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THE DEPARTMENT OF CLINICAL NEUROLOGICAL SCIENCES, WESTERN UNIVERSITY PRESENTS

2024 CNS RESEARCH DAY

TUESDAY, JUNE 11, 2024

8:00 AM TO 4:15 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 2024 CNS Research Day on Tuesday, June 11th 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. Michael D. Hill.

I would like to take a moment to highlight our industry sponsors; Roche, Stryker, 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 for their commitment, Amanda at King's University, Michelle at Aramark and Adam our AV Support. 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 for her incredible planning of today's events.

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

Sincerely,

David A. Steven, MD, MPH, FRCSC, FACS
Professor of Neurosurgery
Richard and Beryl Ivey Chair
Department of Clinical Neurological Sciences
London Health Sciences Centre and
Schulich School of Medicine & Dentistry
Western University

EVENT ITINERARY

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.	**Keynote presentation** *Advancing the treatment of stroke* Dr. Michael D. Hill, MD, MSc, FRCPC, (FESO FAHA FCAHS FRSC O.C.) Calgary Stroke Program, Department of Clinical Neuroscience and Hotchkiss Brain Institute University of Calgary	**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 11:30 a.m.	**Oral Parallel Poster Session #1** *A series of 2-minute presentations.* *Q&A will commence during refreshment break*	**Basement Classrooms KC 005 & KC 006**
11:35 to 11:45 a.m.	**Refreshment Break** (continued) *Poster presentation Q&A*	**Garron/Spriet Lounge**
11:50 a.m. 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**

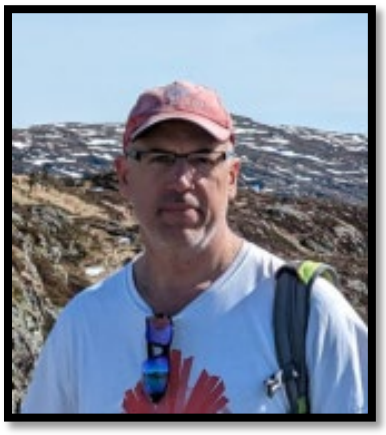
EVENT ITINERARY *(continued)*

1:05 to 1:45 p.m.	**Lunch**	**Garron/Spriet Lounge**
1:50 to 3:00 p.m.	**Oral presentation Session #3** *A series of 5-minute presentations.* *Each presenter will be allotted 3 minutes for questions.*	**Kenny Theatre**
3:05 to 3:35 p.m.	**Oral Parallel Poster Session #2** *A series of 2-minute presentations.* *Q&A will commence during refreshment break.*	**Basement Classrooms KC 005 & KC 006**
3:40 to 3:50 p.m.	**Refreshment Break** *Poster presentation Q&A*	**Garron/Spriet Lounge**
3:55 to 4:15 p.m.	**Closing Remarks and Awards** *Dr. Elizabeth Finger, Research Director, Department of Clinical Neurological Sciences*	**Kenny Theatre**

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

KEYNOTE ADDRESS

DR. MICHAEL D. HILL



Dr. Michael Hill is a Professor for the Departments of Clinical Neurosciences, Community Health Sciences, Medicine and Radiology at the University of Calgary. He is also Director of the Stroke Unit for the Calgary Stroke Program, Alberta Health Services.

Dr. Hill completed undergraduate training at McGill University in biochemistry and went on to the University of Ottawa medical school. He trained in internal medicine at the University of Ottawa and received his FRCPC (Internal Medicine) in 1997. Subsequently, he completed a neurology residency at the University of Toronto and received his FRCPC (Neurology) in 1999. Dr. Hill moved to Calgary to undertake a stroke fellowship and clinical epidemiology training at the University of Calgary and was appointed to faculty in 2001. He then completed his MSc thesis in 2003, and is currently Director of the Stroke Unit at the Foothills Medical Centre, Calgary Health Region.

Dr. Hill's research interests include stroke thrombolysis, stroke epidemiology, and surveillance and clinical trials. He is funded by the Canadian Institutes for Health Research (CIHR) and holds the Heart & Stroke Foundation of Alberta/NWT/Nunavut professorship in Stroke Research. He holds and has held operating and clinical trials grants from the CIHR, Heart & Stroke Foundation of Alberta/NWT/Nunavut and from various industry partners as well as NIH (NINDS). Dr. Hill has also received a number of awards, including the Barnett, The Pessin Award and the ARP merit award and the Performance Recognition award for his role in research and his outstanding publication record.

JUDGES

In addition to having our esteemed Keynote Dr. Michael D. Hill judge the presentations, we are thrilled to announce our 2024 judges;

DR. CHRYSI BOGIATZI

Dr. Chrysi Bogiatzi is an Assistant Professor of Neurology at the Department of Clinical Neurological Sciences, Western University since 2022 and she is leading the National Neurosonology Journal Club at the Canadian Stroke Consortium since 2021. Dr. Bogiatzi earned her medical degree at the Democritus University of Thrace in Greece, followed by a 2 years hands-on training in clinical Neurosonology, under the supervision of Dr. Georgios Tsivgoulis. She then completed a 2-year Masters Degree in Clinical Epidemiology at Western University, followed by 3 years research experience as a research associate in clinical trials in stroke prevention, under the supervision and mentorship of Dr. David Spence. Her Neurology residency was completed in 2021 at McMaster University, followed by 1-year clinical stroke fellowship at the University of Calgary. Dr. Bogiatzi has experience in transcranial and carotid ultrasound, clinical epidemiology and clinical trials, ischemic stroke subtypes, effects of intestinal microbiome in risk of stroke, stroke prevention and acute stroke management.

DR. SEBASTIAN FRIDMAN

Picture and biography not available at this time.

DR. TENEILLE GOFTON

Dr. Tenielle Gofton completed medical school at Dalhousie University (Halifax, Nova Scotia, Canada) followed by Neurology residency training at Western University. She has dual fellowship training in Hospice and Palliative Medicine at Memorial Sloan-Kettering Cancer Center (New York, New York, USA) and in Neurocritical Care and Electroencephalography at Western University. Dr. Gofton is currently an Associate Professor at the Schulich School of Medicine and Dentistry (Western University) in the Department of Clinical Neurological Sciences and has been a faculty member since 2012. She is the acting director of the Neurocritical Care fellowship training program. Dr. Gofton has been an invited speaker at national and international meetings and has received research grant support from national funding agencies. Her research interests and publications are on topics in Neurocritical Care and neuropalliative care. In neurocritical care, Dr. Gofton's research focuses on disorders of consciousness, status epilepticus and neurophysiology as it relates to deceased organ donation. In neuropalliative care, Dr. Gofton investigates challenges and barriers to initiation of neuropalliative care, neuropalliative care in serious neurological illness and neuropalliative education for trainees.

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. MARYAM NABAVI-NOURI

Dr. Maryam Nabavi-Nouri joined the Department of Paediatrics and Clinical Neurological Sciences at Western University as an assistant professor in October 2018. Dr. Nabavi-Nouri received her medical degree from Iran University of Medical Sciences in Tehran in 2009. She completed her paediatric neurology residency at the Hospital for Sick Children/University of Toronto in 2016. Through a fellowship grant from Canadian League against Epilepsy, she finished her Neurophysiology/Pediatric epilepsy fellowship at University of British Colombia with a focus on pediatric EEG interpretation and epilepsy surgery evaluations. She is pursuing a Masters in Clinical epidemiology through London School of Health of Tropical Medicine. She is expanding the pediatric epilepsy research program focusing on multi-center studies to understand the pathophysiology of autoimmune causes of epilepsy, while improving diagnostic accuracy, access to disease-modifying therapies, and patient outcomes. Her research interests further include medically refractory epilepsy, epilepsy surgery, epidemiological studies in epilepsy and global burden of neurological disorders.

DR. STEPHEN PASTERNAK

Dr. Pasternak received his S. B. Degrees in Chemical Engineering and in Life Sciences from the Massachusetts Institute of Technology in Cambridge, Massachusetts. He completed the MD/PhD program at McGill University, Montreal, earning his PhD in the Department of Neurology and Neurosurgery in 1994 and his M.D. C.M. in 1995. Dr. Pasternak then completed his Neurology residency at the University of Toronto Fin 2000, followed by Post-Doctoral training in Cell Biology at the Hospital of Sick Children in Toronto and Fellowship training in Cognitive Neurology at the University of Toronto. Dr. Pasternak joined the Department in 2004 and specializes in Cognitive Neurology.

EVENT SPONSORS

We would like to thank our event sponsors for their contribution to the 2024 CNS Research Day. We are appreciative of your continued support of this event and our Department. We look forward to future collaboration!

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ORAL PRESENTATIONS

PLAT-1

fMRI-based deep brain stimulation programming: a blinded, crossover clinical trial.

B. Santyr, A. Ajala, I. Alhashyan, J. Germann, J. Qui, A. Boutet, A. Fasano, A. Lozano

Importance: Success of deep brain stimulation (DBS) in Parkinson's disease (PD) relies on time-consuming trial-and-error testing of stimulation settings. There is often a long delay between setting changes and visible clinical response.

Objective(s): To prospectively compare a functional magnetic resonance imaging (fMRI)-based stimulation optimization algorithm with >1 year of standard-of-care (SoC) programming in a double-blind, crossover, non-inferiority trial.

Design and Participants: Twenty-seven PD patients undergoing subthalamic nucleus (STN) DBS were prospectively enrolled (within 8 weeks of implantation) for fMRI prior to initiating SoC stimulation optimization. 6.5-min fMRI sessions were acquired using a 30-sec DBS-ON/OFF cycling paradigm. Optimal settings were identified using our published classification algorithm. Subjects then underwent >1 year of SoC programming. Clinical improvement was assessed, after an overnight medication washout period and a minimum of 1 week on SoC or fMRI-determined stimulation conditions with the patient and examiner blinded to the change. The predefined non-inferiority margin was -5 points on the Movement Disorder Society-Sponsored Revision of the Unified Parkinson's Disease Rating Scale, part III (MDS-UPDRSIII).

Results: Subjects underwent an average of 17 months (SD=4) of SoC programming before comparison with fMRI-determined settings. MDS-UPDRSIII improved from 45.3 (SD=14.6) at baseline to 24.9 (SD=10.9) and 24.1 (SD=10.9) during SoC and fMRI-determined stimulation, respectively. The mean difference in scores was 0.8 (SD=8.5; 95% CI -4.5 to 6.2). The non-inferiority margin was not contained within the 95% confidence interval, establishing non-inferiority (p=0.013).

Conclusions and Relevance: We found that fMRI-based programming is non-inferior to conventional clinical programming. Equivalent outcomes may be achieved in 3 hours of early postoperative fMRI compared to >1 year of multi-visit SoC programming. Importantly, settings were compared after 1 week of stimulation, confirming efficacy and sufficient washout. fMRI-based selection of parameters may offer advantages over traditional clinical-based programming including reduction of time and burden of programming.

PLAT-2

Disrupting the Epileptogenic Network with Stereoelectroencephalography-guided Radiofrequency Thermocoagulation

H. Kreinter, PE. Espino, S. Mejía , JG. Burneo, DA. Steven, K. MacDougall, M. Jones, G.Pellegrino, D.Diosy, SM. Mirsattari, J. Lau , A. Suller-Marti

Importance: The biological mechanism sustaining the effectiveness of radiofrequency thermocoagulation (RF-TC) for treating patients with focal drug-resistant epilepsy who undergo Stereoelectroencephalography (SEEG) is unclear. Our study addresses a gap in knowledge regarding the role of RF-TC in disrupting the epileptogenic network.

Objective: To assess the relationship between the location of the ablation within the epileptogenic network and clinical outcomes.

Design: In this retrospective longitudinal study, seizure outcomes were analyzed for consecutive patients who underwent RF-TC and across subgroups depending on the location of the ablation within the epileptogenic network, defined as SEEG sites involved in seizure generation and spread.

Results: Eighteen patients who had RF-TC were included. The median age at SEEG implantation was 35 years (IQR 25.5), and 55.6% were female (n=10). A complete seizure onset zone ablation (C-SOZA) was performed in 12 patients, and a partial seizure onset zone ablation (P-SOZA) in six patients. Ablation of the early spread was performed in three of the C-SOZA patients. Five patients had ablation of an epileptogenic lesion. The number of patients who had follow-up appointments to assess outcomes after RF-TC at 1, 3, 6 and 12 months were 18, 16, 13 and 9, respectively. The seizure freedom and responder rates in the six-month cohort were 23 % (n=3/13) and 85% (n=10/13), respectively. A C-SOZA showed a higher seizure freedom rate compared to a P-SOZA at six months (C-SOZA n= 3/9) (P-SOZA n= 0/4), (p=0.294). Regarding responder rate, C-SOZA demonstrated superior results compared to a P-SOZA at six months (C-SOZA n=9/9) (P-SOZA n=1/4), (p=0.014). Adding the early spread ablation to the C-SOZA did not increase seizure freedom rates at six months but exhibited comparable effectiveness regarding responder rates, indicating a potential network disruption.

Conclusion: A complete ablation of the contacts involved in the seizure onset zone was associated with higher rates of seizure freedom and responder rate. Ablating the early spread improved the responder rate but not the seizure freedom rate, indicating a potential network disruption.

PLAT-3

Segmentation of stereoelectroencephalography electrode contacts using convolutional neural networks

A. Thurairajah, Alaa Taha, Greydon Gilmore, Mohamad Abbass, Mauricio Cespedes, Feyi Ogusanya, Western Epilepsy Surgery Research Collaborative, Jorge Burneo, David A. Steven, Ana Suller-Marti, Ali R. Khan, & Jonathan C. Lau

Importance: Stereoelectroencephalography (SEEG) is a minimally invasive procedure using intracerebral electrodes to determine the seizure onset zone. The localization of SEEG electrodes and individual contacts is crucial for guiding the surgical plan. This process is often performed manually or through semi-automated processes which require additional review.

Objectives: The objective of the following project is to automate the process of contact segmentation via a convolution neural network (CNN) from clinically acquired post-operative Computed Tomography (CT) scans.

