-Analysis

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Importance: Severe COVID-19 infections can result in acute respiratory distress syndrome (ARDS), requiring admission to the intensive care unit and consideration of extracorporeal membrane oxygenation (ECMO). Intracranial hemorrhage (ICH) is the most common neurological complication in patients on ECMO, and is associated with increased mortality.

Objective: To determine the incidence and nature of intracranial hemorrhage (ICH) in COVID-19 patients on ECMO.

Design and Participants: A systematic literature search of MEDLINE, Embase, and MedRxiv databases from December 1, 2019 to July 31, 2021 was performed to identify studies and pre-print articles that described the incidence of ICH in adult COVID-19 patients on ECMO for respiratory failure. The meta-analysis included all studies with 95% or more of its patients on veno-venous (VV) ECMO. A sensitivity analysis with a pre-determined threshold of 90% or more of its patients on VV-ECMO was also performed. Case reports and case series were reviewed for qualitative analyses.

Results: The meta-analysis included fourteen cohort studies (N = 1605 patients) and the estimated incidence of ICH was 10% (95% confidence interval, 6–16%). There was considerable heterogeneity (I2 = 77%, p <0.01) among the studies. The sensitivity analysis included sixteen cohort studies (N = 1687 patients), and revealed an ICH incidence of 10% (95% confidence interval, 7–15%) with similar between-study heterogeneity (I2 = 74%, p <0.01). Intraparenchymal hemorrhage accounted for 84% of all ICHs. There were several case reports of multifocal hemorrhages and fluid-levels within the hemorrhage. Lobar hemorrhages were more frequently reported than subcortical hemorrhages.

Conclusion: In patients on VV-ECMO, the incidence of ICH in COVID-19 patients was 10%, which is approximately three times greater than the 3.6% incidence reported in patients with ARDS from other causes. Intraparenchymal hemorrhages represent the majority of ICH cases.

Humor processing is affected by Parkinson's disease and levodopa

M. Prenger, K. Van Hedger, K. Seergobin, A. Owen, P. A. MacDonald

Importance: Humor is a complex cognitive phenomenon that promotes social and personal well-being. It is currently unclear whether PD patients experience deficits in the cognitive processing of humor as a result of dopaminergic neurodegeneration or treatment with levodopa.

Objective(s): To determine whether humor processing is disrupted by PD-related neurodegeneration and/or levodopa administration.

Design and Participants: PD patients and age- and sex-matched healthy controls were recruited from the Movement Disorders Database at the Western University for this mixed factorial experimental study. PD patients had been diagnosed by a movement disorders neurologist and treated with levodopa for at least 3 months. All participants were screened for cognitive impairment, major depression/anxiety, and dementia and took part in 2 sessions: ON and OFF levodopa with medication order counterbalanced across participants. PD patients took their prescribed dopaminergic medication (ON) and abstained from their medication for 12-16h (OFF). Controls were administered capsules containing 100mg levodopa (ON) and placebo cornstarch (OFF) in a single-blinded manner. At each session, participants listened to 80 audio clips and were asked to categorize each as either a joke or a non-joke and provide a subjective funniness rating from 0 (not funny at all) to 3 (extremely funny).

Results: Ten PD patients (6 males, M age = 71.3) and 10 healthy controls (5 males, M age = 67.8) participated in this study. Relative to controls (M accuracy = 77.38%, 95% CI [70.79, 83.96]), PD patients more often erroneously categorized non-joke stimuli as jokes (M accuracy = 64.25, 95% CI [57.66, 70.84], p < .001), suggesting that PD-related dopaminergic neurodegeneration might contribute to problems identifying humor. Furthermore, controls found jokes to be less funny while ON levodopa (M rating = 2.13, 95% CI [1.86, 2.41]) compared to OFF levodopa (M rating = 2.27, 95% CI [1.99, 2.54], p = .02), suggesting that dopamine overdose might reduce the rewarding nature of humor.

Conclusions and Relevance: Our results demonstrate that disease-related and medication-induced changes might lead to aberrant humor processing in PD, which could negatively impact quality of life for patients.

Investigating The Effect Of Intratumoral Modulation Therapy On Breast Cancer Brain Metastases

M. Uzelac, A. Deweyert, H. Xu, E. Wong, S. Schmid, M. Hebb

Importance: Brain metastases occur in 10-16% of breast cancer patients, severely impeding the survival of these individuals due to limited treatment options at this stage of cancer. Many types of cancer cells are innately vulnerable to low-intensity, intermediate-frequency electric fields (LIEFs) that do not injure healthy brain tissue.

Objective: Our research group is focused on developing Intratumoral Modulation Therapy (IMT), a promising new treatment that uses bioelectrodes to deliver non-ablative LIEFs directly across tumor affected brain regions to induce tumor cell death. The introduction of electric field-based therapy presents a pivotal advance in the treatment of aggressive primary brain cancers; however, the effect on metastatic brain tumors has not been investigated. The aim of this study is to determine whether patient-derived primary breast cancer brain metastases (BCBM) cells and brain-seeking breast cancer cell lines (MDA-MB-231-BR and MDA-MB-231-BR-HER2) are susceptible to IMT fields.

Design: Metastatic breast cancer cells were cultured in 3D spheroid conditions in wells that were custom adapted with implantable electrodes to distribute electric fields across the tumor cells. Cultures were grouped as control, sham (IMT hardware, but no LIEF delivery), or IMT (LIEFs at 200 kHz frequency using a 4V peak-to-peak amplitude sinusoidal waveform for 72 hours).

Results: There was no difference in the appearance or growth rate between groups before intervention. However, following the 3-day experimental period, the sham group showed consistent growth and invasion into the surroundings while the IMT-treated spheroids had fragmented outgrowths and decreased cell density. Analysis using the MTT colorimetric viability assay revealed that IMT produced a significant reduction (mean=19%, p=0.02) in primary BCBM cell survival compared to the sham condition. Similar results were observed with the cell lines (mean=20%; p=0.02). Bioluminescent imaging of spheroids validated the MTT assay results (Primary cells: mean=70%, p<0.001; Cell lines: mean=66%, p<0.001).

Conclusion and Relevance: To our knowledge, this is the first demonstration of metastatic breast cancer sensitivity to low-intensity electric fields delivered from an implantable stimulation source. The results of this study support further investigations into the potential application of IMT for breast cancer metastasis in the brain.

POSTER PRESENTATIONS

POST-1

Immunotherapy responses of patients with suspected autoimmune-associated epilepsy with negative neural antibody testing

N. ALKhaldi, A. Budhram, J. Burneo, M. Sayed, M. Jones

Importance: in patients with refractory epilepsy with negative neural antibody testing, immunotherapy trials may still be pursued in case of possible autoimmune-associated epilepsy (AAE). The value of immunotherapy trials(IMT) in such patients remains unclear. For this reason, we reviewed the immunotherapy responses of these patients.

Objectives: To identify all patients with a clinical picture of possible (AAE) and with negative antibodies or nonspecific results with low antibodies titer detected in serum and/or cerebrospinal fluid (CSF). Review their outcomes after receiving any of (IMT) options available in the Epilepsy Monitoring Unit (EMU).

Design and participant: Observational retrospective cohort study: no interventions. Review charts of patients admitted to the (EMU) with possible (AAE) but negative antibodies or nonspecific results between 2018 and 2021. We included only those who received any (IMT):(methylprednisolone (IVMP) or immune globulin (IVIg) or plasma exchange (PLEX) or rituximab). Fourteen patients were identified. We considered patients responders when their seizure reduction was ≥ 50%.

