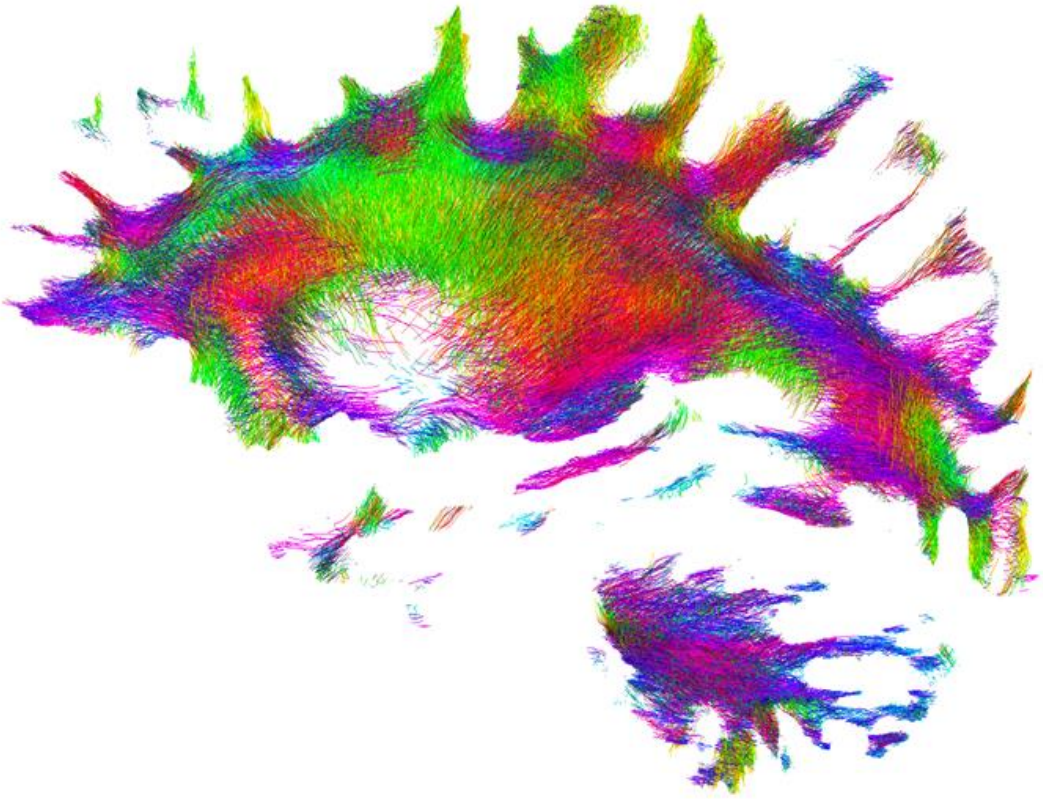
NEURO WORKSHOP

Mercredi 2 décembre, 2020
Virtuel

Wednesday, December 2, 2020
Virtual

CONNECTOMICS IN EPILEPSY

DISEASE BIOMARKERS
MODELS OF COGNITION
AND BIG DATA
NETWORK SCIENCE



It is increasingly recognized that epilepsy is a disorder of whole-brain networks. New techniques to image and to analyze brain connectivity has furthermore given a comprehensive, 'big data' perspective on brain networks, and to detect their alterations in epileptic disorders. In this virtual workshop, we aim to overview how these approaches have provided novel insights into the impact of epilepsy on the whole brain, and how these tools are beginning to deliver clinically useful biomarkers and novel models of cognitive function and dysfunction.

- Organizing Committee

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Program

10:00 **Opening remarks**

10:15 **Session 1: Connectome Biomarkers**

Chairs: Dewi Schrader, University of British Columbia, Andrea Bernasconi, Montreal Neurological Institute, Ed Hogan, Washington University St. Louis

Evolving Network Model for Biomarkers of Treatment Outcome in Focal Epilepsy

Victoria Morgan, Vanderbilt University, USA

The Connectomics and Vagus Nerve Stimulation Outcome Study (CONNECTiVOS)

George Ibrahim, Hospital for Sick Kids, Canada

Connectome Biomarkers in the Early Stages of Epilepsy

Simon Keller, University of Liverpool, UK

11:00 **Session: 1 Q&A**

11:30 **Lunch and Gather Space (Via Zoom)**

12:30 **Session 2: Cognitive Connectomics**

Chairs: Mary Pat McAndrews, University of Toronto, Luis Concha, National Autonomous University of Mexico, Matthias Koepp, University College London

Towards a connectome perspective on cognitive dysfunction in epilepsy: multiscale profiling and dynamic connectivity analysis

Lorenzo Caciagli, Pennsylvania State University, USA

Cognitive Phenotypes in Epilepsy: Moving Towards Precision Neuropsychology

Anny Reyes, University of California at San Diego, USA

Functional Connectivity Patterns Associated Compensatory Memory Reorganization in Epilepsy