Design and Participants: CNNs are a branch of deep learning primarily used in computer vision tasks and medical image segmentation. Our study trains a 4-Layer 3-Dimensional (3D) U-Net, a popular CNN architecture.

CT Images were resampled to be 0.4mm isotropic, and z-score normalised by the mean intensity value and within 1 standard deviation. Ground-truth labels were based on the manually localised contact coordinates. Three-dimensional “patches” were then taken from each image to reduce computational load, with dice-cross entropy chosen as the loss function.

Training data consisted of 72 patients, with 853 implanted electrodes and 8531 contacts. The model was evaluated on a validation dataset of 15 patients (175 implanted electrodes and 1750 contacts).

Results: Empirically a patch size of 95x95x95 voxels demonstrated the best model performance, reducing the “false positive” segmentations seen outside the skull. Qualitatively the model accurately identified each electrode, but failed to segment individual contacts that are “tightly packed” in the imaging and more difficult to seperate.

A quantitative assessment of model performance was done using a connected components count of segmented contacts. In total, the model identified 1182 of the 1750 contacts in the validation set. Model precision (the number of correctly identified contacts divided by the number of model segmentations) was 82.4%.

Conclusions and Relevance: Our results show that convolutional neural networks are a robust method for automatic segmentation of SEEG electrode contacts, requiring minimal pre-processing and no prior information outside of the original post-operative CT scan. Future directions include optimising the model architecture to improve segmentations or exploring additional post-processing algorithms.

PLAT-4

Task-based indices of neurocognitive mechanisms underlying apathy in neurodegenerative dementias: findings from FTD, LBD, and AD

R. Malik, I. Kinley, K. Coleman, O. Dabash, M. Berih, S. Jesso, R. Hegele, D. Mitchell, S. Pasternak, M. Restrepo, R. Ruiz, E. Finger

Importance: These findings serve to characterize mechanisms involved in apathy across neurodegenerative dementias and inform future targeted approaches to treating apathy in patients.

Objective(s): To determine the neurocognitive mechanisms underlying apathy in neurodegenerative dementias.

Design and Participants: The current proposal is a prospective cohort study. Participants with neurodegenerative dementias, including patients with Alzheimer's Disease (AD), frontotemporal dementia (FTD), and Lewy body dementia (LBD), as well as age-matched healthy controls (HC) were enrolled in this study. Patients were recruited from the Cognitive Neurology and Alzheimer Research Centre at Parkwood Hospital in London, and through advertisements in doctor's offices in the community. Healthy control participants were recruited from the community through word of mouth and posters. Participants engaged in a series of computer-based tasks to deficits assess option generation, motivation, and volition, as core neurocognitive domains affected by apathy. Additionally, participants underwent 3T MRI structural scans at the Robarts Research Institute.

Results: This study included 29 participants (18 males). The mean age of participants was 68.52 years old (SD: 7.13, range: 49-80). Participants between 10 and 25 years of formal education (mean: 14.69, SD: 2.78). Participants in the AD, FTD, and LBD groups had significantly less years of education (F(3,25)= 5.44, p<0.01) and lower MoCA total scores (F(3,25)= 8.71, p<0.001) than healthy control participants. Healthy controls had significantly higher AES scores (lower apathy ratings) compared to all three disease groups (F(3,25)=3.39, p=0.03. A PLS was performed with informant-based apathy questionnaire data as the response variables. The predictor variables included main outcome variables from the neurocognitive computer tasks. Results revealed a significant association between fluency (number of options generated) in the open-ended/no time constraints condition and questionnaire items (83.22% of variance explained, r2=0.67, p<0.001). A multiple linear regression model revealed deficits in option generation were associated with atrophy in the anterior cingulate cortex (F(6,15)=6.63, adjusted R2=0.62, p=0.001).

Conclusions and Relevance: The current work highlights deficits in option generation that may underlie symptoms of apathy seen across neurodegenerative dementias. With more testing, these computer-based tests can be leveraged as objective end-point measures of apathy in clinical trials, or as screening measures for apathy subtypes.

PLAT-5

Impact of Competency-Based Medical Education on Neurology and Internal Medicine Resident Elective Experiences

M. Patel, L. Mai

Importance: In the Canadian Competency based medical education (CBME) model, residents must complete a designed list of “Entrustable Professional Activities” (EPAs) within their specialty as a benchmark of pre-specified competency outcomes to qualify for independent practice. Unfortunately, in this model, off-service electives can be seen as a hindrance to timely completion of specialty-specific EPAs and thus risks individual learners focusing on completing individual EPAs at the expense of broadening residents’ experiences through off-service electives.

Objective: To determine the impact of CBME on the diversity of resident experiences and factors motivating resident elective choices.

Design and Participants: A retrospective analysis of rotation schedules was performed for residents in the Neurology program at Western University starting in July 2017 until June 2023 (6 year time span, including 3 years before and after start of CBME). In addition, current neurology and internal medicine residents’ perspectives were collected via the use of a Qualtrics questionnaire comprising of 5-point Likert scales in addition to short answer responses. Quantitative data including the time spent on specialty-specific vs off-service rotations was compared between the pre-CBME and post-CBME groups with descriptive and t-test statistics. Furthermore, qualitative data from short answers was analyzed to identify any emerging themes.

Results: A total of 28 pre-CBME and 14 post-CBME neurology resident rotation schedules were compared to examine differences in rotations and their elective choices. In addition, a total of 37 survey responses were collected. Residents in the pre-CBME cohort had a higher mean number of off-service electives compared to post-CBME for PGY-1 (7.8 vs. 5.2, p<0.0001), PGY-2 (6.8 vs. 4.4, p=0.0004), and PGY-3 (5.8 vs. 4.7, p=0.0003) years. In addition, resident survey responses demonstrated themes indicating a greater sense of restriction in elective choices when comparing pre and post-CBME residents.

Conclusion and Relevance: This study demonstrates a reduced emphasis on off-service electives with the introduction of CBME, thereby limiting the diversity of experiences for residents. Electives permit an individualized approach to broadening skills and experience that is complementary to specialty training and by reducing these experiences, we hinder the ability to produce well-rounded physicians.

PLAT-6

Multi-scale investigation of the A13 subregion in the zona incerta as a neuromodulatory target for Parkinson's Disease

V. Liu, T. Andrews, A. Khan, J. Lau

Importance: The zona incerta (ZI) is a promising neuromodulatory target for alleviating Parkinson's' Disease (PD) motor symptoms in patients. Recent research indicates a dopaminergic ZI subregion, known as the A13, is implicated in emotion processing deficits and chronic pain, whereas its stimulation effectively restores locomotion deficits in mouse PD models.

Objective: To identify the A13 by integrating transcriptomics and ultra-high field (7 Tesla, 7T) MRI-derived phenotypes in healthy volunteers and PD patients.

Design and Participants: We begin by leveraging whole brain spatially registered microarray data from the Allen Human Brain Atlas (n=6) to create ZI clusters via dimensionality reduction techniques, followed by exploring their biological relevance through enrichment analyses. Additionally, our lab had recruited a cohort of healthy volunteers (n=42, age 20-70) and PD patients (n = 46, age 51 - 73) for 7T MRI to generate averaged T1-map and QSM templates in MNI space previously. Combining bioinformatic-derived data with MRI template-derived information, we employed a multi-scale approach to identify the A13 in humans.

Results: From the microarray data from 6 post-mortem brains (age 24-57, 1 female, 5 males), we identified 5 distinct clusters along the rostral-caudal axis in the human ZI, including a putative A13 in the rostromedial ZI region. Consistent with the definition of the A13 region in mice, over-representation analyses show that this region is enriched with dopaminergic markers and genes implicated in PD pathogenesis. Compared to the caudal ZI, we found that this subregion is enriched in genes associated with pain perception and neurogenesis regulation, aligned with previous characterization of the A13 in rodents.

Conclusion and relevance: Despite its significance, the A13 has not been visualized in humans, preventing translation to clinical applications. In this study, our findings show distinctive molecular profiles within the ZI, providing clues to identifying the putative A13 region in humans. Understanding the molecular and MR characteristics of the ZI represents a crucial step in unlocking its full therapeutic potential. By integrating macroscale imaging with transcriptomics, we not only highlight the unique organization within the ZI, but also present potential pathways for improved neuromodulatory targeting and enhancing patient outcomes.

PLAT-7

Neurons in the Lateral Prefrontal Cortex Encode Task Features during Virtual Navigation

M. Abbass, R. Luna, B. Corrigan, M. Roussy, A. Sachs, S. Treue, J.C. Lau

Importance: Our findings suggest that neurons in the lateral prefrontal cortex (LPFC) encode spatial attention in retinotopic and spatiotopic refence frames. These findings contribute to a fundamental understanding of the LPFC and have potential practical implications.

Objective(s): The LPFC is uniquely found in primates and associated with spatial attention and working memory. This function is subserved by neurons that are tuned to spatial locations attended to. Space can be encoded in a retinotopic reference frame (RF) as observed in early visual areas, or a spatiotopic reference frame as observed in higher level visual areas. RF encoding of attended space in the LPFC has not been previously explored.

Design and Participants: Two macaques were trained to perform a modified oculomotor delayed-response task. This task typically requires central fixation on a screen while a transient cue appears, which the subject saccades to after a delay. In our case, we modified the initial fixation position, allowing us to dissociate spatiotopic and retinotopic RFs of covert spatial attention. Macaques were implanted with two 96-channel microelectrode arrays, targeting the LPFC. Task conditions were grouped by RF, and neuron tuning was determined with a multivariate linear regression (alpha=0.05).

Results: A total of 7265 neurons were recorded while the macaques completed the task, and 1816 (25.0%) were tuned to the spatial position covertly attended to. Of these neurons, 1157 (63.7%) were tuned retinotopically, 315 (17.3%) were tuned spatiotopically, and 344 (18.9%) were tuned in both RFs. Spatial location could be decoded with a linear classifier above chance (25%) in both retinotopic (79%) and spatiotopic (55%) RFs.

Conclusions and Relevance: Despite early sensory areas demonstrating retinotopic RFs, our stable perception of space is thought to be mediated by higher visual areas that encode space spatiotopically. Our results further suggest that spatial attention is mediated by LFPC neurons encoding space in both RFs. This may allow the LPFC to transform information between RFs, which can be read from adjacent areas such as the frontal eye fields that control saccades in a retinotopic RF. This has potential practical relevance for brain machine interface research to allow the decoding of attended space in multiple RFs.

PLAT-8

Intracranial Electrotherapy Treatment Planning for Brain Cancer Patients

E. Iredale, S. Schmid, T. Peters, E. Wong, M.O. Hebb

Importance: Our research group has developed a novel anti-cancer electrotherapy treatment planning system for aggressive brain cancers. Besides neurological diseases that employ deep brain stimulation, we found that multi-electrode stimulation has an impact on Glioblastoma (GBM). Current treatment options of surgical resection, chemotherapy, and radiation are not usually effective against GBM. We are investigating a new strategy to treat these aggressive brain tumors, using low intensity electric fields delivered with multiple electrodes implanted directly into the tumor, called Intratumoral Modulation Therapy (IMT). Efficacy of IMT validated in-vitro and in-vivo substantiated the development of a custom treatment planning system for human scale IMT, which was validated on a brain phantom.

Objective: To investigate the robustness of our IMT Planning System (IMTPS), from preclinical to human scale models, considering single vs. multi-insertion sites and post-operative plan adaptation.

Design: Within IMTPS, patient tumors visible in MR images were contoured to define the target volume. The number of insertion sites were then selected, ranging from a single site to a maximum of one insertion site per electrode. The trajectory of each cylindrical electrode, and the voltage and phase shift programming for individual contacts were determined for each patient and insertion site criteria, to optimally cover the tumor with 1 V/cm electric field. Additional treatment plans were created to test the post-operative planning pipeline, by fixing the electrode trajectories.

Results: IMTPS was found to be robust in creating unique IMT 3D field patterns, moving over time to cover patient tumors ranging in shape, size, and location. The number of insertion sites was not found to substantially impact the voltage required for 1 V/cm coverage, but more sites did lessen the maximum delivered current. We found that voltage and phase shift re-optimization through the post-operative planning pipeline mitigated non-optimal electrode placement.

Conclusions and Relevance: Our future goal is to translate IMT technology from bench to bedside, to expand the limited tools available for these difficult brain tumor cases. IMT has the potential to impact the lives of brain cancer patients, with our novel IMT planning system laying the foundation for efficacy evaluation in clinical trials.

PLAT-9

Ganglioside antibody testing at London Health Sciences Centre

CMF Li, Y Chang, L Yang

Importance: Ganglioside antibodies can help diagnose distinct acute and chronic inflammatory neuropathies including axonal variants of Guillain-Barre syndrome, Miller-Fisher syndrome (MFS), multifocal motor neuropathy, and chronic sensory ataxic neuropathies. In clinical practice, ganglioside antibody testing may be pursued outside of these disease phenotypes that are robustly associated with ganglioside antibody positivity; as such, the yield and utilization of ganglioside antibody testing in the clinical setting should be further assessed.

Objective: to evaluate the yield and utilization of ganglioside antibody testing using commercially available line blot at London Health Sciences Centre (LHSC).

Design and Participants: We performed a retrospective chart review of all patients at LHSC who underwent ganglioside antibody testing between April 2019 and August 2023. The disease phenotype was determined for each patient, and the proportion of all tests that yielded a true-positive result was calculated. Ganglioside antibody positivity was classified as a true-positive result if the disease phenotype was robustly associated with the detected ganglioside antibody and there was no other more likely diagnosis.

Results: We identified 92 patients who underwent ganglioside antibody testing. One patient (1%) was classified as having a true-positive result; this patient had GQ1b-IgG positivity with MFS. Among 92 patients tested, 20 patients (22%) had a disease phenotype that was considered to be robustly associated with ganglioside antibody positivity.

Conclusions and Relevance: The yield of ganglioside antibody testing in clinical practice is low. We found that this testing is frequently ordered in patients with disease phenotypes that are not robustly associated with ganglioside antibody positivity, indicating that suboptimal test utilization is a primary contributor to its low yield. Restricting ganglioside antibody testing to patients with characteristic disease phenotypes would be valuable to improving yield and utilization of this testing.

