



# THE DEPARTMENT OF CLINICAL NEUROLOGICAL SCIENCES, WESTERN UNIVERSITY PRESENTS

# 2025 CNS RESEARCH DAY

TUESDAY, MAY 6, 2025 8:00 AM TO 4:00 PM

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 2025 CNS Research Day on Tuesday, May 6<sup>th</sup> 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 50 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. David J. Mikulis.

I would like to take a moment to highlight our industry sponsors; Surgi-One, and Trudell Healthcare Solutions for their generous contribution. 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, moderators and administrative support for their commitment to this event. We would like to acknowledge the support from Amanda, Michelle and other King's University staff for their help in planning today's event. A special thank you to Dr. Elizabeth Finger, Director of Research and the CNS Research Committee for their design of this year's program, and to Alexandra Kylindris, Kristie Lau, and Karen Baptista for their 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**

8:00 to 8:20 a.m.	Registration and Continental Breakfast	Garron/Spriet Lounge
8:25 to 8:35 a.m.	Opening Remarks Dr. David Steven, Richard and Beryl Ivey Chair, Department of Clinical Neurological Sciences	Kenny Theatre
8:40 to 9:35 a.m.	"The Brain Stress Test"  Dr. David J. Mikulis Professor and Full Member of the Institute of Medical Science Temerty Faculty of Medicine The University of Toronto Senior Scientist, The Krembil Brain Institute Director of the Functional Neurovascular imaging in the Joint Department of Medical Imaging The University Health Network The Toronto Western Hospital	Kenny Theatre
9:40 to 9:50 a.m.	Refreshment Break	Garron/Spriet Lounge
9:55 to 11:05 a.m.	Oral Presentation Session #1 A series of 5-minute presentations. Each presenter will be allotted 3 minutes for questions.	Kenny Theatre
11:10 to 11:37 a.m.	Oral Parallel Poster Session #1 A series of 2-minute presentations. Q&A will commence during refreshment break	Basement Classrooms KC 004 & KC 006
11:40 to 11:55 a.m.	Refreshment Break (continued) Poster presentation Q&A	Garron/Spriet Lounge
12:00 to 1:00 p.m.	Oral Presentation Session #2 A series of 5-minute presentations. Each presenter will be allotted 3 minutes for questions.	Kenny Theatre

## **EVENT ITINERARY** (continued)

1:00 to 1:45 p.m.	Lunch	Garron/Spriet Lounge
1:50 to 2:15 p.m.	Oral Parallel Poster Session #2 A series of 2-minute presentations. Q&A will commence during refreshment break.	Basement Classrooms KC 004 & KC 006
2:15 to 2:30 p.m.	Refreshment Break Poster presentation Q&A	Garron/Spriet Lounge
2:35 to 3:35 p.m.	Oral presentation Session #3 A series of 5-minute presentations. Each presenter will be allotted 3 minutes for questions.	Kenny Theatre
3:40 to 4:00 p.m.	Closing Remarks and Awards Dr. Elizabeth Finger, Research Director, Department of Clinical Neurological Sciences	Kenny Theatre

<sup>\*</sup>During the refreshment breaks, poster presenters will be asked to stay beside their poster board for questions and discussion

#### **KEYNOTE ADDRESS**

DR. DAVID J. MIKULIS



**Dr. David J. Mikulis**, MD is Full Professor and Director of the Functional Neuroimaging Research Lab in the Joint Department of Medical Imaging at the University Health Network and the University of Toronto. The primary emphasis of this work has been translational research focusing on the application of novel imaging methods into the clinical environment. He established one of the first fMRI labs in Canada in 1993 and is currently involved in developing advanced neurovascular imaging methods with major program arms including: 1) quantitative measurement and clinical application of cerebrovascular reactivity (CVR) metrics leading to the development of "the brain stress test" (analogous to the cardiac stress test) that assess

the effectiveness of the cerebral circulatory system in meeting the metabolic needs of the brain, 2) high resolution and functional imaging of intra and extracranial blood vessel walls that improves diagnostic accuracy for assessing diseases that directly affect blood vessels, and 3) discovery of a new method for measuring brain blood flow that does not require injection of contrast agents. Research in these areas has improved assessment of the structure, function, and performance of the vascular system in health and disease. These capabilities have further defined the important roles that abnormal vascular performance measures have in the pathophysiology of a number of conditions including for example Alzheimer's and vascular dementias, and in improving diagnostic accuracy of acute concussion. Translation of these methods has been achieved locally, nationally, and internationally confirming the importance of these tools in research and clinical settings.

#### **JUDGES**

In addition to having our esteemed Keynote Dr. David J. Mikulis judge the presentations, we are thrilled to announce our 2025 judges;



#### DR. NEIL DUGGAL

Dr. Neil Duggal is a Professor and consultant neurosurgeon at Western University, with cross appointments in the Departments of ENT, Medical Biophysics, and Robarts Research Institute. He completed his neurosurgical residency in 1999 at Western University and completed subspecialty fellowship in complex spinal surgery, at the Barrow Neurological Institute. He joined the Department of Clinical Neurological Sciences in 2000.

Dr. Duggal has translated clinical problems into successful research collaborations, primarily in developing novel imaging paradigms in patients with cervical myelopathy. He has dedicated 20 years researching the biomechanical, imaging, basic science and clinical outcomes of patients suffering with degenerative spinal disorders. He has repeatedly received tri-council grant support and has been recognized by the American Association of Neurological Surgeons as well as the Cervical Spine Research Society. Dr. Duggal's current research is focused on novel imaging paradigms in patients with degenerative cervical myelopathy and therapeutics measures targeting recovery.

Dr. Duggal is at the forefront of cervical disc replacement surgery and performed the first procedure in North America. With over 20 years of experience, he is recognized internationally for this expertise. He was also the first to introduce and champion minimally invasive spinal surgery techniques and endoscopic pituitary tumor surgery in Southwestern Ontario. He currently acts as the Co-Director of the Western Interdisciplinary Pituitary Group. With a passion for innovation and minimally invasive techniques, Dr. Duggal integrates cutting-edge technology to provide the most current surgical techniques for patients in Southwestern Ontario.



#### DR. JOSEPH MEGYESI

Dr. Joseph Megyesi received his MD from Western University in 1985. He then completed a comprehensive surgical internship and a Master's degree in Biochemistry, also at Western University. He did his neurosurgical residency at the University of Alberta in Edmonton, where he also received his PhD degree in Experimental Surgery. As part of his training, Dr. Megyesi completed a fellowship at Harvard University. Dr. Megyesi joined the Clinical Neurological Sciences Department at

Western University in 1998 and specializes in neurosurgical oncology. He is chairman of

the Scientific Program Committee at the Canadian Neurological Sciences Federation, sits on the Continuing Professional Development Committee at the Royal College of Physicians and Surgeons of Canada and is past-chairman of the board of the Brain Tumour Foundation of Canada. He is currently Professor in the Division of Neurosurgery at Western University.



#### DR. DWIGHT E. MOULIN

Dr. Dwight Moulin received his MD cum laude from Western University in 1973 and then spent four years in general practice. He completed his fellowship in Neurology at Western in 1983 followed by a 2-year Pain Fellowship at Memorial Sloan Kettering Cancer Centre in New York City. He joined the faculty at the Schulich School of Medicine at Western University in 1985 and is currently Professor in the Departments of Clinical Neurological Sciences and Oncology specializing in Pain Medicine. He held the position of Earl Russell

Chair of Pain Research at Western from 2005 to 2020.

Dr. Moulin has published extensively on the role of opioid analgesics in the management of chronic pain and led the first randomized controlled trial of morphine in the management of chronic non-cancer pain. He described the prevalence and impact of chronic pain in multiple sclerosis and Guillain-Barre syndrome – two neurological disorders where significant pain was not previously recognized. More recently he has led a series of observational studies on the long term outcome of the management of neuropathic pain. He has published over 150 scientific papers, book chapters and editorials.

He chaired the Neuropathic Pain Special Interest Group of the Canadian Pain Society from 2005-2014 and led the Consensus Statement on the Pharmacological Management of Chronic Neuropathic Pain – initially published in 2007 and updated in 2014. He was the recipient of the Distinguished Career Award from the Canadian Pain Society in 2012 and he is also a Founding Member of Pain Medicine as a new subspecialty of the Royal College of Physicians and Surgeons of Canada

#### DR. GIOVANNI PELLEGRINO

Dr. Giovanni Pellegrino was trained as Medical Doctor and Neurologist at Campus Biomedico University of Rome (Italy). He developed an interest in multimodal neuroimaging and non-invasive brain stimulation, as well as their application to neurological conditions, with a particular focus on epilepsy.

He furthered his expertise in this field through training at the Danish Research Center for Magnetic Resonance (2012-2013, Copenhagen, Denmark) and at McGill University's Montreal Neurological Institute and Hospital (2013-2016, Montreal, Canada). Between 2018 and 2020, Dr. Pellegrino returned to McGill University's Montreal Neurological Institute and Hospital to complete the Frederick Andermann Clinical and Research

Fellowship in Epileptology and EEG. In 2021, he earned a G.B. Morgagni PhD in Translational Specialistic Medicine – Neuroscience from the University of Padua (Italy) and subsequently received the Italian Habilitation at the rank of Associate Professor of Neurology.

In 2023, he joined Western as Assistant Professor of Neurology – Clinician Scientist. Dr. Pellegrino is also a member of the Western Neuroscience Program and holds a cross-appointment with Department of Medical Biophysics. He has authored over 80 peer-reviewed publications, serves in the editorial board of several peer-review journals, and became recently a Fellow of the American Clinical Neurophysiology Society. At Western, Dr. Pellegrino continues to focus on multimodal neuroimaging, non-invasive brain stimulation, and their application into clinical settings to improve epilepsy care.



#### DR. PATRICIA RICCIO

Dr. Patricia Riccio is an Assistant Professor in the Division of Multiple Sclerosis and Demyelinating Diseases at Western University and a neurologist at London Health Sciences Centre. She completed multiple fellowships in multiple sclerosis and stroke at Western and previously worked as a stroke neurologist in Argentina. Dr. Riccio's clinical and research interests include MS, NMOSD, MOGAD, and neurovascular

diseases. She has authored over 35 peer-reviewed publications and has been actively involved in national and international research projects, grant development, knowledge translation, research data management, and undergraduate medical teaching.



**DR. SHAWN WHITEHEAD**Biography is not available at this time.

### **EVENT SPONSORS**

We would like to thank our event sponsors for their contribution to the 2025 CNS Research Day. We are appreciative of your continued support of this event and our Department. We look forward to future collaboration!





## **ORAL PRESENTATIONS**

Session #1

#### Association of Road Traffic Noise with the Risk of New-Onset Epilepsy

T. Antaya, B. Le, T. Oiamo, P. Wilk, K. N. Speechley

*Importance:* Environmental noise has been associated with the onset and exacerbation of other neurological disorders, but its relationship with new-onset epilepsy has been insufficiently explored.

*Objective:* The study's objective was to assess whether long-term road traffic noise exposure is associated with the risk of new-onset epilepsy among adult residents of Toronto, Canada.

Design and Participants: We conducted a nested case-control study using linked health administrative and environmental data. We included adult residents of Toronto as of January 1, 2010, with no history of seizures or epilepsy. Cases were those who developed epilepsy before December 31, 2016, and were each matched with up to five controls. We measured exposure to road traffic noise using three-year averages of the nighttime average (LAeq, 8 hr), daytime average (LAeq, 16 hr), and the 24-hour average (LAeq, 24 hr) road traffic noise levels at participants' postal code of residence. We estimated the associations of these three-year averages with the risk of new-onset epilepsy using conditional logistic regression models.

Results: We included 4,608 cases and 20,765 controls; 46.3% were female and the mean age was 48.3 (± 17.4). The median [interquartile range] three-year average noise levels were 54.4 [12.9] dB, 63.3 [11.3] dB, and 60.3 [11.8] dB for LAeq, 8 hr, LAeq, 16 hr, and LAeq, 24 hr, respectively. The odds ratios associated with a 10-dB increase in LAeq, 8 hr was 1.043 (95% CI: 0.994, 1.095), 0.999 (95% CI: 0.946, 1.054) for LAeq, 16 hr, and 1.031 (95% CI: 0.980, 1.086) for LAeq, 24 hr.

Conclusions and Relevance: Despite our statistically non-significant findings, there may be an association between long-term exposure to road traffic noise, particularly at night, and the risk of new-onset epilepsy. Considering that little research has been published on the association of environmental noise with the risk of new-onset epilepsy, and given its biological plausibility, future research should continue to explore this potential association.

## A Longitudinal and Systematic Investigation of the Clinical Variables Related to Impulse Control Disorders in Parkinson's Disease

T. Breddy, K. Van Hedger, P. MacDonald

*Importance:* Impulse control disorders (ICD) are experienced by about 20% of patients with Parkinson's Disease (PD) and are associated with serious negative consequences. Currently, clinical predictors of ICD are poorly understood and clarifying the risk factors of ICD can inform tailored intervention strategies.

*Objective:* To analyze the potential temporal relationships between ICD and clinical variables (Anxiety, Depression, REM Sleep Behaviour Disorder (RBD) Symptoms, and Sleepiness) using a large and homogenous sample of de novo patients with PD.

Design and Participants: A systematic sample selection process was used with open-source and longitudinal data from the Parkinson's Progression Markers Initiative. Data from 1,445 eligible patients with PD were screened for eligibility. ICD were assessed using the Questionnaire for Impulsive-Compulsive Behaviours-Current-Short (QUIP-CS). Exclusion criteria include incomplete ICD data, a disease duration of 24 months or greater, or dopaminergic medication use at Baseline. Patients who demonstrated compulsive behaviours outside of ICD domains were also excluded.