Joseph Tracy, Thomas Jefferson University, USA

1:15 **Session 2: Q&A**

1:45 **Coffee and Quiz Time**

2:00 **Session 3: Big Data Network Models**

Chairs: Carrie McDonald, University of California San Diego, Neda Bernasconi, Montreal Neurological Institute, Fernando Cendes, University of Campinas

Network-Based Alterations in the Common Epilepsies: Findings from the ENIGMA-Epilepsy Consortium

Sara Lariviere, Montreal Neurological Institute, Canada

Understanding Treatment Outcomes from Structural Neuronal Networks

Leo Bonilha, Medical University South Carolina, USA

Connectomics in Epilepsy: The Why and Wherefore

Danielle Bassett, University of Pennsylvania, USA

2:45 **Session 3 Q&A**

3:15 **Open discussion (20 minutes)**

Speaker Bios and Talk Abstracts

Victoria Morgan, Vanderbilt University, USA

Dr. Morgan is a Professor of Radiology and Radiological Sciences in the Vanderbilt University Institute of Imaging Science at Vanderbilt University Medical Center. She received her BS in biomedical engineering from Wright State University, and her PhD in biomedical engineering from Vanderbilt University. She is a Fellow of the American Epilepsy Society and the American Institute for Medical and Biological Engineering. Dr. Morgan has been interested in using MRI to quantify the functional effects of temporal lobe epilepsy on the brain since she presented a project to lateralize TLE using functional connectivity in 2002. Since then, she has received funding from the Epilepsy Foundation and sustained support from NIH to continue these investigations.

Abstract: Evolving Network Model for Biomarkers of Treatment Outcome in Focal Epilepsy

For decades the clinical treatment model for drug resistant focal epilepsy included two general steps: 1) identify the seizure focus, and 2) resect as much of it as possible, while minimizing functional or cognitive impairments. However, as numerous technological advances allowed for more confident localization of the focus, treatment outcomes have not improved proportionally. In this talk I will introduce a treatment model for mesial temporal lobe epilepsy that incorporates network evolution over decades of disease before and after surgical treatment. Evidence in support of this model using MRI functional and structural connectomes for understanding and predicting long term treatment outcomes will be presented.

George Ibrahim, Hospital for Sick Children, Canada

Dr. George Ibrahim is a pediatric neurosurgeon at the Hospital for Sick Children and Assistant Professor at the Institute of Biomaterials and Biomedical Engineering, the Institute of Medical Sciences and the Department of Surgery at the University of Toronto. He is also a Scientist in the Neurosciences and Mental Health program as the SickKids Research Institute. His clinical and research interests include the surgical treatment of medically intractable epilepsy, spasticity and functional disorders in children. He plays an active role in the comprehensive epilepsy, dorsal rhizotomy and deep brain stimulation programs at SickKids. His research lab is dedicated to the study of neural networks in children with epilepsy and functional disorders through a combination of connectomic, computational neuroscience and machine learning approaches. His work has yielded insights into personalized treatments for children targeting specific network impairments and the development of novel devices and treatment strategies. His interests also include the intersection of global health, neuroethics and neurosurgery, including the provision of neurosurgical care to the world's most vulnerable children.

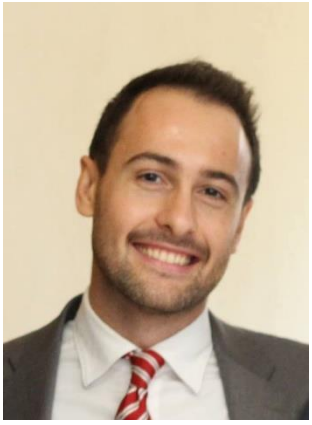
Abstract: The Connectomics and Vagus Nerve Stimulation Outcome Study (CONNECTiVOS)
Vagus nerve stimulation (VNS) is a common treatment for medically intractable epilepsy, but response rates are highly variable, with no preoperative means of identifying good candidates. Multimodal connectomic-based prediction algorithms may enable identification of VNS candidates and the delivery personalized treatments based on an individual's unique neural network fingerprint. A prospective trial, the "Connectomics and Vagus Nerve Stimulation Outcome Study (CONNECTiVOS)" will define the role of connectomic profiling in predicting VNS response. The implication of these studies are far reaching to mitigate surgical risks for patients who may not benefit, and to ensure cost-effective allocation of health care resources.