PLAT-10

Apathy produces selective deficits in cognitive function when controlling for depression in patients with Parkinson's disease

G.K. Badwal, K. Patel, S. Pasternak, H. Ganjavi, R. Renwick, R. Camicioli, O. Monchi, K. Van Hedger, P.A. MacDonald

Importance: This study provides insight into the unique and selective effects of Apathy on patients at-risk for Cognitive Impairment (CI) in Parkinson's disease (PD).

Objective(s): To compare differences in CI among patients with and without clinically significant Apathy in PD, PD-mild cognitive impairment (PD-MCI), and PD-dementia (PDD), controlling for the effects of Depression.

Design & Participants: In a cross-sectional design, multi-site datasets were combined through data-sharing agreements. All participants had a Disease Stage of either PD, PD-MCI, or PDD and were ON dopaminergic medication. Patients were classified as having clinically significant Apathy and/or Depression using standardized questionnaire measures. CI was measured using the Montreal Cognitive Assessment (MoCA). ANCOVA was used to test for a main effect of Apathy, as well as an interaction between Disease Stage and Apathy on CI. Depression, sex, education, and age were included as covariates.

Results: In 442 participants (Female = 121, PD-MCI = 98, PDD = 55), 45 patients met criteria for Apathy, 134 met criteria for Depression, and 55 met criteria for both. ANCOVA revealed a significant main effect of Apathy on MoCA total scores when Depression was included as a covariate. Patients with Apathy had greater CI (M = 23.57, 95% CI 22.69 – 24.45) than patients without Apathy (M = 25.22, 95% CI 24.84 – 25.61, p = .01, ηp2 = .01). Additionally, a significant Apathy by Disease Stage interaction was found on the visuospatial/executive (VSE) subdomain of the MoCA. Patients with PDD and Apathy (n = 18, M = 2.17, 95% CI 1.49 – 2.85) were more impaired on the VSE subdomain than patients with PDD without Apathy (n = 37, M = 3.16, 95% CI 2.78 – 3.54, p = .02, ηp2 = .03).

Conclusions & Relevance: These findings suggest that in patients with PD, Apathy has an impact on CI distinct from that of Depression. Additionally, these findings suggest that Apathy can produce selective impairments in specific cognitive domains based on Disease Stage. These findings highlight the importance of assessing psychiatric symptoms in patients with PD at-risk of CI. Future analyses will investigate additional influences of motor severity and levodopa equivalent daily dosage.

PLAT-11

Chaos to Clarity: Standardizing On-Call Provider Communication

R. Sawaya, K. Cotton, A. Branch

Importance: Communication inefficiencies between nursing and clinical teams can lead to resident pager fatigue and dissatisfaction. Standardizing communication practices can improve workflow, reduce errors, and improve patient outcomes.

Objective: This quality improvement project aims to enhance communication efficiency among nursing and clinical teams while reducing resident pager fatigue. The primary objective is to ensure that by April 2024, 90% of nursing pages to CNS inpatient clinical teams (General Neurology, Stroke Neurology and Neurosurgery) are only for urgent issues.

Design and Participants: The project utilized the Plan-Do-Study-Act (PDSA) cycles and lean methodology to iteratively improve communication processes. To bundle non-urgent communication concerns, clipboards were used as a tool, which clinical teams checked at regular intervals. An infographic and a resident attending the unit improvement huddle were used to educate and engage nursing with the communication strategy.

A qualitative content analysis was conducted on interviews with nurses who work in the CNS department at LHSC. Outcome measures for the initiative include the number of pages received by clinical teams and nursing staff satisfaction. Process measures include consistent use of clipboards by nursing and clinical teams, consistent check-ins with the charge nurse by the on-call resident, and education of nursing and clinical teams. The balancing measure ensures that patient care is not compromised by delays in communication attributable to the initiative.

Results: Clinical experience was crucial in navigating communication practices, especially in distinguishing between urgent and non-urgent issues. Newer nursing staff needed guidance by experienced nursing staff in determining when to escalate issues, emphasizing the significance of mentorship in fostering effective communication practices.

Other root causes for inefficient communication included a lack of agreement on issues considered urgent or nonurgent, a lack of awareness of the residents' schedule, and clinical teams not addressing clipboard issues promptly.

Conclusions and Relevance: The importance of standardized communication is emphasized in our project. The findings highlight the need for ongoing refinement of the paging initiative and education of nursing and clinical teams to ensure effective communication. Future areas of focus include communication with other allied health teams and the establishment of a paging initiative for weekend teams.

PLAT-12

The association of air pollution with new-onset epilepsy

T. Antaya, L. Zhang, B. Le, T. Oiamo, P. Wilk, J. Burneo, K. N. Speechley

Importance: Air pollution has been associated with certain neurological disorders, but its association with epilepsy has been insufficiently explored.

Objective(s): Our objective was to estimate the association of long-term exposure to fine particulate matter (PM2.5), nitrogen dioxide (NO2), sulfur dioxide (SO2), and ozone (O3) with the risk of new-onset epilepsy among adults in Ontario, Canada.

Design and Participants: We addressed our study objective using a nested case-control study design and individually linked health administrative databases. We included Ontario residents aged 18 to 80 on January 1, 2010, and excluded those with a history of seizures or epilepsy. We then identified as cases those who developed epilepsy within five years and matched up to five controls with each case on age and sex using risk-set sampling. We used conditional logistic regression models to estimate the association with new-onset epilepsy for one-unit increases in each air pollutant individually and in a multipollutant model.

Results: We included 24,761 cases and 118,692 controls. In the individual pollutant models, we observed significant associations with epilepsy for PM2.5 (OR=1.047, 95% CI: 1.033, 1.061) and O3 (OR=1.016, 95% CI: 1.012, 1.019). In the multi-pollutant model, the ORs for the associations between new-onset epilepsy and PM2.5, NO2, and O3 were 1.032 (95% CI: 1.015, 1.050), 0.994 (95% CI: 0.990, 0.998), and 1.011 (95% CI: 1.007, 1.016), respectively. SO2 was excluded from the multi-pollutant model, as mean concentrations were very low and considerable data were missing. Due to evidence of non-linearity, we conducted a sensitivity analysis modelling NO2 and O3 using restricted cubic splines. There was no significant association for PM2.5 or O3 in these analyses; however, we observed an interaction between NO2 and O3 and a significant association with NO2. For NO2, a significant OR greater than 1 was observed at a lower concentration of NO2 and a median concentration of O3, and significant ORs less than 1 were observed at median and higher concentrations of NO2 and O3.

Conclusions and Relevance: There was a significant positive association with new-onset epilepsy for PM2.5 and O3 and a significant negative association for NO2. The counterintuitive results observed for NO2 when accounting for non-linearity require further exploration.

PLAT-13

Long-Term Outcomes of Radiofrequency Ablation for Temporal Lobe Epilepsy

R. Wang, A. Parrent, D. Steven, J. Burneo, A. Suller-Marti, J. Lau

Introduction: Radiofrequency ablation (RFA) is a minimally-invasive procedure that has been used for treating medically-refractory epilepsy. However, the long-term efficacy of RFA is unknown.

Objective: We aim to characterize the long-term outcomes of patients from the original series by Parrent and Blume (1999) describing stereotactic RFA for temporal lobe epilepsy (TLE).

Design and Participants: Consecutive patients who underwent stereotactic RFA for TLE were retrospectively reviewed. Baseline demographics, procedural details, and post-operative seizure outcomes until last follow-up were abstracted. Information about additional treatments was collected, if available. Kaplan-Meier analysis was done to estimate seizure-freedom after initial RFA treatment.

Results: 27 patients underwent RFA from 1994 to 2002. There were 14 female (52%) patients and 24 (89%) had mesial temporal sclerosis on MRI. Mean age at time of RFA was 33.1 years (range 12-45 years). Mean time to RFA treatment was 19.6 years (range 5-39 years). 17 (63%) patients underwent left-sided RFA and a mean of 24.3 lesions were made. 15 (56%) patients had further interventions: 4 (15%) patients underwent only repeat RFA, 1 (4%) patient had repeat RFA and anterior temporal lobectomy (ATL), and 10 (37%) patients underwent subsequent ATL only. Mean follow-up was 9.0 years (range 0.5-22.7 years). At last follow-up, 16 (59%) patients were seizure-free with 5 (19%) patients having received one RFA treatment, 2 (7%) patients who received repeat RFA, 1 (4%) patient who underwent repeat RFA and ATL, and 8 (30%) patients who only underwent subsequent ATL. Post-operatively, 6 (22%) patients had visual field deficits and 3 (11%) had hematomas.

Conclusions: Based on the original series describing the technique, stereotactic RFA for TLE is a safe, minimally-invasive procedure with a favourable safety profile and seizure outcome. With resurgence of interest in ablative techniques, it remains to be determined what the role of stereotactic RFA will be as part of the treatment armamentarium for TLE.

PLAT-14

Differential effects of oxytocin on empathy deficits across subtypes of frontotemporal dementia

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

Importance: Oxytocin (OXT) is a promising treatment candidate for improving empathy deficits in Frontotemporal Dementia (FTD). However, given the heterogeneous nature of FTD, including variable degenerative patterns of frontal and temporal regions, OXT may not exert therapeutic effects uniformly across the patient population.

Objective(s): To determine whether OXT differentially affects facial expression recognition, a critical social cue for guiding appropriate behavioural responses including empathy, depending on the integrity of frontotemporal brain networks.

Design and Participants: A double-blind, placebo-controlled, randomized crossover design study was performed where 28 participants with FTD underwent two sessions of fMRI facial expression recognition tasks, once following intranasal administration of 72 IU OXT and once following placebo saline mist. Participants were recruited from the Cognitive Neurology and Alzheimer Research Centre at Parkwood Hospital in London, Ontario, Canada

Seed-based connectivity maps of our regions of interest (ROI; amygdala and insula) were generated to assess neural connectivity on vs off treatment with OXT to determine whether change in functional connectivity with brain regions relevant to empathic processes could be predicted by performance change on the facial expression recognition task following OXT administration.

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

Following OXT administration widespread decreased coupling was observed between the amygdala and occipitotemporal regions, which was also associated with greater improvement in facial expression recognition. Following OXT, the insula demonstrated increased coupling with the cingulate gyrus and decreased coupling with the basal forebrain and occipital gyrus relative to placebo.

Conclusions and Relevance: These findings provide evidence for OXT modulation of functional connectivity between brain regions supporting behavioural performance on an empathy-related task in patients with FTD. Results from this study will help determine whether a specific subset of patients with FTD benefits from administration of OXT to enhance emotion expression recognition and improve empathy deficits.

PLAT-15

**Doesn't consent to having the abstract online*

PLAT-16

In-vivo Accuracy of Autonomous Pedicle Screws Utilizing a Supervisory Controlled 7DOF Robot with Optical Coherance Tomography Guidance: A World First.

B. Johnston, M. Oppermann

Background: Pedicle screw fixation is an important technique in the armamentarium of neurosurgeons for a variety of spinal conditions. Violation of the pedicle can lead to neurovascular injury, with associated morbidity and mortality. Early techniques relied on anatomic orientation. Fluoroscopy and image guided techniques have subsequently improved the accuracy of pedicle screw placement. Due to excellent pose repeatability, robotic technology has been utilized for pedicle placement in an aim to further improve accuracy. All existing surgical spine robotic machines are surgical assist architecture and rely on optical tracking. This work explores the accuracy and precision of a supervisory control architecture robot (8i Robotics) utilizing optical coherence tomography for autonomous pedicle instrumentation. This is the first ever reported use of optical coherence tomography for guidance, as well as autonomous pedicle instrumentation.

Methods: 3 porcine subjects were used with L2, L3, and L4 instrumented with 4.5 x20 mm poly axial screws utilizing the 7dof robot in a scan and plan workflow. Following instrumentation all animals were observed for 24 hours with neurological assessment of hind limb function. Then after sacrifice repeat CT was done to assess post operative screw location. Screws were graded clinically utilizing the Gertzbein-Robbins Scale (GRS) clinical acceptability scale. Precision was assessed by utilizing a customized image processing pipeline to register pre and post vertebral level by level that allowed post procedural screw placement relative to planned location and trajectory. Euclidean error was calculated at screw head and screw tip. All points were normalized to a nominal screw coordinate system, allowing for removal of parallax effect. Scatter error orthonormal to the screw axis at the tip and head was utilized to construct confidence ellipses of certainty of screw axis.

Results: All animals were fully neurologically intact following instrumentation. All (18/18) screws where GRS A with no breach of pedicle. Mean tip and head Euclidean error where 2.47+/- 1.25 mm and 2.25 +/-1.25 mm respectively. The major and minor axes of the confidence ellipse at 99% was 2.19 mm, and 1.28 mm for the tip and 2.07 mm, and 0.42 mm for the head.

Conclusion: 100% of screws obtained satisfactory clinical grading, with intact neurological function in all animals post operatively. Overall accuracy is 2.47mm and 2.25 mm at the tip and head respectively. Although limited sample size it shows the capability of a supervisory controlled 7DOF robot with OCT registration. Screw axis error ellipsoids allow for estimation of safety depending on subject specific pedicle morphology. Further investigation is warranted to further explore robotic capabilities, safety, and cost effectiveness, but nevertheless engenders excitement for autonomous supervised robotic spine surgery.

PLAT-17

Neurodevelopmental implications of genetic frontotemporal dementia revealed through intracranial volume differences in mutation carriers and non-carriers

I. So, GENFI Consortium, ALLFTD Consortium

Importance: There is converging evidence for a neurodevelopmental basis in genetic frontotemporal dementia (FTD). Our group recently observed total intracranial volume (TIV) and cognitive differences between mutation carriers and non-carriers in young adults; here, we extend the examination of neurodevelopmental consequences of FTD mutations into adults.

Objective(s): To investigate TIV and years of education differences between adult gene mutation carriers and familial non-carriers, as measures of the structural and functional outcomes of the genes.