Results: Our sample consisted of 337 de novo patients PD (102 females) between 33 to 85 years of age (M=61.52, SD=9.92): patients with ICD at Baseline (ICD-BL; n =114), patients who develop ICD (ICD; n =126), and patients with no ICD or related behaviours (non-ICD; n =97). The ICD-BL (t = 5.71, pbonf < .001) and ICD (t = 3.70, pbonf &lt; .001) groups had significantly higher Baseline Anxiety compared to the non-ICD Group. The ICD-BL Group had significantly higher Baseline Depression compared to the ICD (t = 2.87, pbonf = .013) and non-ICD (t = 4.95, pbonf &lt; .001) groups. The ICD-BL group also had significantly higher Baseline RBD Symptoms compared to the ICD (t = 2.73, pbonf = .020) and non-ICD (t = 3.88, pbonf &lt; .001) groups. The ICD-BL group had significantly higher Baseline Sleepiness compared to the non-ICD group (t = 3.61, pbonf = .001).

Conclusions and Relevance: Some patients with PD present with ICD symptoms before initiating dopaminergic medications, and these patients also tend to have more clinical symptoms at Baseline. Monitoring and treatment of Anxiety, Depression, RBD Symptoms, and Sleepiness should be incorporated into ICD intervention strategies for patients with PD.

## **Evaluating the Positive Predictive Value of Fixed Cell-Based Assays for Myasthenia Gravis in Clinical Practice**

CMF. Li, MW. Nicolle, K. Sangam, L. Yang, A. Budhram

Importance: Antibody testing for acetylcholine receptor (anti-AChR) and muscle-specific tyrosine kinase antibodies (anti-MuSK) is a cornerstone in the diagnostic evaluation for myasthenia gravis (MG) and historically relied on radioimmunoprecipitation assay (RIPA). Novel fixed cell-based assays (CBAs) for anti-AChR/MuSK have higher sensitivity than RIPA and are now commercially available; however, there is limited data on their diagnostic performance in clinical practice. This is the first single-centre study to evaluate the positive predictive value (PPV) of anti-AChR/MuSK fixed CBA as a first-line test for myasthenia gravis (MG) in a clinical setting.

Objectives: To determine the PPV of anti-AChR/MuSK fixed CBA in routine practice.

Design and Participants: We reviewed the clinical data of all patients with positive anti-AChR/MuSK fixed CBA results at our centre from November 2021 to July 2024. Patients were classified as true-positives if their clinical presentation was compatible with MG and no alternative diagnosis was more likely; all others were classified as false-positives. Test PPV was determined as the proportion as true-positives among all patients with seropositivity.

Results: Among 770 patients who underwent anti-AChR/MuSK fixed CBA testing, 109 (14%) had positive antibody results (Anti-AChR, 105; Anti-MuSK, 4). One anti-AChR-positive patient was classified as a false-positive due to suspected thymic hyperplasia without MG. The remaining 108 patients were classified as true-positives, yielding a PPV of 99%.

Conclusions and Relevance: Our study demonstrates that anti-AChR/MuSK fixed CBA had excellent PPV for MG. Anti-AChR positivity in one asymptomatic patient with suspected thymic hyperplasia was classified as a false-positive result, although the possibility that this represents a true marker of thymic pathology in a patient who may later develop MG cannot be excluded. The high PPV reported herein supports the use of anti-AChR/MuSK fixed CBA as first-line testing for suspected MG in routine practice.

## Subjective Autonomic Dysfunction and Sleepiness in People with Drug-Resistant Focal Epilepsy

H. Gray, H.. Kreinter, M. Elnazali, K. Shoemaker, A. Suller Marti

*Importance:* Sudden unexpected death in epilepsy (SUDEP) is the second leading neurological cause of potential life-years lost. People with drug-resistant epilepsy (PwDRE) are most at risk for SUDEP, which is likely influenced by autonomic dysfunction.

Objective: We aimed to evaluate subjective autonomic functioning and daytime sleepiness in PwDRE.

Design and Participants: This cross-sectional study began recruiting participants from the Epilepsy Monitoring Unit at University Hospital via consecutive sampling in November 2023. Patients with drug-resistant focal epilepsy undergoing stereoelectroencephalography completed the Composite Autonomic Symptom Score (COMPASS-31) and Epworth Sleepiness Scale (ESS).

Results: We present the results of 34 participants (13 females; median age=33.0 years, IQR=11.0). The COMPASS-31 (mean score=27.4, SD=13.8) and ESS (mean score=7.1, SD=3.4; this mean represents higher normal daytime sleepiness) were significantly correlated (r=.42, 95% CI [0.66, 0.09], p=.02). There were no significant correlations between age and total scores on the COMPASS-31 (r=-0.04, 95% CI [-0.37, 0.30], p=0.82) or the ESS (r=-0.12, 95% CI [-0.44, 0.22], p=0.49). There were also no sex differences in ESS scores (t=1.55, 95% CI [-0.57, 4.17], p=.13), but females scored higher on the COMPASS-31 than males (t=3.41, 95% CI [5.82, 23.0], p<.01). There were no differences between seizure onset zones in the temporal lobe(s) (N=20) and multi-focal, extra-temporal or unknown epileptogenic zones on the COMPASS-31 (t=0.18, 95% CI [-9.06, 10.78], p=.86) or the ESS (t=1.29, 95% CI [-0.86, 3.86], p=.21). Participants who were on two or three sodium channel blocking (SCB) anti-seizure drugs (cardiotoxic; N=17) scored higher on the COMPASS-31 than participants on none or one SCB (N=17) (t= -2.15, 95% CI [-18.77, -0.50], p=.04), and higher on the ESS (t= -2.80, 95% CI [-5.08, -0.80], p&lt;.01).

Conclusions and Relevance: In summary, females scored worse on the COMPASS-31 than males, and participants on two or three SCB anti-seizure drugs scored worse on the COMPASS-31 and ESS than participants on none or one SCB. No other clinical factors analyzed show an association with the assessment scores. In routine clinical practice, subjective autonomic symptoms should be assessed in PwDRE, especially females and patients prescribed SCBs. Higher sample sizes, especially for the former subgroup, are warranted.

#### **Intracranial Electrotherapy for Glioma Treatment In Vivo**

E. Iredale, N. Fulcher, V. Luo, E. Fenton, S. Schmid, T. Peters, E. Wong, MO. Hebb

Importance: Glioblastoma (GBM) remains the most fatal form of primary brain cancer, with a median survival of 14 months despite standard treatments of surgical resection, chemotherapy, and radiation. Anti-cancer electrotherapy is showing potential as a new option for aggressive brain cancers, using low-intensity electric fields (1 V/cm) of intermediate frequency (200 kHz). Internal delivery of these fields from multiple bioelectrodes, called Intratumoral Modulation Therapy (IMT), has the potential to provide a sustained, localized GBM treatment approach.

*Objective:* To evaluate the impact of dynamic IMT on GBM growth in vivo and validate treatment planning simulations.

Design and Participants: A 3-electrode preclinical IMT apparatus was implanted into the left hemisphere of the Fischer rat brain (n=22), and F98 glioma cells injected at the center of the pedestal. Bioluminescence imaging (BLI) was performed on post-operative day 4 for each animal pair, prior to the initiation of dynamic IMT stimulation (200 kHz, ±2V amplitude sine waves equally phase shifted). Paired rats received either IMT or sham (no stimulation) treatment for 7 days with continuous voltage and current delivery monitoring. Endpoint BLI was performed on post-operative day 11 (n=11 pairs), and ex vivo 15.2T magnetic resonance imaging (MRI) utilized for analysis of the tumor volume (n=10 individuals). Tumor volume analysis and electric field simulations were performed on our custom IMT preclinical planning system platform.

Results: Tumor volume from ex vivo MRI linearly correlated with endpoint BLI signal (n=10, p<0.01). For treated rats with MRI (n=5), an average 1.71±0.07 V was delivered over the 7 days, with patient specific simulations yielding 100% coverage of the visible tumor volume with 1 V/cm IMT field. The measured electrical current was 5.8±1.3 mA, matching the predicted values from simulations of 5.4±1.1 mA. Over the 7 days, sham tumor burden grew 118.6-fold, while IMT only grew 13.5-fold, an 8.8 times reduction in tumor growth with IMT (n=11, p=0.006).

Conclusions and Relevance: This study provides key preclinical evidence of the efficacy of dynamic IMT against GBM. These results support the translation of IMT to clinical trials, to evaluate safety and efficacy in the human brain.

#### Kinematics of essential tremor

CMF. Li, A. Khan, M. Jog, M. Jog, O. Samotus

*Importance:* Essential tremor (ET), affecting 4.6% of people over 65, is classically described as oscillatory movements of the arms around a central axis that is elicited with postures or movement. Characteristics of ET change with rest, posture, and action. Further characterization of ET, including amplitude and movement axis, at each affected joint (wrist, elbow, and shoulder) can help to better elucidate the nature of ET.

*Objective:* To evaluate the axes of movement and tremor amplitude in ET across the three joints during different tasks (rest, posture, and action).

Design and Participants: A cross-sectional study with 31 participants (12 female, 3 left-hand dominant, average age 69.7) used motion sensors to measure the tremors during two resting, two postural, and two static-loading tasks. Sensors at the wrist, elbow, and shoulder recorded angular tremor amplitude, and the motion was segmented into directional components. There were three degrees of freedom (flexion-extension, radial-ulnar, and pronation-supination) at the wrist, one degree of freedom (flexion-extension) at the elbow, and two degrees of freedom (flexion-extension, and abduction-adduction) at the shoulder.

Results: Tremor amplitude was smallest in resting positions and greatest with weight-bearing tasks (p<0.05). Tremor amplitude was greatest at the wrist across all tasks (p &lt;0.05). At the wrist, there was a bias toward pronation, extension, and ulnar deviation in ET with posture. Pronation-supination contributed most to tremor amplitude at the wrist in most positions, while radial-ulnar had the least contribution. In the shoulder, there was no significant difference in the contributions of flexion-extension and abduction-adduction to ET.

Conclusion and Relevance: This study revealed that tremor amplitude in ET is most pronounced at the wrist and with an oscillatory bias towards wrist pronation, followed by wrist extension. Interventions targeting these particular movements may help to optimize symptomatic treatment of ET and improve patient function.

## Histological and 15.2T MRI characterization of the zona incerta: advancing visualization for precise deep brain stimulation

V. Liu, M. Tsai, A.R. Khan, J.C. Lau

*Importance:* The zona incerta (ZI) is a promising deep brain stimulation target for alleviating motor symptoms in Parkinson's Disease and essential tremor patients. However, its indistinct boundaries and complex internal organization make visualization on standard MRI challenging.

*Objective:* To characterize the ZI and surrounding subcortical regions by establishing spatial correspondence between histochemistry-derived myeloarhictecture and 15.2T MR imaging on postmortem ex vivo specimens.

Design and Participants: The subcortices of perfusion-fixed cadavers (n=5, F=2, M=3) were obtained from Western's Body Bequeathal Program, followed by dissection and T1-weighted MRI (0.1mm³ 3D FLASH, MP2RAGE, magnetization saturation). Tissues were subsequently blockface imaged, serially sectioned, Luxol Fast Blue/Nissl staining to visualize the myeloarchitecture, and aligned with the ex vivo 15.2T sample through rigid, deformable, and landmark-based registrations.

Results: We present the first detailed segmentation of the human ZI and surrounding structures obtained using 15.2T MRI, revealing features previously difficult to discern that are relevant for DBS targeting, including boundaries between the subthalamic nucleus and ZI, the H fields traversing through the rostral ZI, and other small white matter tracts. We have also successfully registered the blockface images to the ex vivo 15.2T image and the standard MNI space, thereby establishing a pipeline for cross-modality visualization of the human ZI at ultra-high field resolution.

Conclusion and relevance: This work provides an in-depth, cross-modality understanding of the ZI, a promising site for neuromodulation in various neurological disorders, and offers insights crucial for DBS target visualization with the potential impact of improving clinical outcomes in the future. Additionally, the computational pipeline developed from this research can be applied to investigate other established DBS targets across scales, thus bridging cell biology and MR imaging in neuroscience research. Given the involvement of ZI in the motor circuitry impacted in PD, particularly the basal ganglia, the findings may also contribute to unraveling the mechanism underlying PD pathogenesis, paving the way for future discoveries for PD research beyond symptomatic treatment. Future work will focus on refining registration and segmentation techniques, conducting immunostaining to obtain cell type-specific information, and expanding the sample size to develop a high-resolution anatomical atlas for precise neurosurgical applications.

## **ORAL PRESENTATIONS**

Session #2

## Functional network differences between unilateral and bilateral deep brain stimulation of the subthalamic nucleus.

B Santyr, A Boutet, M Abbass, A Vetkas, J Germann, A Ajala, J Qiu, G Elias, C Sarica, A Yang, I Alhashyan, S Kalia, A Fasano, A Lozano

*Importance:* The therapeutic efficacy of deep brain stimulation (DBS) in Parkinson's disease (PD) is well established; however, its mechanism and differing therapeutic effects between unilateral and bilateral stimulation of the subthalamic nucleus (STN) remain incompletely understood.

Objectives: We aim to better understand the differences in the therapeutic mechanism by examining network effects using functional magnetic resonance imaging (fMRI) during active unilateral or bilateral stimulation.

Design and Participants: 22 PD patients with bilateral DBS were prospectively enrolled for fMRI. Two groups of 11 subjects matched for age, sex, disease duration, and baseline disease severity were imaged while receiving either left unilateral or bilateral stimulation. The network engagement effects were investigated and correlated with right-sided motor outcomes using the Movement Disorder Society-Sponsored Revision of the Unified Parkinson's Disease Rating Scale, Part III.

Results: Bilateral stimulation does not simply replicate the sum of unilateral effects. When compared to left unilateral stimulation, there is a greater magnitude of signal reduction in the left sensorimotor cortex with bilateral stimulation (p=0.05), and bilateral stimulation nullifies decreases seen in the ipsilateral frontal lobe during unilateral stimulation (p=0.02). This pattern of response is replicated in a single out-of-sample subject. Ipsilateral sensorimotor activity is the strongest predictor of right-sided outcome (bradykinesia p<0.001, R2=0.54; tremor p=0.01, R2=0.28; axial stability p=0.007, R2=0.31). Unilateral stimulation alone was insufficient to demonstrate this association.