Results: 50% (n=7) were female, with a median age of 43.5 years (IQR= 28.75-63.25). All were refractory to ≥ 2 anti-seizure medications. Median age of epilepsy onset was 39.5 years (IQR=23.75-60.25). Median time from epilepsy diagnosis until received immunotherapy was 15.5 months (IQR=12.75 - 21.75). Patients received either IVIG and IVMP (35.7%, n=5) or IVIG alone (28.5%, n=4) or IVIG, IVMP and PLEX (21.4%, n=3) or IVMP alone (7.1%, n=1) or IVIG, IVMP and rituximab (7.1%, n=1). Median follow-up duration was 25 months (IQR=24-31.25). Although non-sustained early immunotherapy responses were common, sustained response to immunotherapy at last follow-up was only observed in 21.4% (n=3). Factors confounding the determination of immunotherapy efficacy were present in all three of these cases (e.g. concurrent changes in ASM, lack of temporal relationship between immunotherapy administration and seizure reduction).

Conclusion & Relevance: Our findings suggest that immunotherapy trials in patients with suspected autoimmune-associated epilepsy but with negative neural antibody testing are largely unsuccessful. This suggests an insufficient therapeutic effect after immunomodulatory treatment or, alternatively, non-immune-mediated mechanisms are causing this type of epilepsy. Critical evaluations of immunotherapy trials in patients with suspected autoimmune-associated epilepsy with negative neural antibody testing are needed.

Characterization of Depression in Fronto-temporal dementia subtypes

R. Ruiz-Garcia, Z. Khazaeipool, S. Pasternak

Importance: Depression is a common syndrome in neurodegenerative disorders. However, descriptions of depression in Frontotemporal dementia (FTD) variants are scarce and have not clearly distinguished depression from apathy, which is highly prevalent in FTD.

Objective(s): To describe the prevalence and clinical features of depression and apathy across FTD variants and describe correlations of depression and apathy with focal brain atrophy patterns.

Design and participants: This retrospective cross-sectional study included participants with possible, probable, or definite behavioral variant FTD (bvFTD), semantic variant PPA (svPPA), and non-fluent variant PPA (nfPPA). Patients with structural brain lesions were excluded. Data extraction was performed through chart review, including demographics, cognitive and behavioral batteries, and depression scales (BDI or GDS). Two blinded raters categorized the atrophy degree of 6 brain regions with a standardized visual scale for FTD using the brain MRI or CT scan that was used to establish the diagnosis. Data were analyzed using chi-square and t-tests.

Results: The total sample included 147 patients meeting inclusion criteria; 81 (57.44%, p=0.492) were males. Of the whole sample,n=82 (55.7%) patients had bvFTD, 34 (23.12%) had svPPA, 25 (17.0%) nfPPA and 6 (4.0%) had a PPA not otherwise specified. There were no significant differences in sociodemographic features. The bvFTD group exhibited higher scores in cognitive batteries compared to PPA groups. FBI total scores were higher in bvFTD group compared with language groups (bvFTD: 36.31, SD 11.31; svPPA: 28.23, SD 14.74; and nfPPA:18.60, SD 13.30, p&It;0.001). The three groups exhibited a similar prevalence of depression. Of bvFTD group 36.1% meet criteria for depression, of svPPA group 36.4% and 33.3% of nfPPA group (X2=1.152, p=0.765). On the other hand, apathy was present in 84.8% of bvFTD patients, in 67.7% of svPPA, and only in 30.4% of nfPPA patients (X2=22.55, p&It;0.001).

Conclusions and Relevance: While apathy was found in a majority of patients with bvFTD and svPPA, depression criteria were also met in one-third of patients (35.5%) in each of the FTD variants. This represents a higher prevalence of depression compared with the general population. Additional analysis will examine correlations between depression and specific brain atrophy patterns.

Quality analysis of stroke thrombectomy outcomes: working versus nonworking hours outcomes from a Canadian comprehensive stroke centre.

M. Bres-Bullrich, S. Aniol, A. Jukes, M. Boulton, R. Kiwan, M. Sharma, M. Mayich, S. Pandey

IMPORTANCE: Mechanical thrombectomy (MT) is a standard treatment in selected acute ischemic stroke (AIS) patients presenting within 24 hours from symptoms onset (SO). Differences in staffing models between regular working hours (WH) and non-working hours (N-WH) can affect the ability to provide timely care and may influence outcomes for patients.

OBJECTIVES: We aimed to determine the impact of a N-WH reduced staffing model on performance metrics and long-term clinical outcomes among patients who underwent MT for AIS at a Canadian Comprehensive Stroke Centre (CCSC).

DESIGN AND PARTICIPANTS: We retrospectively reviewed baseline characteristics of AIS patients undergoing MT at a CCSC (2016/01-2020/04). Patients were categorized into regular WH (8:00 AM to 4:30 PM on weekdays) and N-WH (4:30 PM to 8:00 AM weekdays, statutory holidays, and weekends). The co-primary outcomes were the success of revascularization (TICI) and disability (mRS) at 90 days. Secondary outcomes were presence of intracerebral hemorrhage and MT-related time metrics.

RESULTS: We included 351 patients, mean age 75 [62, 83] years, 42% male, 35% transferred from other centres, 47% received intravenous thrombolysis. Two hundred and twenty patients (63%) were treated in N-WH. The proportion of patients with unsuccessful revascularization (TICI 0–IIa) and unfavourable outcomes (mRS > 3) was significantly higher among patients treated in N-WH (TICI 0-IIa: 22% vs. 13%, p=0.021; mRS > 3: 62% vs. 49%, p=0.0195). Patients treated during N-WH had significantly longer mean time from SO to reperfusion (437 min vs. 416 min, p=0.0176) and CT to groin puncture (83 min vs. 60 min p = 0.0002).

CONCLUSIONS AND RELEVANCE. The present study suggests poorer outcomes and prolonged MT-related time metrics in patients treated with MT in N-WH. Further prospective multicentric studies are needed to fully elucidate the reasons for these increased time points, the impact they play on patient outcomes and the interventions needed to optimize MT workflow and patient care.

Multilingualism as a protective factor against cognitive impairment in multiple sclerosis

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Importance: Cognitive impairment (CI) is common in multiple sclerosis (MS), affecting half of persons with multiple sclerosis (PwMS). Multilingualism has been demonstrated to be a protective factor against CI in Alzheimer's disease (AD), but has never studied in PwMS.

Objective: To explore if multilingualism is a protective factor against CI in PwMS.

Methods: This is a retrospective cohort study of PwMS aged 18-59, with a confirmed diagnosis of relapsing MS, fluent in English, who completed the Minimal Assessment of Cognitive Function in MS (MACFIMS) at the London (ON) MS Clinic. Any PwMS with a history of dementia or developmental delay, daily marijuana use, a major psychiatric disorder, or less than grade 9 education were excluded. We focused on the Brief Visuospatial Memory Test (BVMTR), immediate recall (-IR) and delayed recall (-DR) as it would be the least affected by language, as well as the Symbol Digit Modalities Test (SDMT), as information processing speed is most commonly affected in PwMS. One-way ANOVA was used to compare raw scores on the BVMTR and SDMT between groups (uni- vs. multillingual), while chi-square was used to compare impairment on BVMTR and SDMT between groups.

Results: The cohort consisted of 678 subjects; 73.9% were females, with a mean age of 39.6 (\pm 9.6) years, mean duration of disease of 5.9 (\pm 6.9) years, and mean years of education was 13.9 (\pm 2.2). English was the first language was in 501 subjects (90.6%). 563 subjects were unilingual and 114 were multilingual; 102 subjects were bilingual and 13 subjects fluent in \geq three languages.

There was no significant difference on the BVMT-IR (p=0.195) or BMVT-DR (p=0.100) between groups. Similarly, there was no difference in the number of subjects impaired on the BVMTR-IR (X2 (1, N=678) = 3.167, p=0.057) or BVMT-DR between groups (X2 (1, N=678) = 2.996, p=0.083).

number of subjects impaired on the SDMT between groups (X2 (1, N=678) = 1.023, p=0.312).

Conclusion and relevance: This study shows that multilingualism does not has a protective effect against CI in PwMS and does not play a role in enriching the cognitive reserve, in contrast to studies in Alzheimer's disease This difference may be explained by a different underlying pathological mechanism in these diseases and warrants further study.