Design and Participants: This is a cross-sectional cohort study, consisting of participants enrolled in the Genetic FTD Initiative (GENFI) and ARTFL/LEFFTDS Longitudinal Frontotemporal Lobar Degeneration (ALLFTD) consortiums, which are both prospective and longitudinal in design. Participants (aged 18 to 86 years) included 489 gene mutation carriers and 332 familial non-carriers. Genetic mutations included C9orf72 (41%), GRN (34%), and MAPT (25%).

Results: Four hundred eighty-nine mutation carriers (mean ± standard deviation [SD]; age = 50.2±13.5 years, sex = 56% female, n(C9orf72) = 210, n(GRN) = 151, n(MAPT) = 128) were compared to 332 familial non-carriers (age = 48.3±13.8 years, sex = 61% female, n(C9orf72) = 128, n(GRN) = 127, n(MAPT) = 77). Consistent with our prior findings in young adults, GRN carriers exhibited a trend towards larger TIV compared to familial non-carriers (p=0.06, partial eta squared (η2p)=0.01), particularly in males (p=0.05, η2p=0.04). Larger TIV correlated with higher years of education in male GRN non-carriers (r=0.34, p=0.002), with a trend towards significance in female GRN carriers (r=0.20, p=0.06). MAPT carriers demonstrated smaller TIV than non-carriers (p=0.03, η2p=0.03), observed in both females and males (p=0.02, η2p=0.06; and p=0.03, η2p=0.06, respectively). In male MAPT carriers, larger TIV correlated with higher years of education (r=0.28, p=0.04). Models of C9orf72 and those with education as the outcome did not yield significance.

Conclusions and Relevance: In support of neurodevelopmental implications in genetic FTD, GRN and MAPT mutations are linked to structural neurodevelopmental changes, which correlate with years of education. These findings can contribute to identifying mechanisms resultant from FTD mutations that can impact neurodevelopment. Further research will be essential to validate these mechanisms and ascertain their suitability as targets for developing clinical interventions.

PLAT-18

Hyperpolarization-activated cation channels shape the spiking frequency preference of human cortical layer 5 pyramidal neurons

H. Inibhunu, H.M. Chameh, F. K. Skinner, S. Rich, and T.A. Valiante

Importance: Understanding the contributions of individual ionic currents to neuronal activity is vital, considering the established role of ion channel modifications in neuropsychiatric conditions.

Objective: We combine in vitro characterization of the spiking frequency preference of human L5 cortical pyramidal neurons via the frequency-dependent gain with new analyses of a biophysically-detailed computational model of such a neuron to delineate the connection between the dynamics of the hyperpolarization-activated cyclic nucleotide gated (h-) current prior to spiking and key properties of the frequency-dependent gain.

Design and Participants: Here, we combine the frequency-dependent gain, a measure of spiking frequency preference, and novel in silico analyses to dissect the contributions of individual ionic currents to the suprathreshold features of human L5 neurons captured by the FDG. We confirm that a contemporary model of such a neuron, primarily constrained to capture subthreshold activity driven by the hyperpolarization-activated cyclic nucleotide gated (h-) current, replicates key features of the in vitro FDG both with and without h-current activity.

Results: With the model confirmed as a viable approximation of the biophysical features of interest, we applied new analysis techniques to quantify the activity of each modeled ionic current in the moments prior to spiking, revealing unique dynamics of the h-current. These findings motivated patch-clamp recordings in analogous rodent neurons to characterize their FDG, which confirmed that a biophysically-detailed model of these neurons captures key inter-species differences in the FDG. These differences are correlated with distinct contributions of the h-current to neuronal activity.

Conclusions and Relevance: Together, this interdisciplinary and multi-species study provides new insights directly relating the dynamics of the h-current to suprathreshold spiking frequency preference in human L5 neurons.

PLAT-19

Low-intensity electric field treatment via Intratumoral Modulation Therapy of glioblastoma in a rat neuro-oncology model

N. Fulcher, E. Iredale, A. Elsaleh, C. De Oliveira, S. Schmid, E. Wong & M. O. Hebb

Importance: Glioblastoma multiforme (GBM) is the deadliest brain cancer in human adults and incurable. Existing treatment options include surgical resection when the tumor location and patient status allow, followed by radiation therapy and temozolomide chemotherapy, which affords a median survival of ~14 months. Research into new therapies is evidently imperative.

Objective: Our team has developed a biotechnology called Intratumoral Modulation Therapy (IMT) to deliver low-intensity electric field to attenuate GBM progression.

Design and Participants: N=18 adult Fischer rats received striatal implants of an in-house designed pedestal comprised of a three-prong bioelectrode configuration, and rat-derived glioma cells (F98s) that were modified to express firefly luciferase that enables bioluminescence imaging (BLI) *in vivo*. On postoperative day four, rats were imaged via BLI to confirm adequate tumor size prior to treatment. Rats then underwent IMT treatment or sham (no stimulation) for one week and were imaged again on postoperative day 11 to assess tumor growth. Delivered voltage *in vivo* was confirmed daily during IMT. Subsequently, the rat tissue was processed with plans to assess clinical tumor and proliferation markers, activated glial cells, and general damage to surrounding cells.

Results: Voltage measurements over one week of IMT validated each prong delivered 200 kHz, 1.7 V amplitude sine waves (6 mA current). With each prong's voltage equally phase shifted, an average electric field strength of 1 V/cm covered a 6.0 mm diameter target. We found an attenuation of tumor growth, determined by BLI average radiance comparing pre- and post- treatment tumor size since rats that received one week of IMT had an increase in tumor size of 3.25x post-treatment compared with sham that grew by 49.78x, statistical significance was confirmed via a Mann-Whitney U test (BLI average radiance day11/day4, median; U=15, p=.0122).

Conclusions and Relevance: The results provide novel key information to the field of neuroscience, while bringing us one step closer to offering new therapy options to GBM patients. This data fills a critical gap in advancing IMT towards clinical application. IMT can be applied in conjunction with established therapeutics to prevent GBM recurrences.

PLAT-20

Investigating A Diagnostic Model of PD and Prodromal PD

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**equal contributions*

Importance: No objective diagnostic tests of Parkinson's Disease (PD) have proven accurate, reliable, and generally accessible. This compromises clinical practice and impedes discovery of first disease-modifying therapies (DMTs). Identifying PD patients at symptom onset and pre-motor stages will advance the search for DMTs.

Objective: We sought to develop a PD diagnostic test, using 3 Tesla (T) T1-w magnetic resonance imaging (MRI) and diffusion MRI (dMRI). We investigated its potential to classify patients with rapid eye movement (REM) sleep behaviour disorder (RBD), a prodromal form of PD.

Design, Participants, Methods: This was a cross-sectional study of PD [i.e.,< 12 month since diagnosis; *n*=188; *mean age*=61.7(8.0)], RBD [*n*=86;*mean age*=66.3(6.1)], and age-matched HCs [*n*=208;*mean age*=64.5(4.9)], aged 45-75, from PPMI, ONDRI, CCNA, QPN/MNI, UWO datasets, for a total N=482. Using T1-w and dMRI, we extracted measures of subregions of the striatum, substantia nigra-*pars compacta* (SN*c*), ventral tegmental area (VTA), and cortex. We pseudo-randomly selected 80% of our data for model development and 20% for an independent hold-out set. A bagging, deep neural network classifier was used to develop the diagnostic model using 5-fold cross-validation. Our model was subsequently tested in the (N=97) hold-out set.

Results: We classified PD and RBD from HCs with high accuracy (i.e., ROC/AUC = 86), sensitivity = 0.85, and specificity = 0.81. Clinician accuracy in diagnosing PD is 85-91, with repeated assessments.

Conclusions and Relevance: These findings support the potential of MRI and dMRI, using segmentation of subcortical and cortical regions, to diagnose PD and RBD at the single-subject level. These results present the promise that an automated MRI processing pipeline alone could diagnose PD, relieving the mismatch in PD patients and neurologists/movement disorder specialists. It would also allow prompt referral of early and prodromal PD patients for research in trials of DMTs.

PLAT-21

CEST-MRI characterizes perihematomal pH changes in patients with hemorrhagic stroke: A pilot feasibility study

D. Wong, A. Cronin, R. Bartha, S. Fridman, A. V. Khaw

Importance: Perihematomal edema is a key component of secondary brain injury following intracerebral hemorrhage (ICH) and a predictor of functional outcome. Determinants of perihematomal edema evolution is not well understood, but an altered acidity milieu, reflected by tissue pH changes, may contribute to abnormal metabolism.

Objective: The objective of this study was to test the feasibility of using chemical exchange saturation transfer (CEST) magnetic resonance imaging (MRI) to characterize brain tissue pH in patients with ICH. We present preliminary results from analysis of 3 subjects' imaging.

Design and Participants: 3 adult patients with first-ever ICH underwent 7 Tesla MRI within 48-96 hours after stroke onset, with follow-up imaging within 10 days of stroke onset. CEST images centered on the area of greatest edema seen on fluid attenuated inversion recovery (FLAIR) images, were acquired at 47 frequency offsets (1.2-6.6 ppm) with an isotropic resolution of 3.3. mm^3. A ratiometric contrast, known as amine/amide concentration independent detection (AACID), was calculated where higher AACID values correspond to lower pH values. FLAIR images were used to manually define a region of interest (ROI) that included the perihematomal edema but excluded the hematoma itself. AACID values within this area of edema were compared against a mirrored ROI in the contralateral hemisphere (the control area). AACID values were also compared between the initial visit and follow-up visit.

Results: At the initial visit, average AACID values were elevated in the area of edema versus the control area. At the follow-up visit, average AACID values normalized to that of the control area.

Conclusions and Relevance: Although this pilot study is not powered to make statistical comparisons, it demonstrates that CEST imaging at 7T is feasible in stroke patients with ICH and can visualize changes in perihematomal brain parenchyma acidity. Increased AACID values corresponding to lower tissue pH at 48-96 hours post-stroke may correspond with elevated lactate in perihematomal edematous tissue demonstrated in preclinical studies. Normalization of AACID values within 10 days of ICH could be explained by blood brain barrier breakdown and plasma extravasation with buffering of the acidic shift.

POSTER PRESENTATIONS

POST-1

Stroke Patient Education: A Quality Improvement Initiative

U. Bharaj, M. Patel, J. Mandzia, A. Florendo-Cumbermack

Importance: Quality patient education is a key component for secondary stroke prevention and has been shown to improve patient outcomes and quality of care.

Objective(s): To assess the utility of templates and a resident education workshop in improving patient education provided by learners to stroke inpatients at University Hospital, with a goal of improvement of 50% in quality by April 2024.

Design and Participants: Learners on Stroke service (including 23 neurology residents) participated in this quality improvement study. Focus group discussions and surveys of stakeholders were conducted to elicit challenges to effective patient education. This was organized into themes, using a fish-bone diagram to complete root-cause analysis. Modifiable factors chosen from this list were then ranked by impact by the learners. The resulting Pareto chart identified the most impactful barriers. Two interventions (templates and education workshop) addressing these were tested in PDSA cycles to assess proof of concept, with data collected one month before and after the intervention. Feedback for the interventions was also elicited from stakeholders as balancing measures. Patient education quality was graded using a 10-point scale based on the completeness of documentation. The data were used to adapt the interventions into a tool aiming to sustain the impact of the interventions.

Results: PDSA 1 assessing the utility of documentation templates showed a clear shift towards improvement in the run chart; this was complemented by a 56% improvement in the quality of patient education, but it returned to pre-intervention levels within 2 months. PDSA 2 assessing the educational workshop demonstrated a 60.5% improvement in resident knowledge of patient education topics. Although this did not translate to increased quantity of patient education documentation, its quality was significantly improved. Final tool adapted the interventions into an asynchronous module (educational workshop, reference documents, template how-to-guide) added as orientation for incoming learners.

Conclusion and Relevance: This study demonstrates the utility of templates and education workshops in improving quality of patient education. However, these improvements were short lived and thus require an asynchronous module to address sustainability. We hope this tool can help future learners provide high quality stroke patient education.

POST-2

Positive predictive value of myositis antibody line blot testing in patients with suspected idiopathic inflammatory myopathy

Y. Chang, L. Yang, A. Budhram

Importance: Line blot (LB) is in widespread use for myositis antibody detection, which has an increasingly important role in aiding diagnosis of idiopathic inflammatory myopathy (IIM). Yet, studies of its positive predictive value (PPV) in patients with suspected IIM, which would be of particular relevance to neuromuscular clinicians, are lacking.

Objective(s): To determine the PPV of myositis antibody LB testing in patients with suspected IIM, and examine whether PPV was significantly impacted by intensity of antibody positivity.

Design and Participants: This was a retrospective study of patients who underwent myositis antibody LB testing for suspected IIM between March 2019 and August 2022. Panel-based testing for myositis antibodies was performed by LB (Euroimmun, Lubeck, Germany). Of 207 patients who underwent myositis antibody LB testing during the study period, 100 had a positive antibody result and underwent chart review. Of these 100 patients, 30 were excluded because there was no concern for muscle disease. Based on chart review, each patient was classified as having a true-positive (TP) or false-positive (FP) myositis antibody LB result. Patients clinically diagnosed as having IIM in the absence of a more likely alternative diagnosis were classified as TP, while remaining patients were classified as FP.

Results: Of 70 patients who underwent testing for suspected IIM and had positive myositis antibody LB results, 43 (61%) were female and the median age was 61 years (range: 10-83 years). Forty-four were classified as true-positives, yielding a PPV of 63%. The PPV of patients with weak-positive myositis antibody results (14/30, 47%) was significantly lower than the PPV of patients with moderate-positive or strong-positive myositis antibody results (30/40, 75%) ($p = .02$).

Conclusion and Relevance: Our study found that myositis antibody LB testing in patients with suspected IIM had a modest PPV, underscoring the need for interpretation in the context of all available clinical and ancillary test data to avoid misdiagnosis. The significantly lower PPV in patients with weak-positive results emphasizes the particular importance of clinical correlation in such patients. Further study into the diagnostic performance of various LBs for myositis antibody detection is needed to inform their interpretation in clinical practice.