Conclusions and Relevance: Enhanced engagement of motor circuitry and relative exclusion of non-motor regions in bilateral stimulation, beyond just replicating unilateral stimulation effects, suggests a potential mechanistic basis for better motor outcomes with bilateral stimulation.

## Longitudinal trajectories of neurodevelopmental and neurodegenerative outcomes in genetic frontotemporal degeneration

I. So, Frontotemporal Degeneration Prevention Initiative, E. Finger

*Importance:* Converging evidence hints at neurodevelopmental effects in genetic frontotemporal degeneration (FTD). For some genes, young adult FTD mutation carriers exhibit cross-sectional differences in brain volumes and cognition compared to familial non-mutation carriers. Longitudinal trajectories can more sensitively capture FTD-related neurodevelopmental vs neurodegenerative changes than cross-sectional approaches.

*Objective(s):* To examine longitudinal trajectories of brain volumes, executive function, and plasma biomarkers in young adult carriers compared to familial non-mutation carriers, as measures of neurodevelopmental and neurodegenerative outcomes of FTD-causing genes.

Design and Participants: This longitudinal cohort study comprised participants (18-30 years) from the FTD Prevention Initiative across Europe, Canada, and USA. Genetic groups included C9orf72 (37%), MAPT (50%), and GRN (13%). Linear mixed-effects models were computed to assess longitudinal outcomes between groups, controlling for visit age, sex, scanner (for brain volumes) and education (for executive function); random effects accounted for between-subject variability nested within family membership.

Results: Mutation carriers (n=113) and familial non-carriers (n=102) did not differ in age (mean±SD, 25.8±3.2), sex (56% female), or number of visits (2.2±1.6). Compared to non-carriers, average volumes were smaller in C9orf72 repeat expansion carriers in the thalami (b=2842.5, SE=599.7, p=0.001), insula (b=1176.1, SE=396.3, p=0.016), and medial orbitofrontal cortices (b=911.7, SE=360.4, p=0.032), with significant or approaching significant changes over time (p=0.054, p=0.0005, p=0.015, respectively). MAPT carriers had larger medial orbitofrontal cortices on average (b=-1764.4, SE=646.1, p=0.041) than non-carriers, but this relationship did not vary over time. Average rostral anterior cingulate cortices trended towards being larger in GRN carriers relative to non-carriers (approached significance, p=0.0996), without change over time. No longitudinal changes were observed in total brain or frontal pole volumes, executive function, or plasma NfL or GFAP between groups per genetic group.

Conclusions and Relevance: FTD-causing mutations are linked to longitudinal changes in brain volumes, but not executive function or plasma biomarkers of neurodegeneration, suggesting potential compensatory mechanisms during young adult years. Consistent with prior research, these findings of larger regional brain volumes support neurodevelopmental effects in GRN and possibly in MAPT genetic FTD. Future longitudinal study of youth mutation carriers and non-carriers is necessary to disentangle neurodevelopmental vs. early neurodegenerative changes in FTD.

## Cognitive and Neural Correlates of Olfactory Dysfunction: Exploring the Parkinson's Disease Prodrome

H. Vanderzwet, K. Van Hedger, G. Kang, D. Michels, P. MacDonald

*Importance:* Parkinson's Disease (PD) has non-motor manifestations, including Olfactory Dysfunction (OD), which might emerge years before diagnosis. OD is associated with cognitive decline in PD, highlighting the need to understand OD in prodromal populations.

*Objectives:* This study aimed to determine whether patients with OD, with and without a PD diagnosis, demonstrate cognitive changes compared to healthy controls and patients with PD without OD. A secondary aim assessed microstructural changes in striatum subregions related to OD.

Design and Participants: This cross-sectional study used multisite data from the Canadian Consortium on Neurodegeneration in Aging (CCNA), and the Parkinson's Progression Markers Initiative (PPMI). Participants ages 50-80 completed a standardized smell test (UPSIT/BSIT) and an MRI scan. Hyposmia was defined as having a BSIT or equivalent score at or below 15th percentile for age and sex.

Results: 1255 participants were divided into 4 groups: healthy controls with no hyposmia (n = 446, mean age = 68.3, 237 female), healthy controls with hyposmia (n = 446, mean age = 67.2, 220 female), patients with PD with no hyposmia (n = 130, mean age = 68.2, 46 female), and patients with PD with hyposmia (n = 233, mean age = 64.5, 79 female). A subset (n = 295) was analysed with diffusion MRI processing pipeline output metrics across striatum subregions.

A two-way ANCOVA identified significantly higher MoCA scores in healthy controls with no hyposmia (M = 27.11, SE = 0.11) than healthy controls with hyposmia (M = 26.69, SE = 0.11), t = 2.74, pbonf = .037. No significant differences were found between patients with PD with and without hyposmia. Across all groups, partial Pearson correlations revealed a significant positive association between BSIT scores and limbic surface fractional anisotropy, r(294) = 0.15, t = 2.61, p <.01, and a significant negative relationship between BSIT scores and limbic surface mean diffusivity, r(294) = -0.20, t = -3.39, p <.001.

Conclusions and Relevance: These results highlight differences in cognitive performance and microstructural integrity as a function of OD among participants without a PD diagnosis. Given OD may precede PD, these results suggest findings relevant to a prodromal disease phase.

## Clinicopathological Outcomes and Biomarker Shifting of Breast Cancer Brain Metastases

R. Wang, Q. Zhang, J. Megyesi

Introduction: Breast cancer brain metastases (BCBMs) are a feared complication of breast cancer and associated with a poor prognosis. The molecular and biological events that give rise to BCBMs are not fully understood. The project aims are to characterize the clinicopathological outcomes of patients who underwent surgical resection or biopsy of BCBMs at LHSC and further compare the biomarker profiles between primary tumor and BM.

Methods: Patients who had BCBMs surgically-resected or biopsied at LHSC were identified. Retrospective chart review was conducted to collect patients demographics, details on primary BC and BM diagnoses and treatments, pathology details, and clinical outcomes. Kaplan-Meier curves were generated and uni- and multivariate Cox-regression analyses were conducted to determine clinical outcome predictors.

Results: Seventy-five female patients were identified. Mean age at BCBM diagnosis was 56.1 years and mean time to developing BCBM was 5.4 years (range: 0-23.0 years). Triple-negative (18/75, 24.0%) and HER2+ (14/75, 18.7%) were the most common subtypes. Median overall survival (OS) after BCBM diagnoses was 2.4 years. Solitary BCBM (p=0.0276) and no extracranial systemic disease (p=0.0276) were associated with longer OS after BCBM diagnosis. 51 patients had paired immunohistochemistry (IHC) markers of their primary BC and BMs. 11/51 (21.6%) patients exhibited a subtype switch with hormone receptor loss (5/11, 55.6%) being the most common change. Univariate Cox-regression analyses for these 51 patients demonstrated that triple-negative subtype (HR 2.81, p=0.0075), multiple BMs (HR 3.23, p=0.0024), neurological deficits (HR 3.06, p=0.0058), tumor >3 cm (HR 2.84, p=0.013), and hydrocephalus (HR 4.13, p=0.014) were negative prognostic factors. After multivariate Cox-regression, only triple-negative subtype (3.52, p=0.0033) and multiple BMs (2.34, p=0.047) remained significant. Subtype switching did not appear to impact OS (p=0.31).

Conclusions: The management of BCBM remains challenging with overall survival remaining poor. Within our cohort, a noticeable proportion of patients exhibited biomarker profile shifting between the primary BC and BCBM. This may have clinical implications and further investigations are required. Single-cell and spatial transcriptomic analysis using 10X Genomics Xenium will be pursued to analyze differences between primary BC and BCBMs exhibiting biomarker shifting vs. those that did not.

\*\*Did not consent to having abstract posted online\*\*

\*\*Did not consent to having abstract posted online\*\*

## **ORAL PRESENTATIONS**

Session #3

## Evaluating the Dear MD to Be Podcast as an Equity, Diversity, and Inclusion Resource: A Cross-Sectional Survey Analysis

H. Inibhunu, I. Kherani, C. Osei-Yeboah, M. Bushra, M. Mahendiran, M. Mylopoulos, and M. Law

*Importance:* Equity-deserving groups are communities marginalized from institutional power by oppressive forces. The Dear MD to Be is a medical-student-led podcast created to interview physicians of intersectional backgrounds about their institutional experience. This study aimed to evaluate the podcast as a tool for knowledge, mentorship, and psychological safety for equity-deserving listeners.

Methodology: Between February and March 2022, we recruited medical students across all levels of training from English-speaking Canadian medical schools using email listservs and social media. We disseminated a cross-sectional questionnaire assessing demographics, knowledge gained from podcast engagement, attitudes towards podcasts as a tool for mentorship, and psychological/emotional gains from the podcast content. We conducted descriptive and frequency analyses of quantitative data and applied thematic analysis to qualitative data.

Results: Thirty-eight individuals completed the entire survey from all levels of training, with 97% self-identifying with at least one equity-deserving group. 100% agreed that the Dear MD to Be podcast was an accessible form of mentorship; participants appreciated self-pacing mentorship and interacting with many narratives. Listeners gleaned lessons about wellness, advocacy work, allyship, cultural imposter syndrome, and navigating discrimination. Furthermore, most listeners felt represented, empowered, and legitimized by podcast content.

Conclusions and Relevance: Podcasts can serve as a medium for accessible equity-centered mentorship. By disseminating multiple underrepresented narratives in medicine, the Dear MD to Be podcast serves as a source of EDI knowledge while contributing to learner safety.

#### SEEG in Bilateral Independent Scalp EEG Seizures: Precision or Futility?

A.J. Soni, C.B. Donoso, A. Suller Marti, D Steven, J. Lau, M. Jones, J.G. Burneo, G. Pellegrino.

*Importance:* Stereo-electroencephalography (SEEG) is a crucial tool in presurgical epilepsy evaluation, but its utility in patients with bilateral independent or unclear seizure onset on scalp EEG remains uncertain. Understanding its yield in identifying a single, resectable seizure focus is essential to optimizing patient selection and minimizing unnecessary surgical morbidity.

*Objective:* To determine the probability of identifying a single, unilateral seizure onset zone (SOZ) following SEEG implantation in patients with bilateral independent or unclear scalp EEG onset.

Design and Participants: This is a single-center, retrospective cohort study of adult patients with drug-resistant focal epilepsy (DRE) who underwent SEEG evaluation at London Health Sciences Centre between January 2012 and December 2024. From an epilepsy surgery database of 1,186 patients, 254 underwent SEEG, of whom those with bilateral independent or unclear seizure onset on scalp EEG and subsequent bilateral SEEG implantation were included.

Patients underwent preoperative assessment with scalp video EEG telemetry, brain MRI, and additional ancillary investigations such as FDG-PET, ictal/interictal SPECT, and neuropsychological evaluation. SEEG electrode implantation was tailored based on these findings and reviewed in a multidisciplinary epilepsy surgery conference. Seizure outcomes were classified using Engel outcomes.

Statistical analysis will include descriptive statistics for baseline characteristics and preoperative variables. The primary outcome—the likelihood of a single, unilateral SOZ on SEEG—will be assessed using proportions with confidence intervals. Secondary outcomes includ rates of subsequent resective surgery, neuromodulation, or radio-frequency thermocoagulation (RF-TC), analyzed using logistic regression models to identify associations with preimplantation factors. Seizure freedom outcomes will be evaluated using Kaplan-Meier survival analysis with Cox proportional hazards modeling to determine predictors of sustained Engel class I outcomes.

This study will provide critical insight into the yield of SEEG in patients with non-lateralized scalp EEG, guiding presurgical decision-making and optimizing patient selection for invasive monitoring.

*Results, Conclusions and Relevance:* Data collection has been completed and is in the process of data analysis. Results and conclusions are anticipated to be available by May 2025.

#### Improving management of elevated ICP on the Neurology ward

A. Branch, A. Florendo-Cumbermack

*Importance:* Elevated intracranial pressure (ICP) is a neurologic emergency that can develop in patients admitted to the Neurology ward. This requires prompt management to avoid mortality and morbidity. However, not all residents who cover the neurology services are comfortable with identifying or managing this condition, and this can introduce delays or errors in treatment leading to patient harm.

Objective: To undertake a quality improvement project to improve the timeliness of management of elevated ICP on the Neurology ward by increasing resident comfort with the identification and management of this neurologic emergency.

Design and Participants: An initial survey was undertaken of residents rotating through the inpatient neurology services to establish a baseline of knowledge and comfort with presentation, investigations, and management for elevated ICP. Based on this data and feedback from various stakeholders, an algorithm for initial identification and management of elevated ICP was created for residents to quickly reference on call. This was iteratively improved based on feedback from experts and resident stakeholders. The resource was distributed to residents and a survey was again undertaken to determine any change in resident knowledge and comfort with identifying and managing elevated ICP.

Results: On the initial survey of 23 residents rotating through the inpatient neurology services, only 13.0% of residents rated themselves as "Somewhat Comfortable" or "Extremely Comfortable" in managing elevated ICP. The algorithm was created, and after distribution, 66.7% of 12 residents rated themselves as "Somewhat Comfortable" or "Extremely Comfortable" in managing elevated ICP. Ability to identify at least one clinical finding and at least one imaging finding suggestive of elevated ICP also improved from 82.6% to 100% and 73.9% to 100%, respectively.

Conclusions: Management of elevated ICP is a time-sensitive emergency that many new and off-service residents find themselves uncomfortable with identifying and managing. With the simple intervention of an algorithm provided to residents at the beginning of their inpatient neurology, comfort with and knowledge of this condition increased significantly. This will likely result in faster and more accurate identification and management of this important problem, the measurement of which could be the topic of further quality improvement work.