Association of comorbid psychiatric features with characteristics and long-term clinical outcomes in psychogenic nonepileptic seizures (PNES)

N. Alkhaldi, D. Dongkyung Kim, Y. Yu, M. Alkhateeb, E. Paredes-Aragon

Importance: Comorbid psychiatric diagnoses are common in patients with psychogenic nonepileptic seizures (PNES), that may also have comorbid epilepsy. Identification of psychiatric features associated with clinical characteristics or outcomes may aid with diagnosis, management & prognosis.

Objective: Examine psychiatric profiles of (PNES) patients with/without comorbid epilepsy to identify possible associated psychiatric features with PNES characteristics and outcomes and their prediction for comorbid epilepsy diagnosis.

Design and Participants: Longitudinal data was reviewed retrospectively of all patients with confirmed PNES admitted to the epilepsy monitoring unit (EMU) at London Health Sciences Centre (LHSC) between (May 2000 -February 2010) with follow-up data collected until September 2015.

Results: 271 subjects were included. Mean age at PNES onset was 36 years (6–89). 73.4% (n=199) were female, mean EEG recording time was 6.1days, median time follow-up was 3.3 years (CI 1.6–6.4) .194 PNES without epilepsy, 30 PNES/possible epilepsy, and 47 PNES/epilepsy.

No significant differences were found between PNES patients with/without confirmed epilepsy, or with possible epilepsy with prevalence of depression, anxiety, physical/emotional/sexual abuse, substance abuse, or suicidal thoughts. Patients with confirmed epilepsy reported other neurological (p=0.007) or comorbid other medical disorder (p=0.006) the least. No differences in the prevalence of psychiatric history in patients with differing durations of PNES spells .(n=130) of all PNES patients were on ASMs,(n=64) were not.Prevalence of anxiety was higher without ASMs(40/64)62.5% compared to those on ASMs (58/130)44.6%,(p=0.02). Patients without ASMs were more likely to have at least two out of three disorders of depression, anxiety, abuse (p= 0.01). At final follow up, 80.5% and 87.5 % PNES only patients were able to discontinue and reduce ASMs respectively. No differences in psychiatric history in patients who were able to decrease/discontinue ASMs and those who couldn't. No psychiatric parameter significantly differentiated those who did or didn't experience PNES spell reduction/resolution except for a positive history of substance abuse.

Conclusions and Relevance: All patients had psychiatric comorbidity. The type of psychiatric comorbidity did not reliably differentiate patients with and without comorbid epilepsy and should not be used to estimate PNES patient's epilepsy risk- duration or frequency of spells, or reduction or cessation of spells.

Efficacy and Safety of Using Standardized size of Stents in Patients with Carotid Artery Stenosis

A. Lahlouh, R. Kiwan, J. Mandzia

Objectives: Carotid artery stenosis causes up to 20% of ischemic strokes. Stenting is used as an alternative to endarterectomy in symptomatic patients. Each commercially available stent offers numerous stent diameters/lengths. Most centers thus carefully match each individual stenosis to a specific stent length/diameter stent size. However, this process can be time consuming and costly while the relative benefit of a custom stent sizing versus one-size-fits-all approach has not been well evaluated yet. We hypothesized that a 'one-size-fits-all' default approach to carotid stenting results in non-inferior results to a customized approach.

Design and Participants: We conducted a descriptive retrospective cohort study on patients who presented to our academic carotid revascularization clinic with symptomatic carotid artery stenosis who underwent carotid artery stenting for peri- and post-procedural carotid artery stenting complications. The primary outcomes were periprocedural (within 24 hours of the procedure) or post procedural (within 30 days of the procedure) TIA, stroke, or death. The secondary outcome was the estimated degree of stenosis on follow up ultrasound performed within 6 months of the procedure.

Results: The complication rate -within the first 24 hours- was 4.5% while that during the first 30 days post-procedure was 6.5%. Age and degree of stenosis on post procedural cerebral angiogram were associated with increased risk of complication. Severe restenosis (>70% or occlusion) was reported in 16.8% of patients within 6 months post-procedure.

Conclusions and Relevance: Our study suggests that using a simplified, one-size-fits-all, approach to carotid stenting results in safe and effective outcomes, suggesting a route to possibly simplify a complex medical procedure.

Abstract cannot be posted online due to embargo policies.

Genetic Frontotemporal Dementia Initiative for Neurodevelopment

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Importance: Frontotemporal dementia (FTD) is a highly heritable and currently incurable progressive neurodegenerative disease with group differences in brain structure between pre-symptomatic mutation carriers and non-carriers. Exploring the pathophysiology of genetic FTD in pre-symptomatic early development has important implications for future therapeutic treatments and optimal timing of interventions.

Objectives: We hypothesize genetic mutations (MAPT, C9orf72, PGRN) causing autosomal dominant FTD have neurodevelopmental effects on brain structure and function that can be detected in youth through structural and functional MRI, developmental history, and behavioural and cognitive assessments.

Design and Participants: We are establishing a novel cohort of youths ages 9-18 who have a 1st or 2nd degree relative with genetic FTD recruited from the Genetic Frontotemporal Dementia Initiative (GENFI) network. This will be a multicenter accelerated longitudinal cohort study with participants completing an MRI along with behavioural and cognitive assessments at enrolment and a 2 year follow up. 120 youth with a family history of genetic FTD will be recruited from 10 centres across Canada and Europe and matched against typically developing children from the NIH ABCD youth neurodevelopmental study (n>11,000) using the same assessment and imaging measures.

Results: Not yet available.

Conclusions and Relevance: We aim to determine if the presence of an FTD genetic mutation, specifically MAPT, C9orf72, PGRN, is associated with measurable neurodevelopmental changes in youth at-risk for genetic FTD. Our results will lay the ground work for optimal timing of future molecular interventions and the conceptualization of FTD as a neurodevelopmental disorder.

Predicting the center of the subthalamic nucleus using anatomical fiducials

A. Taha, G. Gilmore, A. Khan, J. Lau

Importance: Deep brain stimulation (DBS) is a well-established neurosurgical procedure employed to relieve symptoms of a wide variety of movement disorders like Parkinson's disease (PD). A few millimeters in placement of DBS electrodes can make the difference between optimal therapeutic outcomes and side effects.

Objective(s): To develop a machine learning (ML) model that utilizes validated x, y, and z coordinates, known as anatomical fiducials (AFIDs), that can be placed within millimeters of accuracy on structural T1-weighted (T1w) MRI scans to predict the location of the subthalamic nucleus (STN; most common DBS target) center.

Design and Participants: AFIDs were applied via 3DSlicer 4.6 on T1w images of 32 healthy participants (age: 46.2 ± 13.5 years; 12 female) acquired at Western University on a 7-T head-only scanner (Siemens Magnetom; Germany). The "ground truth" STN center was computed from the center of mass of STN segmentations derived from high-resolution T2w scans in this same dataset. X, y, and z coordinates were used as features, after principal component analysis, to predict the STN center. Linear and support vector regression (SVR, linear kernel) models were trained (n=27). Euclidean distances (EDs) between the ground truth and predicted center on testing data (n=5) allowed for combined assessment of x,y,and z models. Accuracy was compared to conventional MCP consensus coordinates (±12, -2, -4) via Wilcoxon rank-sum test (p <0.05). The ML models were also externally validated using a randomly selected subset (n=5) from an independent dataset acquired on a 7-T whole body scanner at Maastricht University (Nova Medical, Wilmington, MA).

Results: Total of 20 STN location predictions were made. EDs from model predictions (using top 3 principal components, ~90% captured variation) on testing and external validation data respectively are: 1) 1.16 ± 0.59 and 1.15 ± 0.41 mm (linear regression) and 2) 1.13 ± 0.59 and 1.54 ± 0.55 mm (SVR). All model predictions were significantly more accurate than MCP consensus predictions.