POST-3

Evaluation of the Effect of Quiet Reminders on Sleep Measures in Hospitalized Patients: A Quality Improvement Study

R Sawaya, E Nuro, J AlKharbooshi

Importance: The quality of sleep in hospitalized patients is crucial for promoting recovery and patient satisfaction. Research has shown that disturbances during hospitalization, especially from environmental noise, can negatively impact sleep quality, leading to longer hospital stays and slower recovery. This quality improvement project aims to address this critical care gap by enhancing the sleep quality of hospitalized patients.

Objective: The aim of this study is to assess the effectiveness of posters as visual reminders for hospital staff to maintain a quiet environment during nighttime, with the goal of improving inpatient sleep measures by 25%.

Design and Participants: A pre-post intervention study was conducted using the Plan-Do-Study-Act (PDSA) framework. The intervention consisted of deploying visual posters as reminders for staff to maintain a quiet environment during nighttime hours. Baseline and post-intervention sleep quality measures were obtained from a total of 29 patients in the LHSC CNS ward using the Richards-Campbell Sleep Questionnaire (RCSQ).

Results: Prior to the intervention, the RCSQ scores indicated that 'Awakenings' were a prevalent concern, while 'Time to sleep' was the least problematic. Following the intervention, the RCSQ results showed a decrease in all domains, with a notable reduction in 'Time to sleep', suggesting an unintended adverse impact on sleep quality. However, 'Awakenings' showed slight improvement.

The Pareto chart analysis revealed that noise was the main cause of sleep disturbance, accounting for 37.50% of cases. After the intervention, noise-related disturbances decreased to 21.05%, indicating some effectiveness of the visual reminders. However, other disturbances such as temperature increased (8.33% pre, 15.79% post) or remained unchanged, such as anxiety/stress and mobility/discomfort (both 16.67% pre, 15.79% post), suggesting a shift in the sleep disturbance profile on the ward.

Conclusions and Relevance: Although the intervention showed potential for improvement, the unexpected decrease in sleep measures after the intervention calls for a reevaluation of the approach. The insights gained from this cycle will inform subsequent iterations of the intervention to promote a restorative hospital environment that is conducive to patient sleep.

POST-4

Mesencephalotomy for chronic pain: a systematic and historical review

M. Abbass, B. Santyr, V. Liu, A. Taha, E. Lucar, A. Chalil

Importance: Advances in the medical and surgical treatment of cancers have greatly extended life expectancy. With increased survival comes a desire to improve quality of life and cancer-related pain remains a challenging issue many patients contend with.

Objectives(s): Despite a long history and efficacy in the literature, the use of ablative neurosurgical procedures for pain management has declined. Recently, interest has been reignited as chronic pain management moves to the forefront of symptom treatment of cancer. Here, we review the available literature on mesencephalotomy for chronic pain. We investigate the reported indications, efficacy, and associated side-effects.

Design and Participants: A systematic review was conducted using Embase, MEDLINE, Cochrane Central databases (July 21, 2023) querying for mesencephalotomy in humans for chronic pain. Articles were screened by two reviewers (MA and BS). Appropriate studies had data extracted on the study-type, sample size, age, sex, interventional target, surgical indication, clinical outcome, follow-up time, and adverse events were collected.

Results: Literature search revealed a total of 808 articles and 23 articles comprising 434 patients met inclusion criteria. Age ranged from 17-86 years from 14 articles (n=164), and 63% of patients from 11 articles were female (n=136). Indication was reported in 20 articles (n=420), with cancer-related pain (69%) being the most common indication, followed by central pain (20%). Outcomes were reported in all studies, and moderate to excellent pain improvement was observed in 301 patients (69%).

Conclusions and Relevance: Systematic review identified 23 articles reporting on 434 patients over 80 years. Mesencephalotomy was most commonly used to treat cancer-related or central pain (89%), with most patients demonstrating significant pain relief (69%). However, the literature lacks randomized controlled trials and suffers from heterogeneous reporting of demographic and outcome variables.

POST-5

REVIEW OF DIFFUSE MIDLINE GLIOMA AND THE ROLE OF LIQUID BIOPSY

A. Vivekanandan, S. Pejhan, R. Hammond, J. Megyesi

Importance: Diffuse midline glioma is a tumor recently defined by WHO due to discovered molecular characteristics. The molecular findings affect the diagnosis, treatment and prognosis of this disease. Additionally, liquid biopsy is a method that could potentially be a less invasive means of diagnosing and monitoring CNS tumors.

Objective: To review the clinical presentation, diagnostic findings, treatment challenges and prognosis of the newly defined diffuse midline glioma, H327M-mutant as well as to describe the role liquid biopsy can play in diagnosing and treating CNS tumors.

Design and Participants: Case report of patient diagnosed with diffuse midline glioma and review of literature regarding the disease. Review of literature on the role liquid biopsy can play in diagnosing and treating CNS tumors.

Results: Diffuse midline glioma H3K27 M mutant is a WHO grade 4 CNS tumor that arises from midline structures. It is predominantly a disease of childhood but can occur in adults. Clinical findings tend to occur within a short time frame and include cranial nerve palsies, long tract signs, ataxia and obstructive hydrocephalus. Role of surgical treatment is limited to biopsy due to the precarious location of these tumors. Even biopsy has is its risks due to location. Prognosis is poor with a 2-year survival <10%. Liquid biopsy detects cell-free DNA, such as in CSF. This allows for the diagnosis and treatment monitoring of CNS tumors in a less invasive manner.

Conclusions and Relevance: Diffuse midline glioma (H3K27M-mutant) is a WHO Grade 4 highly morbid tumor that tends to occur in pediatric patients. However, it can be seen in adults as exemplified by our case presentation. Unfortunately, surgical intervention is limited to biopsy given the location of these tumors. However, this is not without risk. Currently, surgical biopsy is the gold standard for diagnosis, molecular characterization, and prognostication, but liquid biopsy is a minimally invasive method that can potentially be used instead in the future.

POST-6

Image Fusion and 3D Road Mapping for Zero Contrast Venous Sinus Stenting in Endovascular Surgery

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Importance: Venous sinus stenting requires an angiography suite with risks of exposure to ionizing radiation and increased cost; however, high-fidelity fusion decreases the need for redundant contrast exposure.

Objective: to determine the feasibility of using image fusion and 3D road mapping in venous sinus stenting.

Design and Participants: Case Report Study.

Results: A 23-year-old male patient was diagnosed with idiopathic intracranial hypertension with papilledema, was previously diagnosed with deep venous thrombosis, and had an unremitting headache unresponsive to medical therapy. The patient underwent venous sinus stenting, and the venous pressure gradient dropped from 26 mmHg to 8 mmHg post-stent. He was followed by ophthalmology, and follow-up showed improvement of papilledema. Acetazolamide doses were tapered, and he continued dual antiplatelet therapy.

Conclusions and Relevance: Image fusion and 3D road mapping for zero contrast can be used in venous sinus stenting in idiopathic intracranial hypertension. Multicentric studies are needed.

POST-7

Evaluating Quality-of-Life in Patients Implanted with Dual Neuromodulation

E. Coskun, A. Suller Marti

Importance: Neuromodulation therapies, including vagus nerve stimulation (VNS) and deep brain stimulation (DBS), have demonstrated efficacy in seizure control and improving quality-of-life (QOL) in patients with drug-resistant epilepsy (DRE). Recently, patients have been treated with dual neuromodulation therapies (DNT), in which the patients are implanted with both devices, showing increased seizure control. However, the number of publications is scarce, and no publications exist regarding the QOL outcomes in patients with DNT.

Objective(s): We aim to describe seizure reduction and QOL change in patients implanted with DNT compared to a single device (VNS or DBS).

Design and Participants: This prospective study reviews the medical charts of patients who underwent either VNS and/or DBS implantation at the LHSC from January 2020 to July 2023. QOL metrics were assessed through the completion of the QOLIE-10 questionnaire. Seizure frequency and QOLIE-10 scores were documented at the follow-ups (baseline, 6-,12- and 24-months).

Results: A total of 55 patients (33 women) underwent neuromodulation implantation. The median follow-up time for the VNS cohort was 12 months (IQR = 6-24), and for both DBS and DNT cohorts, it was 12 months (IQR = 6-12). At the 12-month follow-up, in the VNS cohort (n = 32), the responder rate was 73.91%, while 35% experienced seizure freedom. In the DBS cohort, the responder rate was 50% (n = 2), and 100% (n = 3) of the patients in the DNT cohort were responders. No improvement was found in QOLIE-10 scores during the first 12-month follow-up in any neuromodulation cohort. Notably, seizure frequency reduction did not predict improvement in QOLIE-10 scores.

Conclusions and Relevance: All neuromodulation devices exhibited efficacy in seizure reduction. QOL is subjective, and seizure frequency is not the only predictor of QOL in epilepsy patients. A larger cohort is required to assess the relationship between seizure reduction and QOL.

POST-8

Alexithymia predicts disease outcomes in patients with Parkinson's disease

P. Mangat, K. Van Hedger, T. Stoat, M. Prenger, G. K. Badwal, K. Mutambayi, P. A. MacDonald

Importance: Parkinson's disease (PD) is typically characterized by motor dysfunction; however, it can also involve deficits in cognitive and socioemotional processes. Alexithymia, the difficulty in identifying and describing emotions, impacts socioemotional well-being, and is relevant for disease outcomes in patients with PD.

Objective: This study examines the relationships between alexithymia and disease outcomes, including feelings of anxiety, depression, apathy, and health-related quality of life in patients with PD. Following prior research, we hypothesized that patients with increased alexithymia would also have increased apathy. We also explored whether this relationship extends to other neuropsychiatric symptoms of PD and/or impacts self-reported health-related quality of life.

Design and Participants: This study used a cross-sectional design with 30 patients with PD (10 women) and 38 healthy elderly controls (18 women). A convenience sample was recruited from other studies within the MacDonald Lab, where participants were screened with inclusion criteria for MRI studies and acute pharmacological manipulation of dopamine via medication abstention or administration. For this study, participants completed survey questionnaires assessing alexithymia (Toronto Alexithymia Scale), depression (Beck Depression Inventory), anxiety (Beck Anxiety Inventory), apathy (Starkstein Apathy Scale), and health-related quality of life (Nottingham Health Profile) either during a study session or at home.

Results: Patients with PD had significantly higher ratings of alexithymia compared to healthy control participants ($t(66) = -3.71$, $p < .001$). Among patients, alexithymia was a significant predictor of apathy ($\beta = 0.25$, $p = .02$) and healthy-related quality of life ($\beta = 0.11$, $p = .003$), but not anxiety ($\beta = 0.07$, $p = .48$) or depression ($\beta = 0.13$, $p = .12$), after controlling for age, sex, and disease duration.

Conclusions and Relevance: These findings are consistent with prior research, further demonstrating a link between alexithymia and apathy in patients with PD, and extends those findings to disease-related quality of life. Given that alexithymia does not appear to relate to anxiety or depression, it might be overlooked for treatment in PD, despite the fact that interventions to address alexithymia could improve patient quality of life.

POST-9

Morphometry of the subthalamic nucleus in healthy and Parkinson's disease populations: a systematic review and meta-analysis

Abrar Ahmed, Ali Hadi, Chris Zajner, Chloe Gui, John Demarco, Sandy Wong, Alaa Taha Jonathan C. Lau

Importance: The subthalamic nucleus (STN) is a deep brain stimulation (DBS) target for Parkinson's disease (PD) that is not well visualized using conventional clinical MRI. While knowing the volume and dimensions of the STN may help improve accuracy of DBS targeting these measurements remain poorly estimated in healthy control (HC) and PD.

Objective: We conducted a systematic review and meta-analysis to summarize relevant articles, to determine a global average in STN volume, hemispheric volumes, as well as dimensions related to size (length, width and height). We further sought to identify patterns between STN volume and age, disease duration, and UPDRS III- off L-Dopa scoring.

Methods: Studies from 1980-2024 investigating PD patients or healthy adult patients reporting volume or length, width, height of STN using MRI across different field strengths were included. Exclusion criteria included studies using non-MRI imaging modalities or cadavers/animal populations. Shapiro-wilk, weighted Mann-Whitney U test, Pearson or Spearman correlation coefficient and Hedge's G tests were performed.

Results: 34 studies met inclusion criteria (1356 patients). The average STN volume was 108.71 mm3 +/- 43.09 mm3, and 114.21 +/- 43.3 mm3 in HC and PD respectively (P>0.05). The length, width, and height in PD vs HC were 8.51x 5.80 x 6.90 mm vs 8.54 x 5.38 x 7.84 mm (P>0.05). The volume of the left and right STN in HC was 104.57 +/-33.94 mm3 and 99.26+/- 34.77 mm3 respectively (P>0.05), while in PD it was 105.61 +/- 28.37 mm3 and 104.31 +/- 34.58 mm3 (P>0.05). There was no significant correlation between STN volume and age, disease duration, or UPDRS III- off L-Dopa.

Conclusions and relevance: This study provides a global average for STN volume and size as estimated using MRI in PD and HC. These results provide useful estimates regarding the size of the STN that can be employed to optimize targeting of the STN and may be particularly valuable when the structure is not well seen on clinical images. Further study is required before the results are used in clinical setting.

POST-10

Re-norming Medical Education: Centering Patient Experience and Diverse Bodies in Lumbar Puncture (LP) Instruction

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

Importance: Medical curricula in Canada, which are often developed with limited patient and student input, regularly underrepresent certain body types. Medical education often prepares learners to perform procedures, such as lumbar punctures (LPs), on young, white, able-bodied, males with little body fat. When approaching diverse patients, this educational gap can lead to medical learners' lack of confidence, skill, and knowledge, resulting in poor patient experiences.

Objective: To ameliorate this issue, we integrated the perspectives of patients, clinicians, and students into an LP teaching module that focuses on each patient as an individual.