## MRI micro-structure and morphology predict the development of freezing of gait in Parkinson's disease

N. Rothery, K. Van Hedger, D. Michaels, M. Sharafkhah

*Importance:* Freezing of gait (FOG) in Parkinson's disease (PD) severely impairs mobility and quality of life. Identifying patients at risk of future FOG is critical for guiding earlier interventions to preserve independence.

*Objective:* To determine whether baseline structural MRI measures alone can reliably predict FOG development in early, drug-naïve patients up to 8 years after PD diagnosis.

Design and Participants: Data from 387 individuals in the Parkinson's Progression Marker Initiative (PPMI) database, a multi-site longitudinal data collection effort, were screened. Those with disease duration beyond 24 months, baseline freezing of gait (FOG), or fewer than 5 years of follow-up were excluded, as were patients who exhibited only dopamine-responsive FOG. This yielded a final cohort of 106 recently diagnosed (<24 months), drug-naïve participants with PD. FOG, defined here as persistent, dopamine-resistant freezing, was monitored for up to 8 years. An ensemble-based machine learning model was trained using micro-structural integrity (e.g., mean diffusivity, fractional anisotropy) and morphometric (e.g., volume, surface area) measures extracted from baseline T1-weighted and diffusion-weighted MRI scans. We controlled for age, sex, and baseline motor severity to isolate FOG-specific predictors.

Results: Of the 106 participants in our final cohort, 57 patients developed FOG (25 female); 49 did not (14 female). Differences in baseline characteristics were observed for age (FOG=67.85±8.82, non-FOG=60.05±10.68, P<0.001), sex (P=0.009), and motor symptom severity (MDS-UPDRS-III: FOG=27.71±9.57, non-FOG=16.88±6.78, P&lt;0.001). In a 30% hold-out sample (n=32), the trained model achieved an area under the curve of 0.98, with 100% sensitivity and 87% specificity. Neuroimaging features reflecting micro-structural integrity and morphology in limbic, executive-attentional, and visuomotor networks emerged as key predictors, suggesting that network-specific vulnerabilities, rather than generalized disease severity, underlie FOG predisposition.

Conclusion and Relevance: We identified early structural MRI—based biomarkers which reliably predicted future FOG development in PD, potentially informing proactive clinical strategies. Larger, more demographically diverse cohorts and external validation are needed to confirm these findings and to clarify whether early interventions targeting these network-level vulnerabilities may delay or alter FOG onset.

## Open and Minimally Invasive In-vivo Accuracy of Pedicle Screws with an Autonomous Robotic System

B. Johnston, M. Opperman, V. Yang

*Importance:* Surgical robotics can minimize the discrepancy between surgical preoperative plan and postoperative plan execution.

*Objective:* This work explores the performance of a supervisory-control architecture robot (8i Robotics) for autonomous pedicle instrumentation in both an open and MIS workflow.

Design: Quantitative assessment was conducted in 3 porcine subjects who underwent pedicle instrumentation utilizing the 7dof robot and were observed for 24 hours. An additional 8 porcine subjects (4 open, 4 minimally invasive) had clinical assessment of pedicle screw placement. Post-operative CT assessed screw location. Precision was assessed by a customized image processing pipeline. Euclidean error was calculated at screw head and screw tip. All points were normalized to a nominal screw, and confidence ellipses generated. In two living human patients, guidance accuracy was compared to standard of care navigation, without use of the robotic system for screw placement.

Results: All animals were neurologically intact at 24 hours. All screws where GRS A. There was no clinical difference between clinical assessment of MIS vs Open workflow. Mean tip and head Euclidean error where 2.47+/-1.25mm and 2.25+/-1.25mm respectively. Major and minor axes of the confidence ellipse at 99% was 2.19mm, and 1.28mm, and 2.07mm, and 0.42mm for tip and head respectively. Guidance was successfully obtained in both human cases, with good agreement with standard of care image guidance.

Conclusion and Relevance: 100% of screws obtained satisfactory clinical grading, with intact function in all animals post-operatively. This demonstrates the capability of a supervisory controlled robotic pedicle screw insertion robot in both open and minimally invasive workflow. Furthermore, initial guidance was feasible in living human patients with comparable agreement to current navigation systems. Quantitative assessment of guidance is underway with further accruement of study subjects. This work demonstrates exciting promise for the future of autonomous surgical robotics.

## Resting-State Functional MRI Investigation of Executive Function Networks in School-Age Children with Shunted Infantile Hydrocephalus

B.Y.T. Chung, D. Adil, E. Duerden, R. Eagleson, S. de Ribaupierre

*Importance:* Despite ventriculoperitoneal (VP) shunting, children with infantile hydrocephalus (HCP) often experience long-term cognitive and behavioral challenges, particularly in executive function (EF). The relationship between disrupted functional brain network connectivity and EF outcomes remains poorly understood.

Objective: This study investigates functional connectivity within EF-related brain networks, including dorsal attention, ventral attention, frontoparietal control, default mode, and limbic networks, using resting-state functional MRI (rs-fMRI) and examines associations with EF behaviors in school-aged children with shunted infantile HCP.

Design and Participants: Sixteen children with HCP (mean age: 9.1 years) and 17 typically developing children (mean age: 10 years) were recruited to this cross-sectional study. T1-weighted MRI and rs-fMRI were obtained at Robarts Research Institute, Western University. All patients had VP shunts placed within the first year of life and were clinically stable at recruitment. EF was assessed using the Behavior Rating Inventory of Executive Function, Second Edition (BRIEF2), and the Trail Making Test (TMT).

Results: Patients demonstrated significantly higher Cognitive Regulation Index (CRI) t-scores (M=55.41, SD=6.62, p=0.0027, Hedges' g=1.158) and Global Executive Composite (GEC) t-scores (M=56.00, SD=8.2, p=0.009, Hedges' g=0.970) compared to controls. Patients demonstrated significantly longer completion times for TMT Trail A (M=39.31s, SD=11.50 vs. M=25.94s, SD=10.27, p=0.00013) and Trail B (M=55.63s, SD=11.41 vs. M=37.71s, SD=11.41, p<0.0001) compared to controls.No significant correlation was found between BRIEF2 scores and TMT completion times (r&lt;0.07, p&gt;0.3). Preliminary rs-fMRI findings will provide insight into connectivity disruptions within EF networks.

Conclusions and Relevance: School-aged children with shunted infantile HCP exhibit significant EF deficits in both parental reports and performance-based measures. Differences in cognitive regulation and global executive function suggest long-term neurodevelopmental consequences of early-life hydrocephalus. Further investigation into rs-fMRI-derived network connectivity is critical for understanding EF impairments and guiding targeted interventions.

# POSTER PRESENTATIONS Session # 1 KC 004

## Leveraging the Power of Artificial Intelligence to Understand Cognitive Impairment in Multiple Sclerosis: A Scoping Review

J. Lance, B. Ciftci-Kavaklioglu

Cognitive impairment is a common and disabling symptom among people with multiple sclerosis (pwMS). Artificial intelligence (AI) techniques have emerged as a powerful set of tools for identifying hidden patterns and improving assessment methods, offering potential for advancing understanding of cognitive profiles in MS.

To examine the current applications of AI in understanding cognitive symptoms in MS. Specifically, we aim to explore the type of data used in machine learning models, the scope of different algorithmic approaches, the contributions of these techniques, and key knowledge gaps to guide future research.

This study was designed as a scoping review and conducted in accordance with PRISMA guidelines. A systematic search of PubMed and Web of Science was conducted for articles satisfying the Boolean search "Multiple Sclerosis" AND ("Artificial Intelligence" OR "Machine Learning") AND ("Cognitive" OR "Cognition") in the title, abstract, or keywords. Reviews and non-English papers were excluded.

Of the total of 223 studies identified on the initial search, 31 met the inclusion and exclusion criteria. These studies represented 6,778 individuals with multiple sclerosis (4,696 females). MRI-derived features were utilized in 21 of 31 studies, with subsets incorporating clinical (6/31) and demographic (4/31) data for model training. Several studies explored unique predictive features including microRNA profiles and smartphone keyboard interactions. The Symbol Digit Modalities Test (SDMT) was the most frequently used cognitive impairment metric (21/31, 68%), followed by the Brief Visuospatial Memory Test–Revised (5/31, 16%). Prediction of cognitive impairment was the most common outcome measure (18/31, 58%), cognitive assessment test quality (4/31, 13%) and hidden pattern identification (2/31, 6%). Sample sizes ranged from >500 (7/31, 23%) to <100 (3/31, 26%), with 4 studies (13%) including fewer than 50 participants.

While artificial intelligence methodologies have been used widely to predict cognitive impairment in MS, its implementation remains limited especially in domains of hidden pattern identification using non-MRI data. Furthermore, existing studies in the literature are commonly limited by small sample sizes and inconsistencies in statistical reporting, highlighting the need for larger scale studies with greater standardization and validation.

## Understanding the significance of serum neurofilament light chain across phases and phenotypes of multiple sclerosis: unsupervised machine learning for hidden pattern identification

B. Ciftci, C. S Casserly, J. Lance, P. Malik

Importance: Multiple Sclerosis (MS) is characterized by significant heterogeneity in clinical and radiological trajectories. This heterogeneity is also mirrored in available disease modifying therapies (DMT) that address relapses, progression and progression independent of relapses (PIRA) variably among people with MS (pwMS). Understanding the determinants and implications of PIRA, a novel prognostic concept that has emerged in the era of better radiological disease control is of critical utility. Serum neurofilament light chain (sNFL) is an emerging biomarker to help quantify disease activity in MS. The specific trajectories of sNFL in MS and their relationship to PIRA remain poorly understood.

Objectives: The primary objective of this study is to identify novel phenotypic clusters of people with MS based on their sNFL trajectories and presence or absence of PIRA. It is hypothesized that at least 3 distinct novel phenotypes will emerge. Secondary objectives include identifying determinants of cluster membership and exploring correlations with MRI features and traditional MS phenotypes.

Design and Participants: This is an observational cohort study. Patients enrolled in the comprehensive and longitudinal MS and Neuroinflammatory Disorders Research Registry (REB 01-21-2025, #2025-125523-103929) and consented to being contacted for future research will be screened for eligibility. People aged between 18-60 years, diagnosed with MS (all known traditional phenotypes including relapsing remitting, primary progressive, secondary progressive), with at least one sNFL result, and MRI available will be included.

Results: Data from 350 participants are included. Demographic and clinical variables, sNFL levels, MRI lesion distribution and accrual characteristics are collected. Unsupervised machine learning clustering and feature importance analyses will be conducted using the Scikit-learn package in Python, with train/test/validation dataset splits. For all analyses, dataset is randomly split in train, test and validation sets.

*Conclusion:* This study will enhance understanding of sNFL trajectories across MS phenotypes and stages, offering insight into disease activity pattern.

## Electric field versus temperature effects of intratumoral modulation therapy (IMT) on glioblastoma cell culture

V. Luo, E. Wong, M. Hebb, E. Iredale, A. Elsaleh, T. Zhang, S. Schmid, T. M. Peters

Importance: Glioblastoma (GBM) is a brain cancer with a median survival of 15 months. A proposed treatment termed intratumoral modulation therapy (IMT) involves applying low-intensity, intermediate-frequency electric fields to inhibit tumour growth. While in vitro and in vivo studies have demonstrated IMT's anti-tumoral effects, the heat given off by electric fields (Joule heating) raises the temperature in vitro, presenting a confound during in vitro IMT experiments.

*Objective:* To determine both the electric field effects and the temperature effects of in vitro IMT treatment on GBM cells.

Design and Participants: Patient-derived GBM cells transfected with luciferase underwent 3-day treatments: conventional IMT (heat and fields present); fields-only IMT, or heat-only treatments (39°C and 41°C). A custom printed circuit board delivered electric fields to GBM cells in a 24-well plate with temperature probes centred in wells. Fields (1.0 and 1.5 V/cm intensity, 200 kHz frequency) were produced by a 4-channel waveform generator. After 3 days' stimulation, cell viability was assessed through bioluminescence imaging. The cell viability after IMT treatment normalized to sham controls (IMT hardware present but no fields). Normalized cell viability values were displayed as the mean ± SEM.

Results: At 1.0 V/cm IMT intensity, the GBM cell viability with heat and fields applied was lowest at 0.29  $\pm$  0.02 (n = 8 IMT; n = 8 sham); with fields only, cell viability was 0.55  $\pm$  0.04 (n = 8 IMT; n = 8 sham); and with heat only (39°C), cell viability was 0.40  $\pm$  0.03 (n = 6 treatment and control each). For 1.5 V/cm IMT intensity, the cell viability with heat and fields was 0.08  $\pm$  0.01 (n = 3 IMT; n = 4 sham); with fields only, cell viability was 0.47  $\pm$  0.04 (n = 4 IMT; n = 8 sham); and with heat only (41°C), cell viability was 0.12  $\pm$  0.03 (n = 6 treatment and control).

Conclusions and relevance: The results indicate that the electric field effects of IMT alone are effective at lowering GBM viability, while demonstrating the significant role of heat during in vitro IMT; this supports further investigations of IMT as a glioblastoma therapy.

## Patient-Derived Xenografts in Immunodeficient SRG Rats as a Novel Orthotopic Model of Glioblastoma

Elizabeth Fenton, Niveen Fulcher, Rehanna Kanji, Abdulla Elsaleh, Tony Zhang, Cleusa De Oliveira, Lohiny Balendran, Susanne Schmid

Importance: Glioblastoma multiforme (GBM) is the most aggressive and common primary brain tumor, with limited treatment options and poor prognosis, necessitating improved preclinical models for therapeutic development. The Sprague Dawley-Rag2/Il2rg Knockout Rat (SRG RatTM) is an emerging immunodeficient rat oncology model that represents a promising platform for intracranial GBM xenograft studies.