Conclusions and Relevance: This study demonstrates potential for a new STN-DBS indirect targeting tool, utilizing AFIDs on T1w images alone, with accuracy of approximately 1-1.5 millimeters (superior to MCP coordinate consensus). External validation with PD datasets is ongoing.

Investigating differential effects of oxytocin on improving empathy deficits across structural and functional subtypes of Frontotemporal dementia

S. Yu, L. Oliver, C. Stewart, K. Coleman, J. Kryklywy, R. Bartha, T. Schmitz, E. Duerden, D. Mitchell, E. Finger

Importance: Frontotemporal dementia (FTD) is a progressive neurodegenerative dementia for which the loss of empathy is a key symptom. There are currently no approved treatments for FTD highlighting the urgent need for the development of an effective intervention to address this disruptive symptom causing much social dysfunction and strain on families and caregivers.

Objective(s): To investigate the relationship between structural and functional brain integrity and behavioural response to treatment with oxytocin (OT) in order to determine whether atrophy or dysfunction in specific neural networks may predict symptomatic response to OT.

Design and Participants: A double-blind, placebo-controlled, randomized crossover design study was performed where participants who met diagnostic criteria for FTD underwent two sessions of fMRI facial expression recognition tasks, once following intranasal administration of 72 IU OT and once following placebo saline mist. Participants were recruited from the Cognitive Neurology and Alzheimer Research Centre at Parkwood Hospital in London, Ontario, Canada where 41 individuals met eligibility criteria but 13 declined to participate.

A voxel-by-voxel analysis of the imaging data will be used to classify participants based on patterns of atrophy in the frontal and temporal lobes. Independent component analysis of fMRI data will be used to evaluate patterns of neural activation in networks previously shown to be implicated in socio-emotional skills. Linear regressions will be used to determine if baseline metrics of atrophy in regions of the frontal or temporal lobes and functional connectivity in selected networks predict performance on tasks of facial expression recognition and related empathy measures following OT vs. placebo.

Results: Across the 28 study participants, 15 patients were male, 13 were female, and the mean age was 62.29 (SD = 7.88). Imaging analysis results TBD.

Conclusions and Relevance: Results from this study will help determine whether a specific subset of patients with FTD benefits from administration of OT to enhance emotion expression recognition and improve empathy deficits. With no approved treatments for FTD at the present time, these findings will contribute to our knowledge of how OT may act as an effective intervention addressing a key symptom of FTD.

Development of brain-derived bioscaffolds for neural progenitor cell culture and delivery

J. Terek, L. Flynn

IMPORTANCE: While stem cell-based therapies have been proposed to promote neural tissue regeneration, they face challenges regarding cell survival and fate following transplantation. Three-dimensional (3D) scaffolds fabricated from tissue extracellular matrix (ECM) can be used as an instructive and supportive platform for the culture and delivery of regenerative cell populations within the brain to target tissue damage caused by neurodegenerative disease.

OBJECTIVES: To develop a protocol to decellularize brain tissue and fabricate a novel cell culture platform using the isolated ECM for brain-derived progenitor cells (BDPCs).

STUDY DESIGN: Select decellularization protocols from the literature were tested using porcine brains obtained from a local abattoir, and iteratively optimized to establish an effective detergent-free protocol. Biochemical assays were used to quantify double-stranded DNA (dsDNA), sulphated glycosaminoglycan (sGAG) and hydroxyproline content in both native and decellularized tissues. Spherical microcarrier scaffolds were fabricated from decellularized brain tissue (DBT) and commercially available collagen (COL) via electrospraying techniques. Immunohistochemical staining and compressive mechanical testing were used to characterize the microcarrier composition and stiffness. Ongoing in vitro culture studies are focused on comparing the attachment, growth and neural marker expression of rat BDPCs cultured on the DBT and COL microcarriers under dynamic conditions within spinner flasks.

RESULTS: A novel detergent-free decellularization protocol was established, which effectively removed over >97% of dsDNA from the native tissue while preserving GAGs and collagen. Electrospraying techniques were successfully applied to generate soft and compliant spherical microcarriers, which were stable without chemical crosslinking or other additives. The microcarriers incorporating DBT contained a broader range of collagen types, as well as significantly higher amounts of sGAG. Initial culture studies confirmed successful attachment and expansion of the rat BDPCs on the ECM-derived microcarriers.

CONCLUSIONS AND RELEVANCE: Brain ECM can be successfully isolated using the newly established detergent-free decellularization protocol. Validation with porcine brains showed that the protocol removed >97% of dsDNA while retaining a complex ECM composition including GAGs, collagen and fibronectin. The natural cell-instructive properties of the ECM can be harnessed in the fabrication of microcarrier scaffolds, which hold promise as tissue-specific cell culture and delivery platforms to direct neural progenitor cell phenotype and function.

Usefulness of language mapping during cortical stimulation for presurgical planning in Stereo-encephalography

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Background: Language determination is a pivotal part of presurgical investigations. Presurgical cortical stimulation (CS) with language mapping (LM) in patients with intracranial recordings (SEEG) is a growing practice in some Comprehensive Epilepsy Centers.

Methods: This retrospective study, single center study included patients implanted with SEEG that underwent CS for LM in our Epilepsy Monitoring Unit. We describe frequencies, demographic characteristics of these patients and whether or not CS with LM was useful.

Results: From January 2015 to June2021, a total of 177 patients were implanted with SEEG and analyzed. 95 patients had CS and 44 of these had CS with LM. The mean age was 33 (Ranging from 15-70). During LM, anomia was induced in 26 (58%), speech arrest in 22 (49%), paraphasic errors in 13 (29%), and hesitation in 9 (20%). LM results were recorded as influencing surgical decision in 7 (16%) patients, 4 (9%) did not undergo surgery due to expected language deficits and 3 (7%) proceeded with surgery due to an acceptable risk of language deficit.

Conclusions: Cortical stimulation language mapping is useful for decision-making in presurgical evaluation and should be encouraged whenever involvement of language is suspected when determining the epileptogenic zone.

After-discharges and Interictal epileptic discharges in epilepsy patients who underwent intracranial recording may help predict post-operative outcomes

A. Asim, M. McShane and E. Parades

Importance: Characteristics of after-discharges (AD) and interictal discharges (IED) in epilepsy patients may predict post-operative outcomes

Objective(s): Primary objective: To investigate whether AD morphology helps predict post-operative outcomes measured with the Engel scale.

Secondary objective: To investigate whether frequency of IEDs predict post operative outcomes measured with Engel score

Design and Participants: This is a retrospective study analyzing the data of all patients with drug-resistant-epilepsy who underwent presurgical cortical stimulation mapping using stereoelectroencephalography (SEEG) at LHSC from 2015-2021.

Results: From January 2015 to June 2021, a total of 177 patients were implanted with SEEG out of which 95 (46 males and 49 females, mean age 33 (ranged between 15-70)) underwent cortical stimulation. All 95 patients showed IEDs, however, 88 patients showed ADs upon stimulation. The results below are for the 54 (27 males and 27 females) patients who showed ADs and IED and underwent epileptic surgery.

Aside from 4 patients in whom morphology data was missing, the most common AD morphology observed was spike-waves (n = 14; 28%) followed by polyspike burst (n = 13; 26%), sequential spikes (n = 10; 20%), rhythmic waves evolving into spikes (n = 9; 18%), and lastly rhythmic waves (n = 3; 6%). Those patients with the spike-wave morphology were more likely to have an Engel class I outcome 12/14 (86%) while 1/15 (7%).

Interictal discharges were assessed to be either mild, moderate, or abundant. Most patients had abundant IEDs (n = 49; 91%). Among these patients, 31 (63%) had Engel class I outcome, 7 (14%) had Engel class II outcome, 3 (6%) had Engel class III outcome, and 7 (14%) had Engel class IV outcome.