Simon Keller, University of Liverpool, UK

Simon Keller is an Associate Professor of Neuroimaging at the University of Liverpool with a main interest in understanding mechanisms, developing diagnostic tools and identifying biomarkers of treatment outcome in epilepsy. The primary focus of his research is to develop and apply non-invasive brain imaging methods to understand the biology underlying neurological and neurodegenerative disorders, with a particular focus on using pre-treatment imaging to predict post-treatment outcome. Research in his group is performed at the Liverpool Magnetic Resonance Imaging Centre (LiMRIC) at the University campus and at the Walton Centre NHS Foundation Trust (WCFT). He shares close working collaboration with neurologists, neuroradiologists and neurosurgeons at WCFT, principally, but not exclusively, in context of epilepsy research.

Abstract: Connectome Biomarkers in the Early Stages of Epilepsy
There has been significant developments in understanding brain structural and functional connectivity in refractory epilepsy and how aberrant connectivity may impact on surgical treatment outcome. However, virtually nothing is known about how brain connectivity is impaired in newly diagnosed epilepsy. In this talk, I will present new data from our lab that demonstrates connectivity impairments at the point of epilepsy diagnosis and will consider whether this data can be used to predict future pharmacoresistance.

Lorenzo Caciagli, University of Pennsylvania, USA



MD from the University of Pisa, Visiting Fellowship at the MNI, PhD in Clinical Neuroscience from the UCL Queen Square Institute of Neurology with focus on neuroimaging of epilepsy, supervised by Prof Matthias Koepp. Current position: postdoctoral research associate at the university of Pennsylvania in Prof Danielle Bassett's lab, shaping a training path combining clinical and research activities in the field of epilepsy and cognitive neuroscience. Member of the ILAE Imaging Task Force.

Abstract:Towards a connectome perspective on cognitive dysfunction in epilepsy: multiscale profiling and dynamic connectivity analysis

Growing evidence suggests that the epilepsies are disorders of distributed neural networks. Cognitive dysfunction is a frequent epilepsy comorbidity, but its underlying neural substrates have been rarely investigated from a network perspective. In this talk, I will present results of ongoing work aiming to capture network and connectome substrates of cognitive impairment in common focal and generalized epilepsies. Starting from voxel-based cognitive activation maps, I will illustrate a multi-scale approach that combines the former with profiling of task effects across intrinsic functional systems, and in relation to a macroscale principle of functional connectome organization. Finally, I will discuss results of a dynamic functional connectivity analysis, that aims to track whole-brain network reconfigurations during working memory, and identify shared and syndrome-specific neural signatures across the epilepsy spectrum.

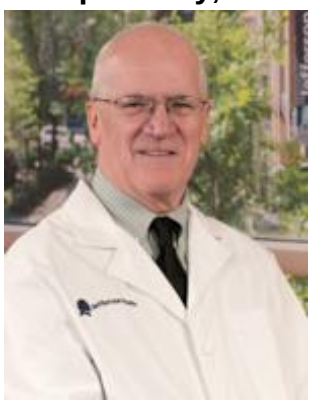
Anny Reyes, University of California San Diego, USA

Anny Reyes is a NINDS/NIH NRSA F31 Fellow, fifth-year doctoral candidate in the SDSU/UCSD Joint Doctoral Program in Clinical Psychology, supervised by Carrie McDonald, focusing in neuropsychology and a doctoral researcher at the UC San Diego Center for Multimodal Imaging and Genetics. Her doctoral research is focused on identifying individual differences (e.g., demographic, cultural, health-related) that can alter the brain's vulnerability to pathology and influence the relationship between brain pathology and clinical phenotypes in patients with epilepsy. Specifically, she is interested in understanding why some individuals with focal epilepsy demonstrate generalized cognitive impairment whereas others demonstrate relatively normal cognitive profiles, despite similar clinical features. The goal of her doctoral dissertation is to identify the neuroanatomical correlates that are associated with different cognitive phenotypes in temporal lobe epilepsy (TLE) in efforts to better understand the heterogeneity in cognitive impairment that is found in this clinical population.

Abstract: Cognitive Phenotypes in Epilepsy: Moving Towards Precision Neuropsychology

Ms. Reyes will provide an overview of the recent paradigm shift to studying cognitive comorbidities in epilepsy. Specifically, she will describe the clinical utility of cognitive phenotyping in epilepsy and how can epilepsy researchers utilize this framework to better understand the underlying neurobiology associated with cognitive impairment across different epilepsy syndromes. Second, she will highlight several studies of cognitive phenotypes that have utilized connectome analysis to understand the network topology associated with different cognitive profiles. Third, she will describe the potential clinical value of phenotyping as a model of precision medicine in epilepsy. Finally, she will highlight the recent efforts of validating phenotypes in large-scale datasets such as ENIGMA-Epilepsy.

Joseph Tracy, Jefferson University, USA



Dr. Joseph Tracy is a Professor in the Department of Neurology at Thomas Jefferson University/Sidney Kimmel Medical College. He is Director of the Cognitive Neuroscience and Brain Mapping Laboratory, as well as Director of the Clinical Neuropsychology Division in the Neurology Department. His major recent project involves development of connectome biomarkers of cognitive and surgical outcome following invasive surgery for epilepsy. Dr. Tracy regularly conducts presurgical brain mapping investigations that are utilized in pre-surgical planning, and then incorporated into his ongoing research.