*Objective:* To determine whether patient-derived GBM cells grow robustly in the SRG RatTM and whether this constitutes a translational preclinical model.

Design and Participants: Patient-derived GBM cells (GBM17, GBM23, and GBM93), obtained from surgical resections, were transduced to express tdTomato-luciferase. These GBM cell lines were subsequently used for stereotaxic implantation. Adult SRG RatsTM were anesthetized with isoflurane and placed in a stereotaxic frame. A unilateral burr hole was drilled at the following coordinate from bregma: anteroposterior + 1.2 mm, lateral + 3.0 mm, dorsoventral - 6.5 mm. Animals received 1 × 106 GBM17 or GBM23 cells in 10  $\mu$ L PBS—injected unilaterally at a rate of 0.2  $\mu$ L/min using a 10  $\mu$ L Hamilton syringe. Tumor growth was monitored using bioluminescence imaging (BLI) for up to 13 weeks. At endpoint, brains were extracted, and post-mortem MRI was performed to confirm tumor presence.

Results: GBM17 and GBM23 cells were each implanted into n = 2 male and n = 2 female SRG Rats<sup>™</sup> (n = 4 per cell line). Two rats implanted with GBM17 exhibited increasing BLI signals, with post mortem MRI confirming obvious tumors at 13 weeks post-operation. The other two rats implanted with GBM17 did not show increases in BLI signals. All rats implanted with GBM23 exhibited increasing BLI signals, with post-mortem MRI confirming obvious tumors in three of these rats. GBM93 implants are scheduled to be performed, and preliminary data will be available soon.

Conclusions and Relevance: These findings indicate that GBM cells can successfully engraft and grow in SRG Rats™, highlighting the model's promise as a preliminary model for preclinical GBM research. Additional investigations involving larger sample sizes and diverse patient-derived cell lines are warranted to confirm reliability and reproducibility before widespread adoption into clinical or therapeutic research applications.

# **Evaluating Spatial Correspondence of Multimodal MRI via Anatomical Landmarks**

J. Zhao, A. Taha, M. Abbass, G. Gilmore, C. Zajner, V. Liu, H. Vahidi, A. Thurairajah, A. R. Khan, J. C. Lau

Introduction. In clinical settings (e.g., stereotactic neurosurgery), errors on the order of ~2 millimeters (mm) are the difference between optimal therapy and complications. Prior studies report registration errors ranging from 1-5 mm, underscoring the need for more sensitive and descriptive evaluation metrics than the currently used voxel-based overlap metrics, which tend to be insensitive to focal misregistrations. We propose the use of homologous anatomical fiducials (AFIDs) which enable a millimetric and vectorized evaluation of registration errors that is more in-line with neurosurgical practice. The present study aims to evaluate whether 34 selected AFIDs surveying the human brain can be accurately placed by novice and expert raters to evaluate image registration across T1w and T2w MRI. Six human raters were recruited to place 34 AFIDs (protocol openly released: https://ataha24.github.io/afids-protocol/index.html) on open-source datasets of paired T1w and T2w MRI acquired at 3T and 7T from 10 healthy participants.

*Methods.* We computed the reliability and accuracy of AFID localization via the anatomical fiducial localization error (AFLE) that describes the variability of AFID placement on one scan between raters as well as via the anatomical fiducial registration error (AFRE) which compares the location of an individual AFID point to the mean location of a template AFID point.

Results. The participants were 25-41 years of age (n = 3 females, n = 7 males). The mean AFLE across all scans and AFIDs was 1.03 + / - 0.55mm and the error between AFID localization on 3T and 7T MRI scans was 0.65 + / - 0.35mm (7 of 34 AFIDs were localized more accurately on 7T MRI). Additionally, the mean AFRE was statistically higher (p &It; 0.001) on 3T (3.12 + / - 1.93mm) when compared to 7T scans (2.86 + / 1.94mm).

Conclusion. This study has validated 34 AFIDs as a reliable and sensitive tool for T2w image registration, striving towards better standardization of neuroimaging and clinical workflows that enhance our understanding of brain structure and function. Future work will expand this protocol to other commonly used imaging modalities (e.g., DWI and CT) and on a clinical dataset.

# Anxiety differentially predicts cognitive flexibility in healthy older adults and patients with Parkinson's disease

G. Badwal, K. Van Hedger, K. Patel, O. Monchi, I. Kathol, H. Ganjavi, R. Camicioli

*Importance:* This study highlights how sex differences and anxiety influence cognitive flexibility in healthy older adults and patients with Parkinson's disease (PD) without dementia or depression.

Objective: To examine the relationship between cognitive flexibility and anxiety in a model accounting for age, sex, years of education, diagnosis of Parkinson's disease (PD), and disease duration.

Design & Participants: Multi-site data from healthy older adults and patients with PD tested ON dopaminergic medication were combined for analyses. Participants >80 years old and those with Montreal Cognitive Assessment (MoCA) <24 were excluded from the study. Anxiety and depression were assessed with questionnaire measures, and participants with clinically significant depression were excluded from the study. MANOVA was used to test for sex differences in cognitive performance. Linear regression was used to identify predictors of cognitive flexibility, measured as the time difference between Trail Making Test A and B (TMT B-A). Longer TMT B-A durations indicated lower cognitive flexibility.

Results: 292 participants (144 female, 159 PD) met the inclusion/exclusion criteria. MANOVA revealed significant sex differences in patients with PD such that female patients (M = 27.593, 95% CI 27.131 – 28.055) outperformed male patients (M = 26.848, 95% CI 26.514 – 27.181) on the MoCA, F(1, 157) = 6.547, p = .011,  $\eta$ p2 = .040. This trend was not observed in healthy adults. Our regression model explained 19.910% ( $R^2$ Adjusted = .179) of the variance in TMT B-A durations, F(7, 284) = 10.090, p &It; .001. Sex was a significant predictor of TMT B-A duration, t = 2.242, p =.026, R2partial =.017, and we found a significant anxiety-PD interaction such that cognitive flexibility was more severely impacted by anxiety in patients with PD than in controls, t = 2.675, p = .008, R2partial = .025.

Conclusions & Relevance: This study highlights the need for sex-specific care provisions to manage cognitive impairment in PD. Furthermore, these findings suggest that anxiety may underlie cognitive flexibility impairment in both healthy older adults and patients with PD. Future studies should investigate the neurobiology of anxiety and cognitive flexibility in healthy adults and PD populations.

# The co-localization of pThr175 tau and DnaJC7: Implications for amyotrophic lateral sclerosis

J. Palik, K. Volkening, N. Donison, M. Hintermayer, M. Duennwald, M. Strong

*Importance:* DnaJC7 is a J-domain chaperone protein that functions in protein folding and interacts with tau. Misfolded tau is found in many neurodegenerative diseases including amyotrophic lateral sclerosis (ALS) with cognitive impairment, Alzheimer's disease, and chronic traumatic encephalopathy (CTE). Tau pathology is preceded by phosphorylation at threonine 175 (pThr175 tau), although the functional significance of the tau interaction with DnaJC7 remains poorly understood.

Objective: To investigate the expression of DnaJC7 and pThr175 tau during the progression of tau pathology in a traumatic brain injury (TBI) model, and human ALS and CTE brain tissues.

Design: A moderate TBI model was induced in Sprague-Dawley rats using a single controlled cortical impact to recapitulate tau pathology seen in CTE. Immunohistochemistry and immunofluorescence were performed to examine DnaJC7 and pThr175 tau expression in cortex and hippocampal tissue from postmortem ALS and CTE cases, as well as in brain tissue from the TBI rodent model. Additionally, in vitro studies were conducted using HEK293T cells exposed to sodium arsenite, an oxidative stressor, to examine DnaJC7 and pThr175 tau expression over 72 hours via western blot analysis.

Results: In the rodent TBI model, we observed a significant increase in total DnaJC7 and pThr175 tau expression in the hippocampus, however co-localization of DnaJC7 and pThr175 tau was significantly decreased 10 days post-injury compared to non-injured controls. Furthermore, positive staining for DnaJC7 was increased in oligodendrocytes and hippocampal neurons in ALS tissue, and the base of sulci in human CTE tissue. Alternatively, oxidative stress did not significantly increase DnaJC7 expression in vitro.

Conclusions and Relevance: These findings suggest that DnaJC7 plays a role in tau pathology and that its interaction with pThr175 tau is disrupted in diseased states. The observed reduction in the DnaJC7-tau co-localization in the TBI model suggests that the function of DnaJC7 may be altered during tau pathology progression. Further studies are required to elucidate the mechanistic basis of the dissociation of DnaJC7 from tau, and its implications for neurodegenerative disease pathogenesis.

# Socioeconomic Disparities in the Health Outcomes of Women with Epilepsy: A Cross-Sectional Study

A. Meira, C. Redhead, M. Elnazal

*Importance:* Women with epilepsy (WWE) face distinct healthcare challenges due to gender-specific risks and outcomes. This study highlights the how social economic factors shape health outcomes of women with epilepsy.

*Objective:* To evaluate the influence of socioeconomic disparities in health outcomes for Canadian women with epilepsy (WWE) concerning folic acid counselling, unplanned pregnancies, contraceptive use, and bone health.

Methods: In 2022 a cross-sectional anonymous survey was launched in the Epilepsy Monitoring Unit and outpatient epilepsy clinic at University Hospital in London, Ontario, Canada. The survey was open to any adult (18+) living with epilepsy who identifies as a woman or was assigned the female sex at birth.

Results: A total of 127 surveys were completed. Participant's ages ranged from 18 to 66. 89.2% (n=71) of participants were White. 71% (n=68) of participants had income less than \$50,000 dollars per year, and 70.3% (n=71) attained a college or university education. 67.7% (n=42) of low-income participants received folic acid counselling compared to 70% (n=7) of high-income participants. 58.3% (n=21) of low-income participants had unplanned pregnancies, compared to 22.2% (n=2) of high-income participants. 65.2% (n=15) of women with a low income were not using contraceptives compared to 60% (n=3) of women with a high income. The most commonly used anti-seizure medications for WWE with low-income are lamotrigine used by 47.11% (n=32), clobazam used by 30.9% (n=21), brivaracetam used by 26.4% (n=18) and carbamazepine, used by 22.1% (n=15). Compared to WWE with high-income were lamotrigine was used by 50% (n=14), brivaracetam by 26.4% (n=18), clobazam by 14.3% (N= 4) and carbamazepine by 7.14% (n=2).

Conclusion: WWE are more likely to earn below \$50,000 despite a large proportion having completed post-secondary education. Women with a low income are less likely to receive folic acid counselling, more likely to have unplanned pregnancies, and be prescribed older medications. More research is needed to understand these associations between lower income and lower levels of education and epilepsy management.

## Using Striatal Microstructural Integrity to Examine Allocentric Visuospatial Dysfunction and Motor Laterality in Parkinson's Disease

K. Mutambayi, K. Van Hedger, P. MacDonald

*Importance:* Brain microstructural integrity reflects the organization of gray and white matter tracts, and abnormalities in both have been implicated in Parkinson's disease (PD). Since striatal dysfunction is a hallmark of PD, assessing changes to striatal microstructure may help link these abnormalities to PD-related cognitive and motor symptoms.

Objectives: This study explores whether asymmetric microstructural changes in right-parietal tractography-based parcellations of the striatum can predict visuospatial impairment in PD. We also sought to examine how these changes relate to motor symptom manifestations, including symptom type (akinetic-rigid [AR] vs. tremordominant [TD]) and lateral asymmetry of motor symptoms (right- vs. left-asymmetric).

Design and Participants: We analyzed data from 379 participants (281 with PD and 98 healthy controls [HC]) from the Parkinson's Progression Markers Initiative (PPMI) and the Canadian Consortium on Neurodegeneration in Aging (CCNA). Striatal microstructural integrity was assessed using mean diffusivity (MD) and fractional anisotropy (FA), while visuospatial orientation was measured with Benton's Judgment of Line Orientation Task (BJLOT). To examine microstructural asymmetries, we computed an asymmetry score for each participant based on left vs. right striatal MD and FA measures, normalized against HC data. Motor symptom type and laterality were assessed using the Movement Disorder Society – Unified Parkinson's Disease Rating Scale (MDS-UPDRS) Part III, while general cognitive ability was evaluated using the Montreal Cognitive Assessment (MoCA).

Results: Among 379 participants, 160 were female and 219 were male. Significant group differences were found for age (F(1, 377) = 5.653, p = 0.017), sex ( $\chi^2$  = 22.857, p < 0.00001), and MoCA scores (F(1, 377) = 6.8986, p = 0.009), with the HC group performing better. In the HC group, males outperformed females on BJLOT scores (p &lt; 0.001), while no sex differences were observed in the PD group. Kolmogorov-Smirnov tests showed significant deviations from HC in striatal MD asymmetry distributions (D = 0.39502, p &lt; 0.00001). No significant deviations were observed for FA distributions. Regression models indicated that MoCA scores ( $\beta$  = 0.2649, SE = 0.0703, t = 3.768, p = 0.000205) and age ( $\beta$  = -0.0675, SE = 0.0220, t = -3.063, p = 0.00243) were significantly correlated with BJLOT performance, while MD and FA asymmetries were not.

Conclusions and Relevance: Although our findings suggest that striatal microstructural asymmetries may contribute to PD-related changes, these asymmetries may be too subtle to predict visuospatial impairment over and above general cognitive ability and age. Future research should focus on more precise posterior parietal parcellations of the striatum to better capture the small effect sizes that may explain the relationship between striatal microstructure, visuospatial dysfunction, and motor symptom manifestations in PD.

## BiTemporal Epilepsy Outcomes in Patients investigated with Stereoelectroencephalography

N. Nasrkhani, J. Lau, K. MacDougall, D. Steven, J. Burneo, G. Pellegrino, A. Suller-Marti

*Importance:* Temporal lobe epilepsy (TLE) is the most common form of drug-resistant epilepsy (DRE), and bilateral TLE (BTLE) occurs in 20–35% of cases. Optimal management of BTLE remains unclear due to limited evidence and small sample sizes in prior studies.