Conclusions and Relevance: The most common AD morphology observed was spike waves in 14 (28%) of the patients. Those with this morphology were more likely to fall under the Engel class 1 outcome post surgical resection. Patients with abundant IEDs were most likely to have an Engel class I outcome post-surgery 31 (63%). The relevance of these findings is that they can be used to predict patient outcomes post-surgery, however, additional samples and more analysis needs to be conducted prior to clinical application of these findings.

Insights from the New-Onset Refractory Status Epilepticus (NORSE/FIRES) Family Registry

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Importance: The New-Onset Refractory Status Epilepticus (NORSE) and Febrile Infection-Related Epilepsy Syndrome (FIRES) Family Registry contributes to an international and systematic effort to examine past medical history, outcomes, and quality of life for people affected by NORSE/FIRES.

Objectives: The objective of the NORSE/FIRES Family Registry is to 1) provide an accessible and internationally available registry into which survivors and surrogates of NORSE/FIRES can enter data into a systematic and rigorous research study, and (2) examine possible risk factors for NORSE/FIRES, assess the spectrum of clinical outcomes, and to better understand the quality of life of survivors for this rare and understudied disease.

Design and Participants: This registry uses REDCap, a web-based database. People permitted to access the registry include survivors, substitute decision makers (for survivors or non-survivors) and physicians. Information collected in this longitudinal cohort study includes past medical history, clinical presentation, disease course, survivorship, clinical sequelae and quality of life, among others. Participants are invited to complete follow-up surveys for up to two years following clinical presentation of seizures. 65% of participants currently enrolled in this study have completed study procedures. Enrollment is ongoing in English, French, and Spanish, and Mandarin and will remain open until 2025.

Results: To date, 58 participants have enrolled in this study (2-78 years, median: 13.5, IQR: 21.5, 21 females and 37 males) from 12 different countries across 5 continents. 36/58 participants are survivors of NORSE/FIRES. At > 6 months after the onset of NORSE/FIRES, survivors experience a mean of >12 seizures per month and remain on a median of 4 (IQR: 2) anti-seizure medications. The median self-reported quality of life amongst all survivors was scored as 4/10 (IQR: 3) and overall intellectual function was rated as 6/10 (IQR: 2.5).

Conclusions and relevance: Preliminary results suggest that survivors of NORSE/FIRES have a high seizure burden and poor quality of life. We hope that this registry will allow for the collection of a wide range of clinical and epidemiological variables which will provide a stepping-stone for future systematic research. The NORSE/FIRES Family Registry is generously supported by the Robert N. Kohn Research Memorial Fund.

Impact of the energy distribution of Interictal epileptiform spikes in mesial temporal lobe epilepsy as a classification tool

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Importance: Interictal spikes (IISs) are known as biomarkers used in the identification of epileptogenic zone (EZ) in focal epilepsy. The quantitative analysis of their morphology using energy has not been deeply investigated to assist in surgical decision and improve surgical outcomes.

Objective(s): To investigate the relationship between the prominence of IISs and their spatial distribution relative to brain lobes and hemispheres using energy.

Design and Participants: From the 80 patients with medically intractable epilepsy (MIE) implanted with depth electrodes (DE), at Western Epilepsy Program, we selected two patients for the analysis. These patients have history of MIE, with the suspicion of temporal epilepsy. We analyzed intracranial recordings exclusively from DE implanted on anterior and posterior hippocampus, left or right. The sampling rate of the recordings was at 2048 Hz. Each waveform's power across all detected spikes were computed and clustered based on their energy distributions. The statistical properties of these spikes and the best-fit distributions were calculated for hippocampus electrodes. The algorithm discriminates these spikes based on their energy waveform distributions based on the electrode's locations. Our algorithm calculates spike waveform energy information in anterior vs posterior and left vs right using Akaike information criterion (AIC) and Loglikelihood criteria.

Results: Data included eight, 24-hour session extracellular recordings from two patients with MIE and history of bitemporal lobe epilepsy. More than 210 hours were extracted from four hippocampus electrodes: anterior, posterior, and left/right. Results indicate that detected spikes on the hippocampus contacts in the left hemisphere are significantly different in anterior than posterior and in each hemisphere. We performed the parametric Kolmogorov-Smirnov test to assess statistical significance; a value of P<0.05 was considered statistically significant. The algorithm uses spatiotemporal characteristics of detected spikes before and after, classifies them based on energy waveform's information, and differentiates them using AIC and Loglikelihood estimators.

Conclusion and Relevance: Our algorithm successfully distinguished IISs in the hippocampus MIE implanted in epilepsy patients and calculates individual electrode's contact information for all detected IIS types. Further analysis will have direct applications in localizing the EZ.

Evidence of a first structural MRI diagnostic biomarker for PD: Surface measures of sub-regions of striatum identify very early-staged PD patients with high accuracy in multicentered data

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Importance: Parkinson's disease (PD) is a neurodegenerative illness that has no diagnostic tests, cures or disease-modifying therapies. PD diagnosis is complex, relying on specialist assessments.

Objective: Using MRI, we parcellated the striatum into sub-regions, allowing us to isolate areas that are first, most, and invariably affected in PD. Extracting MRI measures of connectivity and shape, and using machine learning, we aimed to develop an accurate MRI diagnostic biomarker in very early PD.

Design and Participants: 3T diffusion and T1w MRI data of 100 PD patients (unmedicated, scanned <6months since diagnosis) and 52 healthy controls were obtained from the Parkinson's Progression Markers Initiative. We parcellated the striatum into 7 sub-regions per hemisphere using probabilistic tractography and connectivity to cortical regions. Measures of connectivity (i.e., fractional anisotropy, mean diffusivity, cortical connectivity), volume, and shape (i.e., surface area and surface displacements relative to age-matched norm) were extracted for separate striatal sub-regions. A classifier was trained on data from 80% of PD and control participants. The model was subsequently tested on the remaining 20% hold-out data. Further, we validated our model in an entirely independent dataset of 20 PD [medicated, mean 2.3years-since-diagnosis (SEM)] and 20 healthy controls scanned at Western. Area under the receiver operating characteristic curves (AUC-ROCs) were used to classify individual participants.

Results: Our model distinguished PD patients from healthy controls with 95% AUC-ROC accuracy. The validation accuracy in Western dataset was also 95%. Surface displacement and surface area in caudal motor and executive striatum were most relevant for successful classification.

Conclusions and Relevance: We present a first semi-automated diagnostic biomarker of PD, using only structural and diffusion MRI, common sequences, allowing ready translation to PD research and practice. We achieve 95% classification accuracy at the single-subject level even in very-early unmedicated and medicated PD patients. An MRI diagnostic biomarker would transform PD research and practice. Accurate recruitment enhances power of clinical trials. More important, an easily accessible and highly accurate diagnostic test empowers generalists to care for PD patients, relieving specialists who are already outpaced, even ahead of an anticipated sharp rise in PD prevalence.

Association of outdoor air and noise pollution exposure with seizure risk: A systematic review and meta-analysis

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Importance: Some seizures can be prevented by avoiding known triggers, such as stress and sleep deprivation. If exposure to air or noise pollution increases seizure risk, patients with epilepsy may be able to prevent seizures by avoiding these exposures.

Objective: To systematically synthesize the evidence examining whether exposure to outdoor air and noise pollution is associated with seizure risk.

Design and Participants: We searched EMBASE, MEDLINE, SCOPUS, Web of Science, BIOSIS Previews, LILACS, Proquest Dissertations and Theses, conference abstracts, and the grey literature in January 2022 using terms representing air and noise pollution and seizures. Observational and ecological studies were included if they examined the effect of outdoor air or noise pollution on the risk of unprovoked seizures in humans. The risk of bias will be assessed using the Risk of Bias Assessment Instrument for Systematic Reviews Informing WHO Global Air Quality Guidelines. The characteristics and findings of the included studies were summarized descriptively, and a meta-analysis will also be conducted.