Design and Participants: This project used a co-design framework involving patients, a medical student, a nurse practitioner, neurologists, and educational specialists. We interviewed five patients who underwent LPs at the London Health Sciences Centre and explored their experiences through a trauma-informed approach. We filmed neurologists demonstrating landmarking techniques on nine standardized patients of different body sizes, ages, skin tones (Fitzpatrick Scale), and spinal curvatures, including scoliosis, kyphosis, and lordosis. Our team created a teaching module with patient narratives, instructional videos, and landmarking demonstrations on diverse body types.

Results: In Spring 2024, we plan to hold student focus groups of 6-10 participants each to review their perceptions of the module effectiveness. Qualitative feedback from the participants will be used to refine module content. Our aim is to use a co-design framework to create a medical education resource that is more patient- and student-centred. Our module will be incorporated into Western University's Undergraduate Medical Education curriculum and made available under a Creative Commons license through the Western Open Access Health Education Media Library.

Conclusions and Relevance: Since understanding patient experience is instrumental in providing care, we invited patients to become teachers. Since students are experts in experiences of learning, we invited students to become co-designers. Combining patient, student, educator, and clinician expertise, our module equips learners to deliver LP across varying body types. Our teaching module provides an opportunity for health professionals to re-examine assumptions around the normative body in healthcare and understand the importance of recognizing each patient as an individual to deliver safe LPs.

POST-11

Evaluating Spatial Correspondence of Multimodal MRI via Anatomical Landmarks

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In clinical settings (e.g., stereotactic neurosurgery), errors on the order of 1-2 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 which survey the human brain can be accurately placed via novice and expert raters to evaluate image registration across imaging modalities, such as 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. 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.

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 < 0.001) on 3T (3.12 +/- 1.93mm) when compared to 7T scans (2.86 +/- 1.94mm). 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.

POST-12

Isolating the non-thermal effects of electric field therapy for Glioblastoma: an in vitro investigation

A. Elsaleh, E. Iredale, S. Schmid, M. Hebb, E. Wong

Importance: Treatment of brain tumors using locally delivered, low-energy, intermediate frequency (kHz range) electric fields, called Intratumoral Modulation Therapy (IMT), has shown promise preclinically. Applying IMT fields in vitro creates unwanted increases in temperature in the culture media. We here investigate the electrical properties of the culture media and test a novel water-cooling solution to optimize our in vitro IMT model.

Objective(s): (1) Determine the electrical properties of culture media at different frequencies. (2) Assess the temperature increase in vitro with the application of IMT. (3) Develop a water-cooling solution to distinguish electric field vs. thermal impacts on Glioblastoma (GBM) cells.

Design and Participants: A custom printed circuit board (PCB) was previously fabricated to enable IMT in a 24-well plate. We measured the delivered voltage in culture media at different temperatures (22-50oC) and frequencies (1kHz-1MHz) to derive its electrical properties. Next, temperature increase was assessed in culture media during IMT stimulation in a tissue culture incubator at different field intensities (1-2 V/cm). Finally, water-cooling was applied to cell culture plates, temperature measured, and the effect of IMT on patient-derived GBM cells compared with and without the cooling solution.

Results: Media conductivity was found to linearly increase with temperature. At 37oC, conductivity was found to increase with frequency between 1kHz (0.9 S/m) and 10 kHz (1.6 S/m) then level off between 10kHz-1MHz (1.7 S/m). During IMT application, temperature increases were significantly lower (n=3; $p<0.01$) with water cooling (0.9±0.3oC, 2.7±0.2oC, 4.7±0.2oC for 1V/cm, 1.5Vcm, and 2V/cm respectively) compared to traditional IMT (2.0±0.1oC, 4.3±0.2oC, 7.6±0.6oC). The measurements matched our computer simulations. Water-cooled IMT produced comparable GBM cell death (83±6%, 34±16%, 18±3% vs. 88±9%, 18±5%, 6±4% for non-cooled IMT at 0.5V/cm, 1V/cm, and 1.5V/cm; n=4), suggesting electric fields are the main driver of the observed cell death with IMT, especially at lower field intensities.

Conclusions and Relevance: We measured media conductivity at different frequencies and temperatures, which is rare in the literature, yet is essential to develop accurate computer simulations for IMT. Our novel water-cooling solution was effective at reducing the heat produced from IMT stimulation, and early investigations reveal a robust non-thermal IMT impact.

POST-13

Cognitive impairments in early Parkinson's disease

K. Patel, K. Van Hedger, P. MacDonald

Importance: Cognitive impairment is the most common non-motor symptom in Parkinson's disease (PD). Up to one third of patients with early PD exhibit cognitive impairments. However, previous studies examining cognitive performance in PD have been limited by small sample sizes, heterogeneity in disease severity, and effects of chronic dopaminergic therapy on cognition.

Objective: The aim of this study is to characterize cognitive deficits in early PD using a large, drug-naive sample and robust measures and to elucidate the differential memory deficits in encoding and retrieval.

Design and Participants: This study examined Montreal Cognitive Assessment (MoCA) total and sub-domain performance from the Parkinson's Progression Markers Initiative dataset (n= 714 patients with PD; n= 244 healthy controls). Patients were restricted to ≤ 12 months of disease duration and had not begun dopaminergic therapy. Encoding and retrieval were measured using the Hopkins Verbal Learning Test- Revised in a subset of participants (n= 675 patients with PD; n= 243 healthy controls). Bayesian analyses of covariance were performed on each measure using age, sex, education, and anxiety and depression scores as covariates. Bayes factor's (BF10) were calculated, using JASP, as the ratio of the predictive performance of any given model over the null model (BF10= 1).

Results: Patients had significantly lower scores than controls in MoCA total (BF10= 8.74×10+16), and sub-domains of recall (BF10=1.27×10+13), language (BF10= 234015.89), visuospatial executive (BF10= 3.05×10+11), abstraction (BF10= 299.32), and attention (BF10= 854.83). Patients and controls did not differ in learning slopes (BF10= 0.51) but did differ significantly in retrieval (BF10= 2725.73). BF10 values are presented for the best predictive model, including group as a predictor, except for learning where the BF10 for the first model including group as a predictor is reported.

Conclusions and Relevance: Patients with early PD show worse performance in global cognition, as well as memory, recall, visuospatial, executive, and attentional domains compared to healthy control participants, after controlling for relevant covariates. Furthermore, patients do not show impairments in learning (encoding) but do show impairments in memory retrieval. These findings highlight robust cognitive differences in patients with early PD tested prior to initiating dopaminergic therapy.

POST-14

Developing a patient-derived xenograft model of diffuse intrinsic pontine glioma in the SRG Rat

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Importance: Diffuse intrinsic pontine glioma (DIPG) is the primary cause of brain-tumor related deaths in children and requires further preclinical characterization in patient derived xenograft models. The Sprague Dawley-Rag2/Il2rg Knockout Rat (SRG RatTM) is an emerging immunodeficient rat oncology model, which serves as a promising candidate for DIPG intracranial xenograft.

Objective(s): To determine whether patient derived DIPG cells robustly grow in the SRG RatTM and constitute a translatable preclinical model.

Design and Participants: Patient derived DIPG cells were received from Dr. Michelle Monje at Stanford University and were transduced to express tdTomato-luciferase. For stereotaxic implantation, DIPGXIX and DIPG25 were used, which were cultured post-autopsy from a 2-year-old male and 4-year-old female, respectively. Adult SRG RatsTM were anesthetized with isoflurane and placed in a stereotaxic frame. A unilateral burr hole was drilled at the following coordinate sites from bregma: anteroposterior + 1.2 mm, lateral + 3.0 mm, dorsoventral - 6.5 mm. Animals received 1 × 106 DIPG25 or DIPGXIX cells in 10 µl PBS - injected unilaterally at a rate of 0.2 µl/min using a 10 µl Hamilton syringe. Tumor growth was monitored using bioluminescence imaging. At endpoint, SRG brains will be paraffin-embedded for subsequent immunohistochemical analysis of tumor- and DIPG-specific biomarkers.

Results: DIPGXIX cells were implanted into n =1 female SRG RatTM, which has been imaged over the course of 15 weeks. DIPG25 cells were implanted into n = 4 female SRG RatsTM. After implantation, large tumors were detected via bioluminescence imaging. The peak average bioluminescent signal decreased until ~one-month post-operation then began to trend upwards.

Conclusions and Relevance: This preliminary data suggests that DIPG tumors establish in the SRG RatTM; however, growth is slow at best and does not contribute to decline in health status. Further replication and immunohistochemical analysis are necessary to confirm trends and assess molecular characteristics. Overall, this study focuses on a promising preclinical animal model for DIPG, in which therapeutics can be more reliably assessed.

POST-15

Clinical Predictors of Impulse Control Disorders in Parkinson's Disease

T. Breddy, K. Van Hedger, K. Patel, N. Rothery, M. Sharafkhah, H. Ganjavi

Importance: A sub-group of patients with Parkinson's Disease (PD) experience impulse control disorders (ICD), which can substantially affect their quality of life and daily functioning. Clinical predictors of ICD development in patients with PD are largely unknown, with a few studies demonstrating conflicting results.

Objective(s): To investigate whether anxiety, depression, and sleep problems relate to development of ICD in patients with early-stage PD.

Design and Participants: Data from 1,701 patients with PD was obtained from the Parkinson's Progressive Marker Initiative (PPMI), which is an ongoing, longitudinal, open-source, multi-center study. PPMI exclusion criteria include a clinical diagnosis of dementia or another clinically significant neurological, psychiatric, or medical condition. The presence of ICD was evaluated using the Questionnaire for Impulsive-Compulsive Behaviours-Current-Short (QUIP-CS). Participants were excluded if they did not have sufficient QUIP-CS or PD medication data (n=846), demonstrated ICD at baseline (n=253), had less than six visits during which the QUIP-CS was administered (n=231), had a disease duration greater than 24 months at baseline (n=68), or initially presented with compulsive behaviours other than the main ICD of interest (n=118).

Results: We investigated 185 early-stage patients with PD (75 females) between 33 to 81 years of age (M=61.22, SD=10.07). We contrasted scores on measures of anxiety, depression, and sleep problems at baseline in patients who later developed ICDs within five years (n=52) or did not (n=133) using the State-Trait-Anxiety Inventory, Geriatric Depression Scale, and part 1.7 of the Movement Disorder Society-Unified Parkinson's Disease Rating Scale, respectively. Patients with ICDs reported significantly higher anxiety (M=72.65 vs. 59.87; p < .001), depression (M=2.77 vs. 1.84; p=.017), and sleep problems (M=1.00 vs. 0.65; p=.021) at baseline compared to patients without ICD. Logistic regression analysis revealed that only anxiety significantly predicted ICD after controlling for age and sex, OR = 1.04, CI 0.02 to 0.07, p = .001.

Conclusions and Relevance: Patients with early-stage PD who develop ICD demonstrate significantly higher anxiety, depression, and sleep problems at baseline, though only anxiety scores predicted ICD development. Anxiety screening could alert clinicians to patients at greater risk of developing ICDs, which could inform type and dose of dopaminergic therapy.

POST-16

Implementation and Evaluation of an Interictal Intracranial EEG Classifier

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Importance: Automatic identification of pathological events in interictal intracranial EEG (iEEG) suffers from low specificity, often confusing these events with artifacts. Prior attempts to further incorporate artifact classifications have not thoroughly evaluated the use of external datasets and diverse feature analyses.

Objective(s): Develop a machine learning model to distinguish between pathologies, artifacts, and baseline in interictal iEEG.

Evaluate the efficacy of various features in pathology and artifact identification within interictal iEEG.

Compare deep learning with traditional machine learning methods.

Assess the influence of sampling rates on iEEG classification performance.

Validate the model's effectiveness using continuous interictal data for practical pathology and artifact detection.

Methods: Two public datasets from St. Anne's University Hospital and Mayo Clinic were used to train several models for classifying iEEG data. Feature sets and models underwent comparison through cross-validation, including an analysis of sampling rate effects (1024 Hz vs. 2048 Hz). The best performing model was further tested on continuous iEEG recordings from the London Health Sciences Center.

Results: This study began with an evaluation of the performance of different deep learning models. This analysis favored a simple Convolutional Neural Network (CNN) model using time-frequency maps from the Hilbert Transform. Comparison was performed through cross-validation and the best model was selected based on a balance of simplicity and performance.

Non-deep learning models were also evaluated using discrete wavelet transform (DWT) features as inputs. Random forest (RF) was selected as the best non-deep learning model. This RF model outperformed deep learning models in subsequent external validation using a University of Florida dataset.

Notably, models trained with a 1024 Hz sampling rate showed improved performance, although these differences lacked statistical significance. Ongoing analysis on the RF model with London Health Sciences Center data aims to assess real-world application viability.

Conclusions: Our study underscores the importance of feature selection and model choice in machine learning for iEEG analysis. Surprisingly, deep learning did not surpass traditional methods, and higher sampling rates did not improve accuracy. Following final validation, the RF model will be released for public use, aiming to advance iEEG pathology and artifact detection with machine learning solutions.

POST-17

Development of a prognostic model for Parkinson's disease: predicting the onset of freezing of gait

N. Rothery, M. Sharafkhah, T. Breddy, K. Van-hedger

Importance: Freezing of Gait (FOG) is a debilitating motor symptom associated with Parkinson's disease (PD). Effective therapeutic and preventive interventions for FOG are limited due to insufficient understanding of its pathophysiology.

Objective(s): To develop a reliable prognostic model for FOG that can accurately predict the likelihood of developing FOG within five years of PD diagnosis. Additionally, we will extract biomarkers from the model that represent early pathophysiological changes that predispose the later development of FOG.

Design and Participants: Data from 174 PD patients were obtained from the Parkinson's Progressive Marker Initiative, an ongoing, open-source repository for longitudinal, multi-site neuroimaging and clinical data. Participants were excluded if they had a disease duration longer than 24 months (n=19) or presented with FOG at baseline (n=18). FOG-negative participants were also excluded if they had less than five years of FOG assessment data from diagnosis (n=67). From the MRI scans, we segmented the VTA/SNc and striatum into subregions using automated probabilistic tractography to the cortex. We extracted structural integrity, and connectivity measures, like mean diffusivity and fractional anisotropy, along white-matter bundles, subregional surfaces and within distinct cortical regions.