Objective: The primary objective of our study is to assess seizure outcomes in BTLE patients investigated with stereoelectroencephalography (SEEG) and to compare the effectiveness of different treatment modalities. The secondary objective is to further characterize BTLE as a heterogeneous group based on SEEG findings, neuroimaging results, and neuropsychological assessments.

Design and Participants: This retrospective study analyzed 25 patients with BTLE who underwent SEEG at the LHSC Epilepsy Program between 2018 and 2024. Collected data included demographics, seizure frequency, neuroimaging findings, and treatment outcomes. The primary outcome was seizure reduction, assessed across treatments using ANOVA and post-hoc tests (p &It; 0.05). Secondary analyses explored clinical characteristics (SEEG findings, neuroimaging, and neuropsychological assessments) associated with a >50% reduction in seizure frequency.

Results: Thus far, data from 25 patients (13 females,  $44 \pm 13.3$  years) have been collected. The most common treatment was vagus nerve stimulation (VNS) (N=10), followed by clinical management (N=6), resective surgery (N=6), responsive neurostimulation (RNS) (N=2), and deep brain stimulation (DBS) (N=1). The most effective treatments were resective surgery (84% seizure reduction) and clinical management (68% seizure reduction) followed closely by VNS (65% seizure reduction). The mean ( $\pm$  SD) follow-up period after treatment was 21.6  $\pm$  20.34 months.

Conclusions and Relevance: Despite the limited sample size, findings suggest that resective surgery and clinical management of BTLE such as medication adjustments, may offer improved seizure management for BTLE patients. Further research with larger cohorts is needed to confirm these findings and guide clinical decision-making.

# POSTER PRESENTATIONS Session # 1 KC 006

# The impact of localization and registration accuracy on estimates of deep brain stimulation electrode position in stereotactic space

M. Abbass, A. Taha, G. Gilmore, B. Santyr, A. Chalil, M. Jog, K. MacDougall, A. Parrent, T. Peters, J Lau

*Importance:* Deep brain stimulation (DBS) relies on millimetric accuracy for optimal clinical outcomes. Registration of patient imaging to stereotactic space is essential for studying DBS effects across populations, yet the impact of registration accuracy on electrode localization remains poorly quantified.

*Objective(s):* To determine the extent to which registration accuracy influences estimates of DBS electrode position in stereotactic space and to quantify the contribution of misregistration errors using the anatomical fiducials (AFIDs) framework.

Design and Participants: This retrospective study included 89 patients with Parkinson's disease who underwent bilateral subthalamic nucleus DBS at a single center (2009–2018). Patients' preoperative and postoperative imaging were registered to a common stereotactic space using standard nonlinear registration techniques. Expert raters independently localized DBS electrodes and AFIDs, enabling assessment of registration accuracy.

Results: The study included 89 patients (mean age:  $60.54 \pm 6.12$  years; 31.46% female). Inter-rater localization distances for DBS electrodes and key anatomical fiducials were sub-millimetric (median: 0.63-0.74 mm). AFID registration errors (AFRE) ranged from 1.49 mm to 6.85 mm, with subcortical AFIDs near the DBS target showing the lowest errors. Covariation among AFREs at specific AFIDs indicated systematic spatial misregistration patterns. These spatial patterns explained 28% of the variance in electrode position along the axis of maximum variance, corresponding to a median displacement of 0.64 mm (range: 0.05-2.05 mm).

Conclusions and Relevance: Registration accuracy significantly impacts DBS electrode localization in stereotactic space, contributing to spatial variance that may influence group-level analyses. The AFIDs framework provides a millimetric estimate of registration accuracy, allowing separation of registration-related variance from other sources of electrode position variability. These findings support the use of AFIDs for quality control, optimization of registration parameters, and improved interpretation of DBS research outcomes.

# The effect of acute exercise on neuroelectric indices of cognitive control in epilepsy

M. Daub, G. Pellegrino

*Importance:* Impairment in executive functioning is common in people with epilepsy. Aerobic exercise is an accessible intervention that may benefit cognition.

*Objective:* To determine whether a bout of acute aerobic exercise will improve performance on a cognitive task as measured with behavioural and neuroelectric indices.

Design and Participants: 11 participants (as determined by sample size calculation) will be recruited from the epilepsy monitoring unit at London Health Sciences Center. Participants will be over the age of 18, have a diagnosis of epilepsy and not suffer any pre-existing medical conditions precluding exercise. Participants will participate in an Eriksen Flanker task before and after an acute bout of moderate aerobic exercise during the experimental condition, and before and after 30 minutes of quiet reading during the control condition. Each participant will participate in both conditions on separate days. Electroencephalography will be measured during the cognitive task and event related potentials including the error-related negativity, error positivity, P3, N2 will be measured.

Results: Results are pending. We hypothesize that after an acute bout of exercise, but not after quiet reading participants will demonstrate improved accuracy and response time. Additionally, we expect modulations in ERPs suggesting greater top down cognitive control during trials. This is demonstrated by a larger amplitude P3 across trials and larger amplitude N2 suggesting optimized processing of conflicting stimuli. After error commission, we expect a higher amplitude error related negativity and error positivity.

Conclusions and Relevance: The outcome of this experiment will add to a growing body of literature describing the effects of acute aerobic exercise on cognitive functioning in people with epilepsy. Aerobic exercise is an inexpensive and accessible intervention, though additional evidence is necessary to make any definitive claims regarding its benefits on cognition in people with epilepsy. The present study will add to this body of literature and better inform exercise recommendations in this population.

# Accuracy of Navigated Drilling Versus Low-Speed Motorized Drilling in Cervical Spine Surgery

A. Mastrolonardo, K. Pustovetov, M. Oppermann, V. Yang.

*Importance:* Cervical spine fixation with lateral mass and pedicle screws is a cornerstone of modern spinal surgery but has a substantial risk profile due to the cervical spine's relation to critical neurovascular structures. The primary driver of this risk is the initial act of drilling, which can cause damage or influence the ultimate screw trajectory, making optimization of this step paramount.

Objectives: Our primary goal was to examine the accuracy of two drilling techniques: manual probing hand drilling (HD) with twist drills and low-speed motorized drills (LSMD). We compared drilling trajectories and assessed the degree of cortical breaching. A secondary objective was to compare screw placement between surgeons of varying levels of experience.

Design: Twelve identical cervical spine models were mounted on polyurethane foam for mechanical stabilization, and reference CT images were obtained. Navigation was planned with a 7D surgical system, employing structured light for rapid, radiation-free registration. Drilling targeted the C1 lateral masses, C2 pedicles, C3-C7 right pedicles, and C3-C7 left lateral masses in half of the models, with the opposite pattern for the remaining. Six of the 12 spines were instrumented with HD and six with LSMD. Half of the screws were inserted by a junior resident, while the other half were inserted by a senior surgeon.

Results: Upon completion of the drilling, accuracy was assessed with two methods: spatial 3D comparisons were created with the 7D software, and the Neo classification system was applied for breach assessment. Analyses were performed, calculating Euclidean distances, pooled by drilling technique and surgeon. Bland-Altman plots visualized the agreement between planned and actual trajectories, identifying differences via chi-square tests.

Conclusions: While the project is currently underway, data is actively being prepared.

# Reducing Wait Times for Urgent Neurology Clinic Patients Using Quality Improvement Methodology

J. Al-Tawari, A. Florendo-Cumbermack, D. Zok, B. Pilgrim, K. Cotton

*Objectives:* Patients with urgent neurological issues who do not require admission but need timely Neurology assessment currently experience prolonged wait times at the Urgent Neurology Clinic (UNC), often up to three weeks. This project aims to reduce wait times to three business days by June 30, 2025, and sustain this improvement.

Design and Participants: Quality improvement methodology was used to analyze the problem. Key stakeholders include Neurology faculty, residents, UNC administrative staff, referring physicians, and decision support services. Data was gathered through surveys, focus groups, and referral tracking.

Methods: Surveys were administered to Neurology faculty and residents to evaluate inefficiencies in triage and referral processes. QI rounds and focus groups engaged stakeholders in identifying key issues and potential solutions. UNC administrative staff provided workflow feedback. Referral data tracking, supported by decision support services, helped analyze trends and define contributing factors. A triage criteria survey guided the development of a standardized triage process and improvements to the UNC referral form to enhance efficiency and reduce inappropriate referrals.

*Measures of Success:* The primary outcome measure is UNC wait time, tracked using a run chart. Process measures include declined referrals, inappropriate referrals received, and the number of patients seen daily. Balancing measures include physician satisfaction, administrative burden, and triaging time.

*Results:* Key contributors to prolonged wait times include high volumes of inappropriate referrals due to unclear clinic criteria, variability in triage decisions, and inconsistent patient volumes among neurologists.

Potential solutions include updating the referral form for more detailed clinical information and refining triage criteria using faculty feedback. UNC referral criteria will be disseminated to emergency physicians, family physicians, and triaging physicians to ensure appropriate referrals. Faculty development will focus on standardized triage criteria and alternative care pathways, such as directing concussion cases to the ABI clinic and dementia cases to the Ambulatory Geriatrics clinic.

Conclusion: This ongoing QI project aims to streamline referral and triage processes for timely urgent neurology care. Targeted interventions are expected to reduce wait times while maintaining efficiency and stakeholder satisfaction.

# Lack of Comprehensive Neural Antibody Testing: A Contributor to Diagnostic Delay in Autoimmune Encephalitis

J. Al-Tawari, MA. Tarnopolsky, JG. Burneo and A. Budhram

*Background:* Autoimmune encephalitis is an immune-mediated neurologic disorder, for which prompt recognition and treatment are crucial to prevent irreversible neurological damage. Neural antibody testing is integral to diagnosis, but limited testing panels may yield false-negative results and lead to to diagnostic delays.

Objectives: This report illustrates two cases of autoimmune encephalitis with diagnostic delay due to negative limited antibody testing, emphasizing the critical role of comprehensive neural antibody testing in timely diagnosis.

Methods: Case series.

Results: Two patients were evaluated: a 19-year-old woman presenting with subacute encephalopathy, focal seizures, and cortical/subcortical lesions (patient A), and a 26-year-old man with rapidly progressive cerebellar syndrome and encephalopathy (patient B). Both initially underwent limited neural antibody testing which was negative, resulting in diagnostic uncertainty and referral to neurometabolic evaluation for suspected mitochondrial disease. Both patients developed visible sequelae of neuroinflammation on neuroimaging, highlighting the importance of prompt diagnosis and treatment to mitigate irreversible structural injury. Comprehensive neural antibody testing performed later in the disease course eventually confirmed a diagnosis of autoimmune encephalitis in both patients (coexistent anti-GAD65 and anti-GABA(A)R detected in patient A, anti-mGluR1 detected in patient B). Both patients experienced clinical improvement following immunotherapy, but had neurologic disease sequelae.

Conclusions: These cases highlight that limited antibody panels may contribute to diagnostic delay in autoimmune encephalitis. Negative antibody results may significantly reduce suspicion for autoimmune encephalitis but, as illustrated by our cases, can be falsely reassuring if only limited testing has been performed. Comprehensive neural antibody testing is essential in patients with a high clinical suspicion of autoimmune encephalitis, even when initial results are negative. Prompt accurate diagnosis facilitates timely immunotherapy and may mitigate long-term neurologic disease sequelae.

# Prophylactic Endovascular Coiling Prior to Surgical Removal of Nail: Case Report and Literature Review of Cranial Nail Gun Injuries

A. Vivekanandan, A. Mastrolonardo, R Al-Bader, A. Mascarenhas, R. Johnston

*Importance:* Penetrating injury to the brain via a nail gun is uncommon, and thus there is no protocol for management. Surgical removal of the nail can inadvertently lead to significant hemorrhage if vascular damage has occurred. Therefore, cerebral angiography and endovascular management are crucial when there is suspicion for vascular injury. Pre-emptive endovascular coiling can play a critical role in preventing hemorrhage during surgical extraction.

Objective: Our primary objective is to review the literature on the management of cranial nail gun injuries and present a case where we prophylactically embolized the contralateral posterior communicating artery adjacent to the nail tip. This pre-emptive measure prevented potentially inaccessible catastrophic bleeding during surgical removal from the ipsilateral side of nail entry – an uncommon, but valuable technique.

Design and Participants: Case report of a patient with a self-inflicted nail gun injury to the brain and review of the literature on the management of cranial nail gun injuries. A comprehensive literature search was conducted through Scopus, Medline, Embase and Pubmed databases. Title/abstract and full text screening was performed with Covidence software.

Results: From a total of 1097 studies, 143 were included after screening. Mechanism of injury included accidents, assault and intentional self-inflicted injuries. The vast majority of patients were male. Presentation varied from a comatose state to GCS 15 with no neurological deficits. Complications included hydrocephalus, traumatic pseudoaneurysm formation, and infection. Pre-operative cerebral angiography was not standard but was typically performed when vascular injury was suspected. Management varied from observation to surgical removal of the nail, with or without endovascular management. Prophylactic coil embolization to avoid bleeding prior to removal of nail was seen in only 2 other cases.

Conclusions and Relevance: Cranial nail gun injuries occur in a variety of settings. Vascular injury represents a potentially devastating sequelae that requires prompt and effective treatment. We described a case where preoperative endovascular embolization of the posterior communicating near the nail tip prevented the possibility of devastating hemorrhage that would have been difficult to access intraoperatively.

# Evaluation of registration accuracy and precision in magnetic resonance images with relevance to stereotactic neurosurgery

D. Wong, A. Taha, G. Gilmore, B. Santyr, M. Abbass, T. Peters, J. Lau

*IMPORTANCE:* Brain image registration is crucial for precise targeting of brain structures for stereotactic neurosurgery. Common registration algorithms optimize image similarity metrics based on intensity. The assumption made is that this approach will also accurately and precisely register key anatomical brain structures.