Results: We screened the titles and abstracts of 4881 citations, retrieving 46 articles for full-text screening, with ten included in the review. The studies were conducted in Asia (n=6), North America (n=2), South America (n=1), and Australia (n=1). One study estimated the effect of a period of higher air pollution relative to periods of typical air pollution and reported that it increased seizure risk. The other nine studies estimated the effect of one or more specific air pollutants, but only seven clearly reported the results of a multivariable analysis. The effect of PM10, SO2, and NO2 was reported in all seven studies, CO in six, and PM2.5 and O3 in five. PM2.5 and PM10 significantly increased seizure risk in one study, SO2 in two studies, and O3 in one. NO2 and CO significantly increased risk in three studies and decreased risk in another. None of the included studies estimated the effect of general or source-specific noise pollution.

Conclusions and Relevance: Evidence suggesting that air pollution affects seizure risk is inconsistent, and research on the effect of noise pollution was not identified. Additional research is necessary to elucidate their effects.

Funding: Lawson Health Research Institute's Internal Research Fund; Schulich School of Medicine & Dentistry's Collaborative Research Seed Grant; Jack Cowin Endowed Chair in Epilepsy Research at Western University; Government of Ontario's Ontario Graduate Scholarship; and Western University's Western Graduate Research Scholarship.

Post-surgical depression and suicide in patients with temporal lobe epilepsy: A systematic review

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Importance: Epilepsy is associated with a high rate of psychiatric comorbidities, including depression and suicide, which contribute to the illness burden of patients with temporal lobe epilepsy (TLE).

Objectives: The purpose of this systematic review was to synthesize existing literature assessing the effect of TLE surgery on (1) depression prevalence, (2) depression severity, (3) the incidence of de novo depression, and (4) the incidence of attempted and completed suicide post-operatively.

Design: A search of the literature was conducted using Ovid Medline, Embase, Clarivate Web of Science, Cochrane Library, and ProQuest Dissertations and Theses. Studies were included of patients with TLE who underwent TLE surgery and that reported outcomes of: pre- and post-operative depression prevalence or severity, the incidence of post-operative de novo depression, or the incidence of post-operative attempted or completed suicide.

Results: The literature search yielded 2,127 records related to TLE surgery and post-operative depression or suicide. After review of 116 relevant full-length articles, 18 articles met the final eligibility criteria. Compared with the pre-operative period, the majority of studies reported a reduced or similar prevalence (n=12) and severity of depression (n=5) after TLE surgery. The incidence of post-operative de novo depression (n=11) ranged from 0% to 38% over follow-up times ranging from three months to nine years. The incidence of attempted or completed suicide (n=4) ranged from 0% to 3% over follow-up times of one to four years after TLE surgery.

Conclusions and Relevance: The effect of TLE surgery on depression and suicide remains complex. Although most results did not show an increase in depression prevalence or severity post-operatively, many studies did not assess the statistical significance of changes in depression prevalence or severity after TLE surgery. Appropriate psychosocial follow-up for patients after TLE surgery should be considered given the potential risk of exacerbating depression symptoms, the risk of de novo depression, and suicide after TLE surgery. Future studies in this patient population are needed to improve understanding of the effect of TLE surgery on the prevalence and severity of depression and the incidence of de novo depression and suicide after TLE surgery.

Translation of microsurgical skills from simulation training to the operating room

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Importance: Microsurgical skills are inherent in many neurosurgical procedures. Therefore, it is prudent to provide neurosurgical residents with opportunities to practice these skills.

Objective: The objective was to investigate whether participation in a live rat femoral artery model simulation translated to improved performance in the operating room in neurosurgical procedures.

Design and Participants: We looked at the operative evaluation forms for different neurosurgical procedures for 11 residents in PGY5 who participated in the rat simulation, 11 residents in PGY6 who participated in the simulation, 3 residents in PGY5 who did not participate in the simulation and 3 residents in PGY6 who did not participate in the simulation. Each resident was evaluated on superficial exposure, deep exposure, and primary maneuvers for each operative case. Residents were marked as being unable to, being able to do the step supervised, or being able to do the step independently. A chisquared test was used to compare the performance of those who did and did not participate in the simulation in each PGY year (PGY5 and PGY6).

Results: Within the PGY5 year, more operative evaluation forms marked residents being able to superficially expose independently within the group who participated in the simulation compared to those who did not (p=0.003). This was not the case for deep exposure or primary case maneuvers. Within the PGY6 year, more residents who did participate in the simulation were able to conduct deep exposure and primary maneuvers independently compared to those who did not partake in the simulation (p=0.007 for deep exposure, p=0.00057 for primary maneuvers). This was not seen for superficial exposure.

Conclusions: Participating in simulations may provide some benefit to residents and translate into better performance in the operating room. These could provide residents with more opportunity to practice microsurgical skills outside of the operating room. More study is required to establish whether participation in simulation training for microsurgical skills translates into better performance in the operating room for neurosurgical cases.

Feasibility of retrospective EEG research focused on critically ill children in an academic tertiary care children's hospital

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Importance: Continuous electroencephalography (CEEG) is a valuable and increasingly utilized resource in pediatric critical care. Analysis of CEEG utilization and yield can provide important insights regarding judicious use of CEEG, and can help recognize and mitigate barriers to EEG access for critically ill children.

Objectives:

- 1. Discuss feasibility and challenges in the retrospective review of CEEG data.
- 2. Develop recommendations on standardized recording, review and storage of continuous EEG data.

Design and Participants: Before pursuing a retrospective cohort study evaluating utilization and yield of CEEG in children admitted to the pediatric critical care unit (PCCU), we wanted to evaluate the feasibility of this research. After collating the list of all patients who had undergone EEG monitoring between January 1st, 2016, to December 31st, 2020 in the PCCU, we evaluated if our study information could be found in electronic medical records (PowerChart, Natus Neuroworks database, PACS, etc.) and paper charts. We conducted meetings with stakeholders (neurologist & PCCU physician) to review feasibility data and discuss potential solutions to overcome some of these barriers.

Results: We found that 429 EEGs were performed in the PCCU during this period and 30 could be excluded. The total EEG recording duration was rarely specified and could not be reliably inferred from any source, including the Natus EEG archive files and EEG reports. This is because continuous EEG recordings are routinely "trimmed", but not standardized. Some recordings labelled 'Routine EEG' were actually continuous and were likely initiated as a routine (20 min) EEG and converted to a continuous EEG (based on clinical/EEG abnormalities). Of the 399 EEG reports, 80 documented electrographic seizures (ESz) detection among 42 different patients. Clinical history documentation was available, but confirmation of management changes based on CEEG was deficient.

Conclusions and Relevance: This study identifies several barriers to retrospective CEEG research in our institution. It is likely that these or similar issues exist in other centers with limited EEG resources. This affects our ability to calculate ESz detection latency and burden, while limiting a systematic analysis of early recording features. We recommend that institutions consider standardizing EEG report formats, improve clinical documentation detailing EEG-based management changes, and eliminate/standardize CEEG "trimming" practices.

The LHSC/Western Brain Tumour Tissue Bank: A Global Resource

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Importance: A brain tumour tissue bank can serve as an important source of tissue for neuro-oncology research. The LHSC/Western Brain Tumour Tissue Bank (BTTB) provides high-quality brain tumour tissue specimens that are used globally for neuro-oncology research.

Objectives: The LHSC/Western Brain Tumour Tissue Bank was established approximately 35 years ago. The objectives of this study were to: 1) establish an up-to-date accounting of the brain tumour specimens in the BTTB; 2) compare the quality control measures used to assess specimen quality against those used in other comparable tissue banks; 3) determine the scope of tissue distribution globally.

Design: The records of the BTTB were reviewed with the assistance of the BTTB co-ordinator. Number and type of brain tumour specimens were recorded. The quality control measures used in the BTTB were compared to those published in the literature. The location of laboratories to which brain tumour tissue had been distributed was determined.