Results: We investigated 70 PD patients (26 female) aged 38- 82 (M=60.32, SD=10.25). At baseline, differences between patients who developed FOG within five years (n=29) and those who did not (n=41) were observed for age (M=64.31 vs. 57.50; P<.01) and MDS-UPDRS-total score (M=36.34 vs 24.95; P=.001). Larger group differences were observed in measures from the parcellated subregions of the striatum and VTA/SNc (P<.005) compared to unparcellated measures (P<.05). Differences were also found in distributed regions of the cortex (P<0.01). Following feature selection, a model classified patients who developed FOG from those who did not at the single-subject level with good performance during 10-fold cross-validation as measured by AUC (M=0.88, SD=0.17).

Conclusions and Relevance: Using Diffusion MRI and automated segmentation, we identified pathophysiological changes in microstructural integrity and connectivity that reliably predict the future development of FOG in patients with early PD. Further development of a prognostic model for FOG could be instrumental for patient planning in clinical settings enriching clinical trials with patients expected to develop FOG, enhancing efficiency and reducing costs.

POST-18

Targeting Pannexin 1 to uncover its role in glioblastoma multiforme

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Importance: Glioblastoma multiforme (GBM) is an aggressive and heterogenous tumor in the central nervous system with a median survival time of 14 months which highlights a need for new therapeutic interventions. Pannexin 1 (PANX1) is a channel forming protein that is overexpressed in GBM relative to normal brain and this study investigates the potential of PANX1 to be used as a therapeutic target for GBM.

Objective: To determine the role of PANX1 in GBM and the effect of pharmacological PANX1 inhibition on tumorigenic properties.

Design: Two patient-derived glioblastoma tumor fragments and patient-matched non-neoplastic brain fragments were embedded in paraffin and used for immunohistochemical staining of PANX1. Five patient-derived glioblastoma cells were immunoblotted for PANX1 and GBM17 was chosen as a representative cell line for this study. Probenecid (PBN) and Spironolactone (SPIR) are Health Canada approved drugs that have been repurposed as blockers of PANX1 and can cross the blood brain barrier. The blockers were used to determine the effect of PANX1 inhibition on malignant properties and on the expression of PANX1 interactors, F-actin and B-catenin, in GBM17. In addition, PANX1 expression and inhibition was studied in the rat glioma cell line F98 to determine the potential of F98 cells to be employed for a syngeneic allograft to study PANX1 inhibition.

Results: PANX1 expression appears diffuse in GBM tumor fragments and immunofluorescence in GBM17 reveals mostly intracellular localization. Treatment of GBM17 with PBN and SPIR reduced both cell growth and migration and did not affect PANX1 expression or localization. However, the inhibitors disrupted F-actin expression and β-catenin localization. PANX1 is also expressed in rat glioma cells with an intracellular localization and its growth was significantly reduced with SPIR however not with PBN.

Conclusion and relevance: GBM has a poor prognosis due to heterogeneity and limited drug accessibility. This study furthers our understanding of the tumor promoting role of PANX1 in GBM and demonstrates the potential of PANX1 inhibitors to be used as GBM therapeutics. This study also provides evidence warranting F98 syngeneic allografts to further understand the effects of PBN and SPIR in-vivo.

POST-19

PST As a Screening Tool for Cognitive Impairment in MS in the Clinic Setting

M. R. Everest, S. A. Morrow

Importance: Cognitive impairment, most frequently in information processing speed (IPS), is estimated to affect 65-85% of persons with MS (PwMS), and is standardly accessed using the in-person oral Symbol Digit Modalities Task (SDMT).

The self-administered iPad Processing Speed Test (PST) has been proposed as a possible alternative.

Objectives(s): To examine the relationship between the PST (iPad) and SDMT (oral) in PwMS, and if this relationship is affected by manual dexterity differences.

Design and Participants: This prospective, single-site study recruited PwMS aged 18 years and older, with an Expanded Disability Status Scale (EDSS) <8.0. At one time-point, in-person, all participants completed the Nine-Hole Peg Test (9HPT), SDMT and PST, in that order. For the purpose of this analysis, only dominant hand 9PHT was used. 9HPT scores were divided into quartiles. Pearsonâ€™s correlation (r) was used to compare SDMT and PST scores, first for the whole cohort, and then within each 9HPT quartile.

Results: Participants (n = 100) were mostly self-identified female (75%) with a mean age of 46.2 (SD = 12.4) years, with a mean years of education of 14.2 (SD = 2.3) and a median EDSS score of 2.0 (Min = 0.0, Max = 7.0). SDMT (Raw score M = 59.4, SD = 11.3) and PST (Raw score M = 55.6, SD = 11.3) scores were significantly correlated (r = 0.83, P<0.001). Mean 9HPT in the dominant hand was 22.2 seconds (SD = 6.2). In all 9HPT quartiles (Q), the SDMT and PST were significantly correlated (Q0: r = 0.76, P<0.001) (Q1: r = 0.82, P<0.001) (Q2: r = 0.67, P<0.001) (Q3: r = 0.88, P<0.001). Notably, the correlation between the PST and SDMT was strongest amongst participants with the lowest manual dexterity.

Conclusions and Relevance: This study demonstrates the validity of the iPad PST screening tool as comparable to the oral SDMT for PwMS, without the need for an administrator, regardless of manual dexterity/9HPT performance.

POST-20

Association Between Statin Use and Stroke-Related Epilepsy: A Nested Case-Control Study

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Importance: Research suggests that statins may reduce the risk of epilepsy after a stroke. However, whether this association differs between sexes is unclear. As sex differences between men and women in this association is a potentially clinically important finding, effect modification by sex requires further exploration.

Objective(s): The primary objective of this study was to assess whether sex modifies the association between post-stroke statin use and stroke-related epilepsy. Our secondary objectives were to assess whether statin characteristics and other risk factors affect stroke-related epilepsy risk within groups defined by sex.

Design and Participants: We conducted a nested case-control study using linked health administrative datasets. Participants were included if they were discharged from inpatient treatment for an ischemic stroke, between the ages of 66 and 105, and did not have a history of epilepsy, seizure or epilepsy risk factors, or statin use. Patients with epilepsy were matched on age, sex, and month with up to 10 controls who had not yet developed epilepsy. The index date was defined as the epilepsy diagnosis date for cases and their matched controls. To address our primary objective, we used a conditional logistic regression model to estimate the adjusted odds ratio for statin use in the 100 days prior to the index date between those who did and did not develop epilepsy, including an interaction term between sex and statin use. To address our secondary objectives, we estimated the odds ratios for statin use and all covariates within groups defined by sex and the adjusted odds ratios for statin characteristics (i.e. type and intensity) among statin users stratified by sex.

Results: The final sample included 1,009 patients who developed epilepsy and 6,522 matched controls. Statin use did not significantly affect the risk of epilepsy in the entire sample or the stratified analysis, and we did not observe a statistically significant interaction between statin use and sex (p-value=0·07). Compared to statin non-users, males taking simvastatin had a significantly increased risk of epilepsy (OR 3·30; 95% CI 1·03-10·52). Among statin users, there was a lower risk of epilepsy among females taking rosuvastatin compared to females taking atorvastatin (OR 0·70; 95% CI 0·51-0·95). Other risk factors were similar between sexes; however, alcohol abuse and depression or anxiety were associated with epilepsy only among males.

Conclusion and Relevance: Although the risk of epilepsy did not significantly differ between males and females, some risk factors for epilepsy differed between sexes and should be further explored.

POST-21

A Retrospective Analysis of Stereoelectroencephalography Application Accuracy: Single Canadian Center

K. Al Orabi, Greydon Gilmore, Mohamad Abbass, Arun Thurairajah, Alaa Taha, Brendan Santyr, Ana SullerMarti, Jorge G. Burneo, Sandrine de Ribaupierre, Keith W. MacDougall, Andrew G. Parrent, David A. Steven, Jonathan C. Lau

Importance: Stereoelectroencephalography (SEEG) is a stereotactic neurosurgical procedure utilized in specific cases of drug resistant epilepsy to characterize epileptogenic zones and networks. Accurate implantation of SEEG electrodes is essential for maximal efficacy and safety.

Objective(s): In this study, we sought to analyze the factors contributing to the accuracy of robotically and frame-based implantation of SEEG electrodes.

Design and Participants: A series of 200 patients who underwent robotic SEEG implantation and 31 frame-based SEEG were included (between 2013 to 2024). Euclidean and radial electrode trajectory distances were calculated between the planned target (defined on preoperative T1w imaging) and the actual target (based on postoperative CT). The effects of target location and patient factors on accuracy were investigated.

Results: This study included 200 patients who underwent robotic SEEG implantation (50.0% female, mean age 34.26 ± 13.03 yrs, mean number of electrodes 11.66 ± 2.96) and 31 patients who underwent frame based SEEG implantation (51.61% female, mean age 33.48 ± 10.73 yrs, mean number of electrodes 10.23 ± 2.31). For robotic SEEG, Euclidean error at entry was 1.67 ± 1.12 mm and at target 2.30 ± 1.19. The radial error at entry was 1.23 ± 0.85 and at target 1.59 ± 1.04. For frame based SEEG, Euclidean error at entry was 3.16 ± 1.68 mm and at target 3.05 ± 1.52. The radial error at entry was 2.04 ± 1.41 and at target 2.27 ± 1.52.

Conclusions and Relevance: SEEG electrodes can be placed within millimetric accuracy with robotic assistance. Factors such as target location can influence placement accuracy. Future directions include further elucidating the association between target location and accuracy, further exploring possible covariates such as trajectory angle and length. This framework can be applied prospectively to optimize SEEG implantations, enabling increasingly accurate and tailored investigations of patients with epilepsy.

POST-22

Late-Onset Ornithine Transcarbamylase (OTC) Deficiency resenting with coma and status epilepticus

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Importance: Late-onset ornithine transcarbamylase deficiency is increasingly being diagnosed in older people. Therefore, it is important to include an ammonia level in the assessment of encephalopathic adult patients, regardless of age.

Objective(s): This case report outlines the clinical presentation, diagnostic challenges, and management of a 71-year-old male with a previously undiagnosed late-onset Ornithine Transcarbamylase (OTC) deficiency presenting as hyperammonemic encephalopathy.

Design and Participants: We will provide an overview of the clinical, laboratory, and imaging investigations for a patient with late onset OTC deficiency diagnosed post-mortem.

Results: The patient presented with delirium in the context of a recently diagnosed giant cell arteritis (biopsy proven) being treated with prednisone. Despite empiric antimicrobial treatment for suspected meningitis, and lumbar puncture, the patient's level of consciousness rapidly deteriorated. Continuous EEG revealed non-convulsive status epilepticus with multifocal spikes and occipital seizures. An MRI showed extensive cortical diffusion abnormalities. The patient died from hyperammonemic encephalopathy and diffuse cerebral edema after administration of valproic acid administered for ongoing seizures. Subsequent genetic testing revealed hemizygosity for OTC:c:622G.

Conclusion and Relevance: Late-onset OTC deficiency is a rare but potentially fatal cause of hyperammonemic encephalopathy. This case underscores the importance of considering urea cycle disorders in patients presenting with unexplained coma, seizures, or cerebral edema, irrespective of age. Prompt diagnosis, aggressive intervention, and awareness of potential triggers, including protein-rich enteral feeding and valproate use, are crucial for preventing irreversible neurological damage.

POST-23

The spectrum of cognitive outcomes following admission to hospital for refractory status epilepticus: a scoping review

A. AL Wahaibi, K. Kazazian, T. Gofton

Importance: Refractory Status epilepticus (RSE) is a life-threatening neurological emergency that is associated with high mortality and morbidity. There is growing evidence to guide management, but there remains limited information regarding outcomes after hospitalization especially with respect to prolonged RSE.

Objective(s): This scoping review will examine the spectrum of cognitive outcomes following admission RSE from all etiologies. Secondary questions include exploring why specific approaches to cognitive assessment were used and whether there are differences in cognitive outcomes for patients with RSE with an identified etiology compared to NORSE.

Design and Participants: This scoping review follows established methodology. A comprehensive literature search was conducted using MEDLINE and EMBASE. The search strategy was designed by clinical librarian and the literature search was completed in September 2023. Conference abstracts without full text and publications without an English language translation were excluded.

Results: Of the 2439 studies, 15 studies met inclusion criteria. 4/8 studies described the specific test used when they reporting neuropsychological or psychometric evaluation. One study assessed cognitive outcomes by standardized IQ tests and two studies used Telephone Interview for cognitive status (TICS). One pediatric study described a wide spectrum of cognitive outcomes withdescribing their approach. There were 5 studies reported using a comparison group to contextualize the results. The data could not be combined for statistical analysis because the approach for cognitive assessment was different between studies.

Cognitive outcomes were reported after RSE at different timepoints, which varied from between 3 months after onset of RSE to greater than one year, and some did not specify the timing of assessment. Short term memory was commonly reported as impaired in adults whereas mild to moderate mental retardation was reported in children. With impairment in multiple domains was described. There were no reports of return to baseline function in children.

Conclusions and Relevance: A large portion of patients admitted with RSE developed cognitive impairment. The majority of studies did not provide justification for their approach to cognitive assessments. Further research is required in order to improve consistency regarding the timing and approach to cognitive testing when evaluating outcomes after RSE.

POST-24

Examining neural substrates of freezing of gait with structural MRI in patients with Parkinson's disease

Mojtaba Sharafkhah, Hooman Ganjavi, Brian Corneil, Kathryne (Kasey) Van Hedger, Jessica Grahn. Co Author: Nathan Campbell Rothery

Importance: Freezing of gait (FOG) is a treatment-resistant motor symptom of Parkinson's disease (PD). Using MRI, researchers can evaluate white matter (WM) structural changes in subcortical regions in PD patients with and without FOG to better understand this symptom and assess the potential for new therapeutic approaches.

Objective: To compare the integrity of WM tracts using diffusion MRI measures in standard subcortical regions (i.e., striatum, ventral tegmental area (VTA), substantia nigra pars compacta (SNc)), and parcellated regions of the striatum and VTA/SNc between PD patients with and without FOG (i.e., PD-FOG and PD-nFOG).