*OBJECTIVE:* This study evaluates a standard image registration algorithm's accuracy and precision in registering key anatomical structures using a previously developed anatomical fiducials (AFIDs) framework.

DESIGN: Key anatomical structures in three publicly available and four locally acquired brain MRI datasets were annotated using the AFIDs framework. Multiple raters annotated the same AFIDs in a publicly available group template (Montreal Neurological Institute [MNI] MNI2009bAsym template). The average location across raters was considered the ground truth. The seven datasets were registered to the group template using a standard image intensity-based registration method. The AFIDs in these datasets were transformed into MNI space using transformation matrices derived from the registration.

The sample distribution for each AFID in MNI space was modelled using principal component analysis (PCA). Accuracy was assessed by calculating the Euclidean distance between the sample distribution's centroid and the ground truth location. Precision was assessed by calculating the simple and weighted, normalized means of the principal axes' eigenvalues.

A bootstrapped analysis was conducted to further assess accuracy. The distribution of the raters' AFIDs on the MNI template was used as the reference distribution. PCA was used to determine the centroid of both the sample distribution and the reference distribution. Bootstrapping was used to generate sample and reference centroid distributions with large n. The percent overlap between these distributions served as an additional accuracy metric.

RESULTS: Bootstrap analysis showed minimal overlap between sample and reference distributions for most AFID locations across datasets, suggesting that traditional image-similarity based registration lacks anatomical registration accuracy. Euclidean distance showed that well-defined anatomical structures (e.g., anterior/posterior commissures, genu, splenium, etc.) were more accurately registered, while periventricular structures were less accurately registered. The weighted, normalized mean of eigenvalues showed that almost all sample distributions were anisotropic and not normally distributed. Analysis of the simple mean of eigenvalues showed periventricular areas were least precisely registered.

*CONCLUSIONS:* The AFIDs framework can be used to quantify the accuracy and precision of the registration of key anatomical structures. The accuracy and precision metrics defined in this study could be optimized in novel image registration algorithms to help improve registration of anatomical structures.

# POSTER PRESENTATIONS Session # 2 KC 004

# Multiscale analysis of mesial temporal lobe epilepsy: Anatomo-Electrophysio-pathologic differentiation

PN Nambiar, K. Alorabi, J. Lau, A. Thurairajah, A. Suller-Marti

*IMPORTANCE:* Mesial temporal lobe epilepsy (mTLE) is now considered a heterogenous condition with variable long-term post-surgical outcomes. Hippocampal sclerosis (HS) is associated with different patterns of architectural changes in post-surgical histopathology.

High resolution MRI has not been previously used in combination with neither stereoelectroencephalography (SEEG) nor the histopatological results of the resected tissue. We believe that combining MRI, SEEG and histology will allow us to identify anatomical and physiological patterns not previously seen and establish different subtypes of mTLE.

*OBJECTIVES:* - Identify patients with suspicion of mTLE, pending to be implanted with SEEG, complete a high resolution MRI and hippocampus subfield reconstruction for each case.

- Identify the seizure onset zone and segment groups depending on the findings.
- Correlate the data obtained from the subfield hippocampus localization of the seizures using SEEG with the findings in the pathology obtained from their resection
- Classify different anatomical-histological-neurophysiological groups depending on epilepsy surgery outcomes (using Engel Classification).
- Establish predictor factors of good surgical outcomes in patients with mTLE.

DESIGN AND PARTICIPANTS: Retrospective analysis of patients with mTLE with 1) SEEG Patterns 2) MRI 3) Post temporal lobectomy tissue analysis 4) Engel Classification. HippUnfold method was used to segment hippocampus on MRI.

RESULTS: Of 109 patients investigated with SEEG, 11 patients were analyzed so far. Low voltage fast activity was seen in 215 seizures, low-frequency periodic spikes in 21, sharp activity at &It;13 Hz in 58, rhythmic spike sharp wave activity in 86, and other types were less frequent. MRI revealed unilateral mesial temporal sclerosis (MTS) in 6 (54.55%), bilateral MTS in 2 (18.18%), and was normal in 3 (27.27%) patients. Histopathology showed ILAE grade I in 3 (37.5 %), II in 4 (50 %), IV in 1 (12.5%) patient. 63.63% had Engel Class I at 6 months. HippUnfold analysis and SEEG electrode coregistration was done in one patient and will be attempted in the rest.

*CONCLUSION:* Our study highlights a strong correlation between SEEG findings and histological analysis in mTLE. A multidimensional classification will help predict long term outcomes.

# Mapping the Limbic Connectome Using in vivo Diffusion MRI: Feasibility and Reliability

D. Deniz, B. G. Karat, A. R. Khan, J. C. Lau

Importance: The limbic system is an essential network of brain regions and tracts that support emotion, memory, and behaviour, yet its structural connectivity remains incompletely characterized due to the challenges of non-invasive brain imaging, including low anisotropy in subcortical regions, and the small and complex nature of limbic structures. Diffusion MRI (dMRI) tractography provides a unique opportunity to recapitulate the white matter tracts of the limbic system, however, the reproducibility of these connections across independent imaging sessions has not been systematically evaluated.

Objective: To assess the test-retest reliability of limbic system tractography using the Human Connectome Project (HCP) test-retest database and to investigate the impact of tractography parameters on connectivity reproducibility.

Design and Participants: The HCP dataset is composed of 3T diffusion-weighted images acquired at 1.25 mm isotropic resolution, with multi-shell b-values of 1000, 2000, and 3000 s/mm². Anatomical selection of core limbic structures, including the hippocampus, amygdala, cingulate gyrus, mammillary bodies, and anterior thalamic nuclei was performed using FreeSurfer-based segmentations. We applied multi-shell, multi-tissue constrained spherical deconvolution (MSMT-CSD) to compute fibre orientation distributions (FODs) and used MRtrix3 for both ROI-seeded and whole-brain probabilistic tractography. Streamline filtering was performed using Spherical-deconvolution Informed Filtering of Tractograms (SIFT2) to correct for reconstruction biases. Connectivity matrices were generated using the apparent fibre density (AFD) between ROIs and were used to calculate the intraclass correlation coefficients (ICC) and weighted Dice Similarity Coefficients (wDSC) between the test and retest scans. We systematically evaluated the impact of step size and angular threshold on test-retest reliability. In addition to this, we integrated an ROI-seeded tractography module within the SCATTR pipeline, refining streamline selection based on anatomical constraints.

Results: Preliminary analysis with the MRtrix3 pipeline shows limbic tractograms (n = 45). Ongoing work includes generating tractograms with varying step sizes and angular thresholds as well as computing the reliability of the produced connectivity matrices.

Conclusion and Relevance: This study offers a feasible and reproducible framework for investigations into the limbic system, with potential applications in neuromodulation, neurodegenerative diseases, and psychiatric disorder research. The proposed parameter optimization strategy combined with ROI-seeded tractography provides critical insights for refining dMRI-based connectomic analyses, ensuring applicability in clinical and research contexts.

# Assessing heat shock transcription factor 1 as a therapeutic target in high-grade glioma

E. Fenton, N. Fulcher, R. Kanji, A. Elsaleh, C. D'Oliveira, S. Schmid, M. O. Hebb

Importance: High-Grade Gliomas (HGG), including Glioblastoma Multiforme (GBM) in adults and Diffuse Midline Glioma (DIPG) in children, are highly aggressive and treatment-resistant tumors with poor prognoses. The heat shock response, regulated by Heat Shock Transcription Factor 1 (HSF1), has emerged as a promising therapeutic target in various cancers; however, its specific role in HGG progression remains poorly understood.

Objective(s): To evaluate the therapeutic potential of HSF1 inhibition in HGG tumorigenesis in vitro and develop an optimized preclinical model for testing HSF1-targeting therapies.

Design and Participants: Patient-derived GBM and DIPG cell lines were treated with DTHIB, an HSF1 inhibitor, at various concentrations to assess its impact on tumor growth and viability. Cell proliferation was monitored using IncuCyte® live-cell imaging, while viability was assessed via bioluminescence imaging and MTT assays. Downstream effects of HSF1 depletion were examined through qPCR analysis of heat shock protein expression. For in vivo studies, patient-derived GBM and DIPG cells were implanted into the striatum of Sprague Dawley-Rag2/Il2rg Knockout Rats, an emerging immunodeficient model for oncology research. Tumor growth was tracked using bioluminescence imaging, with postmortem MRI used to confirm tumor presence and volume. Brain tissue was further analyzed through immunohistochemistry to quantify HSF1 expression.

Results: In vitro, DTHIB treatment reduced GBM cell growth (n=3 each cell line; p=0.0005 & p=0.0042) and viability (n=3 each cell line; p<0.0001) in a dose-dependent manner, while DIPG cells exhibited more variable responses. The qPCR analyses confirmed that DTHIB decreased expression of HSF1 target genes in GBM cells, including HSPB1 (n=3; p=0.0173), HSPA1A (n=3 each cell line; p=0.0236 & p=0.0007), and HSP90AA1 (n=3 each cell line; p=0.0035 & p=0.0358) after 24 hours. In vivo, tumors were detected via bioluminescence imaging and MRI, with tumors exhibiting higher HSF1 expression compared to contralateral brain (n=5 paired samples; p&lt;0.0001).

Conclusions and Relevance: These findings highlight the therapeutic potential of HSF1 inhibition in HGG tumorigenesis and further support its investigation as a treatment strategy. Additionally, the use of Sprague Dawley-Rag2/Il2rg Knockout rat xenografts enhances preclinical modeling, providing a valuable tool for further testing HSF1-targeted therapies in vivo.

## Pannexin 1 as a potential therapeutic target for glioblastoma multiforme

R. Kanji, D. Johnston, M. Huver, N. Fulcher, E. Fenton, A. Deweyert, M. Hebb, S. Penuela

*Importance:* Glioblastoma multiforme (GBM) is the most common malignant brain tumour, with a median survival time of 14 months despite standard treatment. Pannexin 1 (PANX1) is overexpressed in GBM relative to normal brain, and its inhibition reduces GBM growth in-vitro, warranting further investigation into its potential as a therapeutic target.

*Objective:* To characterize PANX1 expression in GBM tumour fragments, assess the effects of its inhibition or deletion in-vitro and evaluate preclinical models for studying PANX1 inhibition.

Design: GBM tumour fragments (N=7) and patient-matched non-neoplastic brain tissue (N=6) were stained for PANX1 using immunohistochemistry (IHC). PANX1 expression was also analyzed in patient-derived GBM cell lines, and CRISPR/Cas9-generated PANX1 knockout (KO) cells along with pharmacological inhibition with Probenecid (PBN) and Spironolactone (SPIR) were used to investigate the expression of cancer-promoting molecules. PBN and SPIR were tested in combination with temozolomide (TMZ) to evaluate the effects on GBM cell growth. In addition, PANX1 expression was examined in the rat glioma cell line F98 to investigate its suitability for syngeneic allograft models.

Results: PANX1 had diffuse and variable expression in GBM tumours. PANX1 deletion in patient-derived GBM cells significantly reduced YAP expression, a key regulator of GBM growth and migration. However, pharmacological inhibition did not replicate these effects, suggesting a channel-independent role of PANX1 in GBM. Treatment with SPIR and PBN did not alter the effects of TMZ on GBM growth in-vitro, and PBN alone reduced cell growth to the same extent as TMZ alone. In F98 rat glioma cells, PANX1-25K was the dominant isoform, and only SPIR significantly reduced cell growth. In-vivo, PANX1 was detected in human GBM xenografts but showed low expression in F98 allografts, suggesting limitations in using the F98 model for PANX1-full-length targeted studies.

Conclusion and Relevance: Our findings suggest that PANX1 plays a role in GBM, potentially through mechanisms beyond its channel function. While PANX1 deletion impacts key oncogenic molecules, pharmacological inhibition does not mimic these effects, emphasizing the complexity of PANX1's role in GBM. Additionally, differences in PANX1 isoform expression across rat models highlight the need for careful model selection for PANX1-25K or PANX1-full-length targeted studies.

# Listening to Learn: Designing a Lumbar Puncture Module Based on Medical Learner Feedback

E. Lin, W. Koopman, D. Dilkes, C.S. Casserly

Importance: Medical training on lumbar puncture (LP) techniques is often based on young, thin, ablebodied white males, underrepresenting patients with diverse body types. Thus, learners may feel underprepared when encountering patients with different anatomies or complex needs. To address this, we created an LP module that demonstrated the procedure across diverse bodies. This module was developed through a co-design framework in collaboration with patients. Medical learners, as the primary audience for the module, are an equally important source of design information. This year, we focused on improving the module learning experience by gathering in-depth learner feedback and integrating it into the module.

*Objective:* To assess learner perspectives on the module's effectiveness and use qualitative feedback to guide iterative improvements on learning experience and module content.

Design and Participants: We conducted three focus groups with 13 medical learners: one with neurology and neurosurgery residents (n=3), and two with Schulich medical students (n=5 per group). Sessions were led by Dr. Wilma Koopman, using a qualitative, open-ended question style to elicit learner reflections on the module's content, delivery, and clinical relevance. Discussions explored experiences with trauma-informed care, challenges in LP technique, and suggestions for module enhancement. Transcripts were analyzed thematically.

Results: Learners valued the module's inclusion of diverse body types and recognized its role in challenging assumptions about the 'normative' body. Four key themes emerged from learner feedback. Clinical Relevance: Residents recommended clarifying normal opening pressure values and adding guidance on troubleshooting low CSF flow. Trauma-Informed Care: Residents felt the module acknowledged the invasive nature of LPs but requested more examples of empathetic language and communication techniques. User Experience: Medical students recommended improved navigation, more consistent voiceovers, and clear transitions between module sections. Curricular Integration: All participants agreed that the module would be most impactful when paired with supervised, hands-on training.