Results: Since 1995 there have been 1536 adult brain tumour specimens collected in the BTTB. There are approximately 3 vials per case, not including paraffin blocks. This includes 713 primary intra-axial central nervous system (CNS) tumours, 229 meningeal tumours and 285 metastatic tumours. Since 1995 there have been 223 pediatric brain tumour specimens collected in the BTTB. This includes 53 pilocytic astrocytomas, 32 medulloblastomas and 27 ependymomas. The quality control measures used in the BTTB appear to exceed those used by other brain tumour tissue banks as determined by literature review. The BTTB has sent tissue specimens to neuro-oncology laboratories around the globe and numerous publications have resulted from experiments using the brain tumour tissue supplied by the BTTB.

Conclusions: The LHSC/Western Brain Tumour Tissue Bank has collected a large and diverse number of high quality brain tumour specimens since its founding. It serves as a global resource, and the supplied tissue has led to many research publications in neuro-oncology.

Endovascular Treatment of Ruptured Intracranial Infectious Aneurysms

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Importance: Ruptured Intracranial Infected Aneurysms (IIAs) are relatively rare, but they portend high mortality. To our knowledge, there are no Canadian case-series on IIA, as well there is a relative paucity of international published experiences.

Objectives:

- 1. To share the experience of a single Canadian tertiary centre in managing ruptured IIA
- 2. To conduct a systematic review of literature of the last 10 years.

Design and participants: We did a retrospective case review series of adult patients with ruptured IIA treated at our institution. Secondly, we conducted a systematic review of literature on ruptured IIA between 2011-2021 inclusive.

Results: At our institution, of a total 8 cases with ruptured IIA, 4 were treated endovascularly and 2 by surgical bypass. For the systematic review, we included 9 non-comparative studies with a total of 509 patients (318 males) and at least 437 ruptured IIA aneurysms. Favourable outcome was specified for 63.3% of patients (n=57). Regarding ruptured IIA, favourable clinical outcome was described in 59.3% (n=16).

Conclusion: This study highlights a single Canadian tertiary centre experience in the management of IIA and compares it to the global trends of the last 10 years in a systematic review.

Predictors of management decisions for subdural hematomas

E Toyota, D Steven

Importance: Subdural hematomas (SDHs) are one of the most common pathologies in neurosurgery and are increasing in incidence. Consistent guidelines on management—observation versus early operative evacuation—are lacking, leading to variations in practice patterns.

Objective: To characterize the incidence of SDHs presenting to community hospitals in southwestern Ontario and identify what influences a surgeon's decision to transfer patients to a tertiary care centre.

Design and Participants: All outside calls to adult neurosurgery in London via OneNumber between July 2020 and June 2021 will be screened for patients with subdural hematomas. Demographic data, exam findings, and neuroimaging features will be compared between patients who were managed in the community and those who were transferred to LHSC for further treatment to determine significant predictors of management strategies.

Results: Data collection is currently undergoing. Preliminary analysis of 100 outside calls identified 33 patients with SDHs. Nine of 9 patients with symptomatic lesions and 1 additional patient who was neurologically intact were transferred to London. All 23 patients with asymptomatic SDHs were monitored in the community setting.

Conclusions & Relevance: Neurologic status at presentation has a strong influence on how patients with SDHs are managed. Subsequent analyses will characterize the role of hematoma chronology and thickness on management. This study will assist junior neurosurgical residents in decision-making on the management of SDHs.

Canadian use of Marijuana Post-Legalization Among Patients with Epilepsy

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Importance: Marijuana has long been used as an alternative treatment for epilepsy and the adverse effects of anti-seizure medications and it has become increasingly mainstream since Canadian legalization in 2018. However, data is lacking on marijuana's benefits and prevalence, while usage among epilepsy patients is growing.

Objective: This study aims to evaluate marijuana usage in patients with epilepsy.

Design and Participants: We conducted a Canadian cross-sectional survey investigating usage and perceptions of marijuana in patients suffering from epilepsy. 264 surveys were completed by patients (n=219;83.3%) or their caregivers (n=44;16.7%).

Results: The mean respondent's age was 32.4(IQR=24-39) and 74.2%(n=193) were female. 23.4(n=61) are on disability and 48.5%(n=126) have been experiencing spells for >10 years. Spell frequency <1 per month (n=104;40.2%) and generalized epilepsy (n=139;55.4%) were most common. 76.0%(n=200) of participants have used marijuana and 44.5%(n=73) use marijuana for their epilepsy. However, 55.2%(n=90) started using marijuana before their epilepsy was diagnosed. 40.4%(n=65) use marijuana multiple times per day. Most consume cannabis products in the evening (n=108;69.7%), amount used has a median of 5g per week (IQR=0.5-10) and smoking is the most used method of consumption (33.5%, n=54). 65.4%(n=100) of users feel more comfortable using marijuana compared to other pharmaceuticals because it is "natural", but 40.6%(n=63) had some type of side effect, including impaired thinking. 80.3%(n=126) of users and 70.5%(n=43) of non-users believe that there is stigma towards marijuana users. Among all respondents, 71.6%(n=156) report stigma lessening since legalization. 78.8%(n=126) of marijuana users have discussed their usage with their doctor. In addition, 53.8%(n=84) reported no change in their marijuana usage after legalization.

Conclusions and Relevance: Marijuana use among epilepsy patients is a controversial subject, increasingly discussed in Canada since legalization. Our study shows a high prevalence of epilepsy patients using marijuana. Healthcare providers should provide appropriate counselling on the benefits and limitations.

The Role of BOLD Signal Variability in Pediatrics: A Systematic Review with a Focus on Potential Clinical Applications

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Importance: BOLD signal variability is intra-individual variation in the functional magnetic resonance imaging signal and is often correlated with cognitive functioning metrics such as neural flexibility. Given the present knowledge of BOLD signal variability's behavior during aging, pediatric BOLD signal variability may be vital to new advances in understanding neurodevelopment.

Objectives: To identify and characterize the types of BOLD signal variability metrics used in studies including pediatric populations, and to identify common associations trends and outcomes involving BOLD signal variability.

Design and Participants: A systematic review of the literature was conducted. Inclusion criteria were restricted to articles that were quantified using any metric of BOLD signal variability and possessed individuals under the age of 18 within the study population. The definition of BOLD signal variability was any measure of intra-individual variability that measured the BOLD response. 5 Databases were searched: Psychinfo, Healthstar, Medline, Embase, and Scopus on January 10, 2022.

Results: 17 cross-sectional studies including both male and female pediatric participants were included. A total of 8 studies quantified variability as the amount of deviation from average BOLD signal activation, 7 used complexity-based metrics, 3 used correlational measures of variability, and 1 used variation of the hemodynamic response function. In total, 10 methods of quantifying the BOLD signal's variability were identified. Although outcomes vary widely between different studies, associations and trends in BOLD variability were commonly found with age, factors specific to a mental or neurological disorder, performance or activity during psychological and behavioral tasks, changes in brain structure, or changes in regional variability.

Conclusions and Relevance: Establishing trends in how the BOLD signal changes with age across various conditions may lead to establishing developmental milestones in defined pediatric populations. It also may lead to the potential use of BOLD variability as a biomarker of symptom severity or a risk factor of mental disorders. However, studies identified were prone to bias due to their methods being primarily cross-sectional. Studies that establish clinical trends and a low risk of bias will need to be conducted before clinical applications BOLD signal variability can be properly utilized by physicians.

Quality of Life in Elderly Epilepsy Patients implanted with Vagus Nerve Stimulators

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Importance: Older epilepsy patients are a fragile group with higher risk of comorbidities and at times, less tolerant to anti-seizure medications (ASM). Many of these patients are medically resistant (MR) to ASM and other treatments are required and there is a lack of understanding regarding how improvement of seizures could have an improvement on their quality of life.

Objectives: The goal of this study is to analyze the rates of quality of life(QOL) and how they relate to seizure frequency in MR elderly patients who undergo VNS implantation.

Design and Participants: We interrogated the database of the Epilepsy Program, Western University. We selected MR patients ages 50 or older who were implanted with VNS and who had completed QOLIE-10 questionnaires prior to implantation as well as 6 and 12 months after.