Design and Participants: Twenty-nine PD-FOG and 41 PD-nFOG underwent 3T MRI through the Parkinson's Progression Markers Initiative (PPMI) and had 5 years of assessment following PD disease diagnosis including demographic, cognitive, and behavioral characteristics. We used automated probabilistic tractography to segment the striatum into 6 subregions and the VTA/SNc into 4 subregions. Mean diffusivity (MD) and fractional anisotropy (FA) were measured along WM bundles and subregional surfaces in both the whole striatum and VTA/SNc, as well as in the 10 parcellated subregions.

Results: Patients with PD-FOG had higher mean bundle MD of the occipital striatum (p-value = 0.047, η^2p = 0.058) and mean bundle MD of the executive (p-values = 0.025, η^2p = 0.074), rostral motor (p-values = 0.024, η^2p = 0.075), and caudal motor of the VTA/SNc (p-values = 0.02, η^2p = 0.07) compared to patients with PD-nFOG. However, Surface FA and MD of the parcellated striatum and VTA/SNc did not differ between PD-FOG and PD-nFOG. Based on logistic regression analysis, significant FA/MD parcellated striatum (p = 0.021, AUC = 0.777, accuracy = 0.814) and VTA/SNc (p = 0.043, AUC = 0.75, accuracy = 0.729) could be useful predictors of FOG appearance.

Conclusions and Relevance: Diffusion MRI measures (i.e., FA and MD) of parcellated nigrostriatal subregions, which degenerate first in PD, can be used to predict the appearance of FOG during the first five years following PD diagnosis. This work has the potential to develop diffusion MRI biomarkers of FOG, which is an important initial step toward developing novel therapeutic approaches.

POST-25

Stereotactic charting of the human brain using automated anatomical fiducials

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Importance: Brain landmark localization is crucial to neuroimaging studies and clinical workflows. For instance, identification of salient brain regions like the anterior (AC) and posterior commissure (PC) is common in brain alignment, and neurosurgical procedures use the AC-PC line as a reference for surgical targeting.

Objectives: We aimed to establish and validate an open and modular infrastructure to automatically localize anatomical landmarks, enabling millimetric and morphometric mapping of the adult brain across lifespan.

Design and Participants: Anatomical Landmarks. We previously identified and validated an open-access protocol for the placement of brain landmarks called anatomical fiducials (AFIDs). Our protocol describes 32 points surveying brain tissue (i.e., grey/white matter and ventricles).

Datasets. We curated 4 international MRI datasets (1.5-, 3-, and 7-Tesla) with different disease backgrounds (healthy, abnormal ventricles, and neurodegenerative) on which we have manually localized a total of 20,000 AFIDs.

Machine Learning. The aforementioned dataset (N = 173) was split across training (70%), validation (10%), and testing (20%) subsets. A convolutional neural network (CNN; U-Net architecture) was trained to localize AFIDs from T1w MRI scans. Euclidean distance (ED) between the predicted location and ground-truth was used for model assessment.

Research and Clinical Applications. Leveraging predictions of AFID coordinates, we build a brain growth chart for AC-PC distance by applying our model on healthy control scans across the adult human lifespan.

Results: The overall median ED error across all landmarks was 1.28 +/- 4.78 mm. We subsequently focus downstream analysis on AC and PC due to their clinical relevance.

The median AC and PC ED error was 0.42 +/- 0.35 mm and 0.82 +/- 0.28 mm, respectively. This is in keeping with previously reported rater localization error and motivated us to reliably apply our model across human aging.

Across an expanded dataset of ~2,000 healthy scans (age: 18-100 years, Female: 54.8%), AC-PC distance decreased with age. The mean AC-PC distance for males and females was 26.62 +/- 1.42 mm and 25.84 +/- 1.43 mm, respectively.

POST-26

Investing the cellular mechanisms of Thr175 tau phosphorylation in traumatic brain injury

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

Importance: Traumatic brain injury (TBI) has been linked to the progressive neurodegenerative disease chronic traumatic encephalopathy (CTE), which is characterized by phosphorylated tau aggregates. TBI has been demonstrated to increase pThr175 tau, which induces GSK3β activation, pThr231 tau and tau fibril formation.

Objectives(s): The objective of this study was to investigate the mechanisms driving Thr175 tau phosphorylation and CTE-like pathology. We examined the ability of candidate kinases ERK and JNK to phosphorylate Thr175 in vitro and examined the effect of GSK3β inhibition by lithium chloride treatment on tau pathology in vivo using a rat model of TBI.

Design and Participants: To investigate the phosphorylation of Thr175 in vitro, HEK293T cells were co-transfected with 2N4R tau and either active or inactive ERK and JNK. Levels of pThr175 and downstream targets were determined by Western blot analysis.

Three-month-old female Sprague Dawley rats were subjected to a single controlled cortical impact injury. Rodents were treated daily with 60mg/kg of lithium chloride beginning three days before or three days after the injury, while controls were administered saline. Tissue was collected on days 1, 3, 5, 7 & 10 post-injury.

Results: Overexpression of active ERK and JNK resulted in a significant increase in pThr175 and pThr231 tau compared to the inactive mutants. Only overexpression of ERK induced a conformational change, oligomeric tau, and pathological PHF tau formation, suggesting that phosphorylation of Thr175 by ERK and JNK activates unique pathways.

Inhibition of GSK3β by lithium selectively reduced pThr231 tau compared to controls. Notably, the greatest effect was seen with pre-injury lithium in the hippocampus, where neurons appeared to be selectively spared. We infer that neuronal vulnerability may be due to the presence of calcium-regulating proteins calbindin 1 (Calb1) and mitochondrial calcium uniporter (MCU), as pThr231 pathology was associated with a decrease in Calb1 and an increase in MCU expression.

Conclusion and Relevance: We demonstrate that both ERK and JNK are capable of phosphorylating Thr175 tau; however, only ERK induces oligomeric and pathological tau formation. Further, we show that in animal models of TBI, inhibition of GS3Kβ reduces pThr231 pathology, suggesting that GSK3β may be an ideal target for TBI and CTE treatment.

POST-27

Discriminating between Parkinson's disease and essential tremor: executive striatal subregion microstructure and its correlation with cognitive deficits

N. Osagie, M. Gilchrist

Importance: Identifying striatal microstructure differences between Parkinson's disease (PD) and essential tremor (ET) provides the opportunity to differentiate between these diseases with MRI. This would inform differential diagnostic biomarkers and ameliorate patients' long wait times for assessment.

Objective: This study compares executive striatal subregion surface mean diffusivity (MD) between PD, ET, and healthy controls (CTs), and its correlation with executive function.

Design and Participants: Sixteen PD patients, 16 ET patients, and 16 CTs participated in a cross sectional study. Participants were matched for age and sex. Patients were recruited through the Movement Disorder Database, and CTs were contacted through a volunteer database. Participants underwent a structural MRI, measuring ipsilateral and contralateral surface MD. They completed the Montreal Cognitive Assessment (MoCA), and scores from the visuospatial/executive (VE) and delayed recall (DR) tasks were analyzed. Group means (±SD) were compared using a one-way ANCOVA and post hoc comparisons. Correlations between surface MD and MoCA scores were analyzed within all groups.

Results: Preliminary results from 16 participants (PD: n = 6, mean age = 66; ET: n = 4, mean age = 69; CT: n = 6, mean age = 66; 6 females), show PD patients had significantly greater ipsilateral striatal surface MD (M = 1.00 x 10-3, SD = 1.41 x 10-4) than CTs (M = 8.09 x 10-4, SD = 8.72 x 10-5; padj = 0.029), and slightly greater ipsilateral surface MD than ET patients (M = 8.18 x 10-4, SD = 4.39 x 10-5; padj = 0.063). There was no significant difference in MoCA subscores between PD (VE: M = 4.00, SD = 1.55; DR: M = 3.67, SD = 1.03), ET (VE: M = 4.25, SD = 0.50; DR: M = 3.25, SD = 1.71), and CTs (VE: M = 4.50, SD = 0.55, padj = 0.701; DR: M = 4.00, SD = 1.55, padj = 0.802). There was no correlation between MoCA subscores and striatal surface MD values (padj > 0.05).

Conclusions and Relevance: Preliminary results provide support for the identification of group differences between PD, ET, and CTs using MRI. We found greater MD values in the executive subregion of the striatum of PD patients, but not ET patients, compared to CTs. However, this difference did not correlate with lower VE or DR scores on the MoCA. These results lay the foundation for identifying neuroimaging biomarkers that could simplify PD/ET diagnosis procedures in clinical settings.

POST-28

**Doesn't consent to having the abstract online*

POST-29

De Novo High-Grade Diffuse Leptomeningeal Glioneuronal Tumour in Children: A Case Report and Review of the Literature

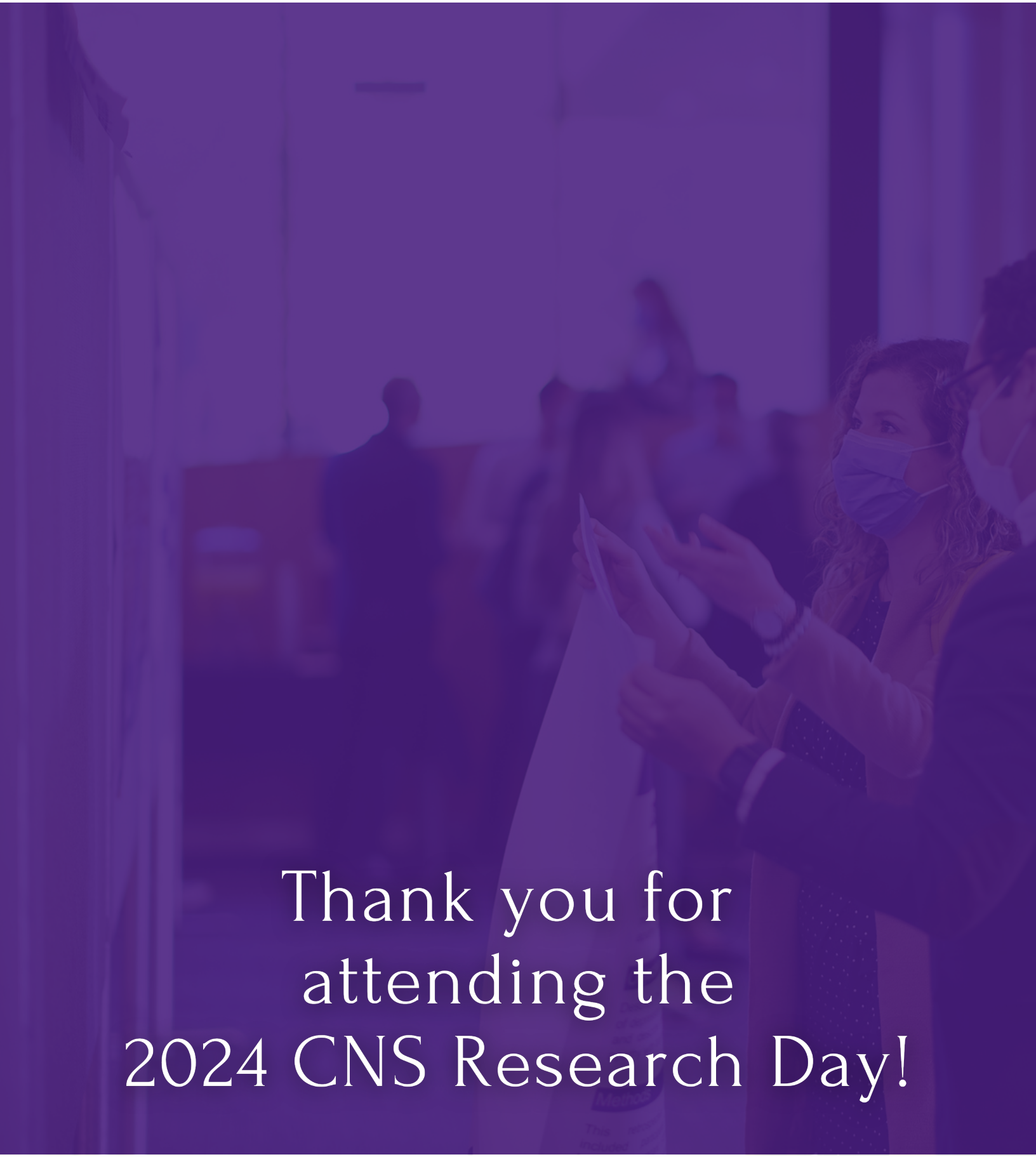
E. Lúcar Figueroa, J.W. Loggie, M. Abbass; M. Son; M.T. Jurkiewicz, E. Spinelli, P. Lessard Bonaventure, R.R. Hammond, L.C. Ang, S. de Ribaupierre

Importance: Diffuse leptomeningeal glioneuronal tumour (DLGNT) is primarily seen in the pediatric population. Given their rarity, specific WHO grades have not been assigned to DLGNTs or their subtypes.

Objective(s): We report a case with high-grade characteristics and review the literature to assess patterns in their presentation, challenges with diagnosis and targeted treatment.

Results: A 16-year-old male with a 6-month history of progressive neurological decline. MRI demonstrated extensive leptomeningeal enhancement along the neuroaxis as well as numerous intradural and intramedullary spinal lesions. Spinal thoracic open biopsy revealed DLGNT with 1q gain and anaplastic morphology, more in keeping with aggressive behavior, WHO grade 3. Despite repeated treatment with chemotherapy and radiation, further tumor progression was observed. To date, there are 28 reported cases of de novo “high-grade” DLGNTs in the literature.

Conclusions and Relevance: De novo “high-grade” pediatric DLGNTs have an aggressive clinical course. Given nonspecific symptoms and radiologic findings, initial diagnosis of DLGNT may be elusive. Thus, early open tissue biopsy is crucial. Moreover, their diagnosis require complementary and novel approaches such as high-throughput next-generation sequencing and microarray-based genome-wide association studies including DNA methylation arrays. In addition, standardized and targeted treatments are lacking.



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