Conclusions and Relevance: Learner feedback was instrumental in refining the module's content and design. Our iterative, co-designed approach improved the module's educational value and modelled inclusive, patient-centered procedural care. By listening to learners, we strengthened an innovative teaching tool that prepares future clinicians to perform LPs with greater confidence, compassion, and skill.

# Hippocampal Volume Positively Predicts Memory Function in Patients with Infantile Hydrocephalus and Healthy Controls

R. Ragguett, L. Meng, D. Adil, R. Eagleson, S. de Ribaupierre

*Importance:* Cognitive outcomes following infantile hydrocephalus are poorly understood. Further characterizing these outcomes following treatment for hydrocephalus may help to set expectations for patients and families.

*Objectives:* Determine whether children with treated hydrocephalus have worse memory function compared to healthy controls and assess if hippocampal volume is a predictor of memory function.

Design and Participants: In our cross-sectional, convenience sample study, we screened 68 participants - 21 patients with ventriculoperitoneal shunt treated hydrocephalus and 47 healthy controls. Participants were included if they completed an anatomical T1 scan, neuropsychological testing, and were under the age of 13. Participants completed the working memory task Mr. Peanut. Hippocampal volumes were extracted and verified by an expert. Hippocampal volumes were age and intracranial volume corrected, and Mr. Peanut scores were age corrected, each using an analysis of covariance approach.

Results: Fifty-four participants were included in the study - 37 healthy controls (18 females, age  $\bar{x}\pm\sigma$  = 9.15 ±2.16 years) and 17 children with hydrocephalus (8 females, age  $\bar{x}\pm\sigma$  = 9.49 ±1.55 years). There was no significant difference for age and sex between groups (p > 0.05). Healthy controls had larger right, left, and total hippocampal volume compared to hydrocephalus patients (all p < 0.005). Healthy controls performed significantly better on the Mr. Peanut task ( $\bar{x}\pm\sigma$  = 2.18±0.65) compared to hydrocephalus patients ( $\bar{x}\pm\sigma$  = 1.69±0.50, p = 0.0014). The multiple regression model was significant (adj R2 = 0.20, F(3, 50) = 5.411, p < 0.0027). A larger hippocampal volume ( $\beta$  = 1.67e-04, p = 0.05) predicted a greater Mr. Peanut score. Gender and whether the participants had hydrocephalus, were not significant predictors of Mr. Peanut performance.

Conclusions and Relevance: In summary, healthy controls have a greater hippocampal volume and perform better on memory tasks compared to children with hydrocephalus. Further, greater hippocampal volume was a significant predictor of better memory performance. Our results agree with a recent meta-analysis in healthy children which demonstrated that greater hippocampal volume was associated with better performance on memory tasks. We continue to contribute to the limited literature characterizing the cognitive deficits in infantile hydrocephalus post treatment.

## Care partner characteristics and reporting of symptoms and progression in FTD

K. Coleman, G. Zou, E. Finger

*Importance:* Studies in Frontotemporal dementia often report on primary outcomes that rely heavily on care partner reported measures due to participants' significant loss of insight into their own symptoms. Observer based reporting makes exploring possible sources of care partner based variability important to understand and measure.

*Objectives:* To determine whether care partner characteristics are associated with FTD symptoms and progression as reported by care partners.

Design and Participants: The National Alzheimer's Coordinating Centre has collected clinical, symptom and neuropsychological data in neurodegenerative diseases since 2005. This study plans to perform secondary data analysis on a convenience sample of data collected from participants with a diagnosis of frontotemporal dementia including language variants. To be included, participants must have completed at least one baseline visit and/or to look into how progression of disease is reported a full baseline and a 1 year follow up visit.

Results: Analysis has not yet been completed.

Demographics will be reported by FTD subtype, sex, age, education, severity at baseline, care partner relationship, care partner sex, care partner education and care partner age. The main outcomes of this study will be based on the revised self-monitoring scale, Interpersonal reactivity index and Neuropsychiatric inventory-Q and their association with a care partner characteristic after adjusting for participant baseline severity rating.

Conclusion and Relevance: This study hopes to identify areas of future research opportunities to better elucidate the impact of care partner characteristics on symptom and progression reporting in FTD. Identification and management of these potential sources of bias may impact future clinical trial design and analysis in FTD.

# The effects of antiseizure medications on sexual hormones and functions in males with epilepsy: a systematic review and meta-analysis

R.G. Couper, P. H. Espino, M.P. Vicuna, J.G. Burneo

The fertility effects of antiseizure medications (ASMs) have been highlighted in females of reproductive age, however, the effects in males have not been extensively analyzed. This review aims to summarize the existing evidence of how ASMs affect sexual hormones and functions in males with epilepsy.

We searched Embase, PubMed, and Medline databases in January 2024 to identify studies measuring sexual hormones, sexual function, or sperm parameters of males with epilepsy taking any ASM except valproic acid and were compared to a control group. A systematic review summarizing the effects of valproic acid on sexual function was published in 2018, therefore we excluded valproic acid to avoid duplicating existing evidence. Risk of bias assessments were specific to the study type and included the National Institute of Health (NIH) Quality Assessment Tool for Observational Cohort and Cross-Sectional Studies, NIH Quality Assessment Tool for Before-After (Pre-Post) Studies, and the Cochrane Risk of Bias-2 tool for randomized trials.

The systematic review included 32 studies, and the meta-analysis included 22 studies. Using random effect models, we calculated mean differences or rate ratios for studies assessing the association between ASMs and male sexual hormones or functions. Analyses were run for each combination of individual ASM or ASM characteristic, outcome, and comparison group. Males taking oxcarbazepine had significantly higher levels of testosterone, luteinizing hormone, and follicle-stimulating hormone compared to healthy controls. Conversely, there was no evidence of differences in any outcomes between levetiracetam or lamotrigine and comparison groups. Analyses that included untreated males with epilepsy rarely differed from males taking ASMs, highlighting the potential importance of epilepsy on altered sex hormones and functions. However, results should be interpreted cautiously as many analyses included only a few studies and had high heterogeneity.

# POSTER PRESENTATIONS Session # 2 KC 006

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## **Useless Hand (of Oppenheim) Syndrome**

#### J. Al Kharbooshi

*Importance:* Useless hand (of Oppenheim) syndrome is a rare yet typical manifestation of multiple sclerosis (MS) that is often underrecognized and might cause an extensive and possibly unnecessary investigations for what is a known problem in MS. This classic syndrome is easy to recognize once it's known and is associated with typical neuroimaging findings.

Objective: To report a patient with useless hand (of Oppenheim) syndrome with neuroimaging findings that led to a diagnosis of MS.

Design/Participants: Case report

Results: A 47-year-old man presented to clinic with right hand numbness. He was diagnosed with clinically isolated syndrome 10 years prior. Now, he had a three-day history of right thumb and index finger numbness which then progressed to affect his right arm and right leg. He had difficulty using his right hand. Physical examination revealed pseudoathetosis of his right hand. His strength was normal. He had normal sensation on pinprick testing of the face, arms, and legs. He had markedly abnormal proprioceptive testing in the right arm compared to the left arm. Magnetic resonance imaging revealed a short-segment right posterolateral cord lesion at upper C2 that demonstrated incomplete peripheral enhancement.

Given his clinical history, examination, and imaging findings, he was diagnosed with relapsing remitting multiple sclerosis. His presenting syndrome was consistent with the useless hand (of Oppenheim) syndrome. He improved with pulse steroids and was subsequently started on disease modifying therapy.

Conclusion and relevance: Hermann Oppenheim initially described the useless hand phenomenon or the "de-afferented hand secondary to posterior column demyelination" in 1911 as a specific albeit rare manifestation of multiple sclerosis, in which a hand loses its functional utility due to dorsal column (position, vibration, two-point discrimination) sensory deficits with occasional presence of involuntary movements resembling that of a sensory ataxia, while maintaining relatively intact motor function. Oppenheim observed a connection with high cervical cord lesions predominantly affecting the posterior column. While the prevalence of useless hand syndrome remains uncertain, it is a rare presentation of multiple sclerosis.

## Glioblastoma Masquerading as Metastasis in a Routine Follow Up of a 79-Year-Old Female

R Moshref, A Elashaal

*Importance:* Glioblastoma needs to be identified as a differential in multiple brain lesions, because a multimodality treatment is needed with gross total resection, radiotherapy, and chemotherapy to increase survivability to a median of 21 months.

*Objectives:* To identify that multiple glioblastomas are a rare presentation that represent 12% of cases of glioblastoma and which can be in the form of multicentric or multifocal.

Design and Participants: Case report.

Results: We report a 79-year-old female, a previous smoker, who was complaining of headache and generalized weakness, who was discovered to have multiple brain lesions. She was treated with craniotomy and partial resection. Final histopathology showed glioblastoma IDH1 R123H wild type, World Health Organization (WHO) grade 4. She was then transferred to hospice care after the goals of care meeting was done.

Conclusions and Relevance: Glioblastomas have a dismal prognosis overall despite multidisciplinary management. In multiple brain lesions, glioblastoma should be one of the differentials.

## **Resident Well-being in Neurology**

#### R. Sawaya

*Importance:* Wellness and burnout are critical issues in medical education. Addressing these issues is essential for the well-being of residents and, ultimately, for patient care.

*Objective:* To identify stressors, evaluate existing wellness initiatives, and inform interventions to improve wellness among neurology residents.

Design and Participants: A longitudinal, anonymous online survey was conducted annually from 2023 to 2025. Participants were neurology residents (12-14 per year) at the London Health Sciences Centre. The survey included the Resident Wellness Scale and 5-point Likert scale ratings for overall wellness, wellness at home, and wellness at work, with free-text feedback options.

Results: In 2025, the average overall wellness score out of 5 was 3.9, with wellness at home (4.5) exceeding wellness at work (3.6). Overall wellness improved over the three years, with overall wellness scores of 3.0 in 2023, 3.4 in 2024, and 3.9 in 2025. The Resident Wellness Scale showed the highest ratings in the Social Support (SS) and Institutional Support (IS) domains, and lowest ratings in the Ability (AB) and Meaningful Work (MW) domains. The highest-rated items included: "Felt supported by your co-workers", "Knew who to call when something tragic happened at work", and "Had an enjoyable interaction with a patient". The lowest-rated items included: "Reflected on how your work helps make the world a better place", "Was eager to come back to work the next day", "You felt connected to your work in a deep sense". Differences were noted between junior and senior residents' ratings in the wellness domains, and these shifted over the years.

Conclusions and Relevance: This study highlights an improving but evolving landscape of well-being for neurology residents. While social and institutional support are strengths, addressing residents' sense of competence and meaningful work is critical. Disparities in wellness between home and work may require targeted interventions. These data suggest the need for ongoing qualitative data collection and tailored approaches for junior and senior residents to promote a more supportive residency experience.

# Bilateral fetal posterior communicating artery mirror aneurysms in the setting of subarachnoid hemorrhage

P. Chan, G. Hatipoglu Majernik, M. Boulton, S. Pandey

*IMPORTANCE:* Bilateral fetal variant PCA and mirror aneurysms on PCOMs in the same patient is a unique case presentation and according to our knowledge this is the first case report to present this entity.

OBJECTIVE(S): To demonstrate how anatomical variants can affect aneurysm treatment decision making where both endovascular and microsurgical treatments are available.

DESIGN AND PARTICIPANTS: This is a case report of a 90-year-old female patient presented with a subarachnoid hemorrhage.

*RESULTS:* On further investigations, she was found to have a right PCOM aneurysm which was thought to be the site of rupture hemorrhage. She was also found to have a mirror left PCOM aneurysm and bilateral fetal variant PCAs. The patient underwent a successful balloon-assisted coil embolization of the right PCOM aneurysm and recovered well.

CONCLUSIONS & RELEVANCE: While fetal-type variance of the posterior cerebral arteries is common, the co-existence of mirror PCOM aneurysms, with associated rupture as case report, has not previously been presented. Although the presence of a fetal variant PCA is associated with increased risk of aneurysms, it does not increase rupture risk of aneurysms. Treatment of fetal-type PCOM aneurysms requires particular considerations for preservation of the posterior cerebral artery.

# Systematic review: mental health outcomes in Guillain-Barré syndrome and chronic inflammatory demyelinating polyneuropathy

CMF. Li, S. Wong, C. Li, N. Fabiano, A. Iansavitchene, MW. Nicolle

*IMPORTANCE:* In Guillain-Barré Syndrome (GBS) and chronic inflammatory demyelinating polyneuropathy (CIDP), patients can experience significant mental health challenges that affect their quality of life. However, the burden of these mental health disorders in these populations remains unclear.

OBJECTIVE: To determine the frequency and risk of mental disorders in GBS and CIDP.

DESIGN AND PARTICIPANTS: A systematic review was conducted to identify primary studies that reported mental health outcomes in GBS and CIDP. Two independent reviewers screened studies, conducted full-text reviews, extracted data, and performed quality assessments; all discrepancies were resolved by a third party.

*RESULTS:* A total of 19 studies were included. In GBS, three studies used the ICD or DSM criteria and reported that up to 82% of patients were diagnosed with anxiety, 67% had depression, 25% had brief reactive psychosis, and 22% had post-traumatic stress disorder. While the risk of anxiety disorders following GBS normalized after three months, the risk of depressive disorders remained elevated for two years. In CIDP, 30-50% of patients reported mental health symptoms, but no studies formally reported mental health diagnoses. Active disease and neuropathic pain were associated with increased depressive symptoms in CIDP.

CONCLUSIONS AND RELEVANCE: In GBS and CIDP, patients may experience symptoms that fulfill criteria for mental health diagnoses, but the limited literature suggests that these disorders are often underdiagnosed and undertreated in these populations. In GBS, the risk of mental health disorders is highest in the acute period and remains elevated for up to two years. In CIDP, patients with active disease and neuropathic pain have worse mental health outcomes. Given the significant burden of mental health symptoms in these patients, clinicians should be encouraged to conduct timely assessments of risk factors and implement targeted interventions as part of comprehensive patient care.