Results: Results from 7 MR elderly patients with VNS were analyzed. The participants' mean age was 56.4 (IQR= 62-52) and 57.1%(n=4) were male. Prior to surgery, patients had tried a mean of 7.5 (n=7) ASM (IQR=10-6). The most common type of seizures were generalized tonic clonic in 57.1% (n=4) and focal with impaired awareness in 57.1%(n=4). The mean frequency of seizures was 6.8per month (IQR=16-4). The mean QOLIE-10 score for patients was 3.1 (n=6) (IQR=3.54-2.63). When asked how afraid they were of having a seizure in the next 4 weeks, 33% (n=2) reported that they were "very afraid". 16% (n=1) of patients reported that their epilepsy-related QOL distresses them overall "very much". After VNS implantation, no major side effects were reported and only 40%(n=2) had mild side effects including coughing and choking sensation. The mean frequency of seizures at 6 months was 0.5 per month and 50% (n=2) were seizure-free. The mean QOLIE-10 score 6 months after surgery was 3.63 (n=3) (IQR=4.27-2.45).

Conclusions and Relevance: Low rates of QOL are common among elderly patients with MRE. VNS is safe in the elderly population with mild side effects. However, there is no data regarding how the VNS can impact the QOL in that population.

Impact of VNS in Quality of Sleep in Patients with Medically Resistant Epilepsy

J. Seth, G. Couper, G. Burneo, A. Suller

Importance: Vagus Nerve Stimulation (VNS) is a relatively common treatment used in patients with medically resistant epilepsy. However, the impact of VNS on quality of sleep of epileptic patients is very limited.

Objective: The objective of this systemic review is to evaluate the current evidence surrounding the effects of VNS on the quality of sleep of patients with epilepsy.

Methods: A systematic review followed the PRISMA protocol. A database analysis was conducted on Medline, Embase, and Cochrane to find studies that examined the effect of VNS on the quality of sleep of patients with medically resistant epilepsy. The search terms used an adapted for each database were as follows: (VNS OR Vagus Nerve Stimulation OR Neuromodulation) AND (epilepsy or epilepsies OR epileptic OR seizures) AND (Quality of Sleep). Only studies published from January 1, 2001 to December 30, 2020 were included. The studies included were randomized clinical trials, case studies or reports, cohort studies and systematic reviews. Abstraction of data was completed by two members of the team using Covidence.

Results: A total of 75 papers were reviewed and 16 studies from eight countries were included in the analysis. A total of 93 patients with ages ranged from 10 – 49 were included in the analysis of VNS and sleep quality. 51 patients aged 12 – 40 were included in the analysis of VNS and obstructive sleep apnea (OSA). Analyzing the change in the quality of sleep after VNS was evaluated using the Multiple Sleep Latency Test. The literature showed that at low stimulus intensities, VNS treatment improves daytime sleepiness in patients. However, VNS setting titration has a dose-dependent effect on OSA where higher VNS frequencies are related to higher apnea events.

Conclusions: Since seizure control is closely linked to the quality of sleep, it is advisable for clinicians to evaluate patient specific sleep parameters while considering VNS as an adjuvant therapy for patients with medically resistant epilepsy. Limited data is available on the impact of VNS on quality of sleep. Further studies are required to evaluate the improvement of sleep in patients with VNS.

Predicting outcome of patients with psychogenic non-epileptic seizures with confirmed or probable concomitant epilepsy

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Importance: This study is clinically significant in the context of PNES, where ASMs confer the possibility of physiological side effects and toxicity unless otherwise indicated for other co-morbidities such as epilepsy.

Objective: To examine predictors of ASM reduction and discontinuation, and PNES spell reduction and resolution in PNES patients with confirmed or strong suspicion of co-morbid ES.

Methods: A retrospective analysis of 271 newly diagnosed PNES patients admitted to the EMU between May 2000 and April 2008, with follow-up clinical data collected until September 2015. 47 patients met our criteria of PNES with either confirmed or strong suspicion of ES.

Results: Patients who did not have a reduction in spell frequency had much more documented generalized seizures (47.8 vs 8.7%), while those with reduction in spell frequency were borderline more likely to have focal seizures (78.3% vs 52.2%) and significantly more likely to have come off all ASMs by the time of final follow-up (21.7 vs. 0.0%). In terms of demographic differences between patients that reduced their ASMs (n=18) and those that did not (n=27), the former were more likely to have neurological co-morbid disorders (p=0.004). Similarly, they had more unknown (non-generalized, non-focal) seizures (33.3 vs 3.7%). Additionally, patients who reduced their ASMs by final follow-up experienced much higher rates of PNES resolution and PNES spell frequency reduction. On hierarchical regression analysis, higher level of education and absence of generalized seizures remain as positive predictors of PNES spell reduction (p=0.042, 0.015), while presence of some other neurological disorder besides epilepsy (p = 0.04) and being on more ASMs at EMU admission (p = 0.03) were positive predictors of ASM reduction by final follow-up.

Conclusions and relevance: PNES patients with either confirmed or strong suspicion of ES have distinct demographic predictors of PNES spell frequency and ASM reduction by final follow-up. The positive relationship between reduction in PNES spell frequency and discontinuation of ASMs at final follow-up elucidates that tapering medication in a safe environment may reinforce PNES diagnosis and absence of comorbid ES in both patients and physicians, resulting in the observed improvement at final follow-up.

Regional Epilepsy: Case Description and Literature Review

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Importance: The classification system for epilepsy is primarily based on the spatial distribution of the seizure onset zone (SOZ). Accurate classification of epilepsy is vital for determining the best approach for the treatment and ascertaining prognosis.

Objective(s): The objective of this study is to develop a holistic understanding of the characteristics regarding the novel phenomenon of regional epilepsy (RE) by assessing a case report and comparing the findings to previous RE reports.

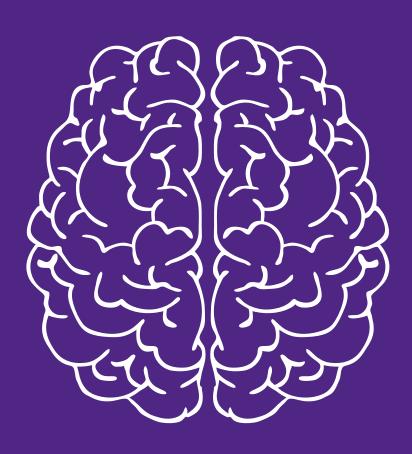
Design and Participant(s): Case report presentation of a 31-year-old female with diffuse medically resistant focal epilepsy admitted to the Epilepsy Monitoring Unit at the Epilepsy Program at Western University. In addition, a literature review will assess whether findings regarding RE are consistent.

Results: A diffuse epileptogenic zone was seen in the patient's scalp recording at the seizure onset and she was implanted with depth electrodes. Her SOZ was identified over a large area in her left posterior temporal-parietal region. Currently, RE is defined as having a SOZ that spans more than 5 electrode contacts (>4 cm), identified through intracranial monitorization. Neural regions including the insula and orbitofrontal cortex have been identified as common onset zones for RE. Regional seizures may demonstrate retention or impairment of awareness commonly seen through focal seizures. RE "syndromes" have been reported as symptomatic or idiopathic and these patients are not candidates for epilepsy resective surgery. Broad neocortical resections are associated with higher rates of seizure freedom but involve a significant risk of postoperative neurologic deficits. Moreover, patients with extensive epileptogenic networks have an increased risk of seizure recurrence after surgery.

Conclusion and Relevance: Although patients with RE are not good candidates for resective surgery, other treatments need to be evaluated. Responsive neurostimulation has been identified as a potential therapy, however, future studies should classify early characteristics of RE. Classification of early RE onset will allow for the precise implementation of responsive neurostimulation which may then prevent early propagation of seizures. Further data concerning diagnosis, management, and impact of RE is needed to improve outcomes.







Thank you for attending the 2022 CNS Research Day!