Abstract: Functional Connectivity Patterns Associated Compensatory Memory Reorganization in Epilepsy

Temporal lobe epilepsy (TLE) is associated with impairment in episodic memory. A substantial sub-group, however, is able to maintain adequate memory despite temporal lobe pathology. What has been missing from prior work in cognitive reorganization is a comparison of TLE patients with intact status from those who are memory impaired. Little is known about regional activations, functional connectivities (FC's), and/or network reconfigurations that implement changes in the primary computations or the support functions that drive adaptive plasticity and compensated memory. We used task fMRI on 54 unilateral TLE patients and 24 matched healthy controls (HC) during performance of a paired-associate memory (PAM) task to address three questions: 1) what regions implement PAM in TLE, and do such regions vary as a function of performance, 2) are there unique FC's present during memory encoding that account for intact status through the preservation of primary memory computations or the supportive computations that allow for intact memory responses, and 3) what memory encoding features are most distinctive: the magnitude and location of regional activations, or enhanced functional connections to key structures such as the hippocampus? Result revealed a unique profile of non-ictal, non-dominant hemisphere regions (e.g., right posterior temporal regions) were most important to intact memory status in LTLE, involving increased regional activity and modulatory communication with the hippocampi, all feature that were missing in memory impaired LTLE. The profile involved areas that are neither contralateral homologues to left hemisphere memory areas, nor regions traditionally considered computationally primary for episodic memory. None of these areas of increased activation or functional connectivity were associated with advantaged memory in HC's. Our emphasis on different performance levels yielded insight into two forms of cognitive reorganization. Computational primacy, where LTLE showed little change relative to HC's, and computational support where Intact LTLE showed adaptive abnormalities. The analyses isolated the unique regional activations and mediating FC's that implement compensatory reorganization in LTLE. The results provided a new perspective on memory deficits by making clear that memory deficits arise not just from knockout of a functional hub, but from the failure to instantiate a complex set of reorganization responses. Such responses provided the computational support to ensure successful memory. The findings demonstrated that by keeping track of performance levels, we can increase our understanding of adaptive brain responses and neuroplasticity in epilepsy.

Sara Larivière, The Montreal Neurological Institute (The Neuro), Canada

Sara Larivière is a CIHR doctoral fellow, fourth-year PhD candidate in the Integrated Program in Neuroscience at Mcgill in Montreal, and a researcher in the Multimodal Imaging and Connectome Analysis (MICA) Laboratory at the Montreal Neurological Institute (MNI) supervised by Dr Boris Bernhardt. Her research focuses on the effects of epilepsy surgery on the developing brain as well as leveraging big data to study multiscale network alterations in the common epilepsies.

Abstract: Network-Based Alterations in the Common Epilepsies: Findings from the ENIGMA-Epilepsy Consortium

Ms. Larivière will provide an overview of whether, and how, healthy brain network architecture governs whole-brain atrophy in temporal lobe and idiopathic generalized epilepsies. Specifically, she will highlight how open access big data initiatives such as the ENIGMA Consortium, the Human Connectome Project, the Allen Human Brain Atlas, and the ENIGMA Toolbox can be leveraged to reveal shared and distinct network descriptors of atrophy in the common epilepsies.

Leo Bonilha, Medical University South Carolina, USA

Dr. Leonardo Bonilha is a Professor of Neurology at the Medical University of South Carolina. He is the Director of the MUSC Epilepsy Center and Vice-Chair for Research in Neurology and MUSC. His research is focused on 1) mechanisms associated with treatment outcomes in epilepsy, and 2) the neural bases of language. He leads a multidisciplinary translational research laboratory that employs machine learning and analytical approaches to structural connectome imaging from diffusional MRI.

Abstract: Understanding treatment outcomes from structural neuronal networks.

Surgery can lead to complete seizure control in many patients with temporal lobe epilepsy (TLE). However, approximately one third of patients with TLE remain with seizures after surgery and the reason for suboptimal treatment outcomes is not well understood. Using novel analytical methods to map neuronal networks, it is possible to evaluate atypical patterns of neuronal network organization in TLE and therefore redefine the concept of “lesion” from a network perspective. This presentation will review and discuss human brain connectome approaches combined with machine learning to better understand the pathophysiology of TLE in relationship with treatment outcomes.

Danielle Bassett, University of Pennsylvania, USA

Prof. Bassett is the J. Peter Skirkanich Professor at the University of Pennsylvania, with appointments in the Departments of Bioengineering, Electrical & Systems Engineering, Physics & Astronomy, Neurology, and Psychiatry. Bassett is also an external professor of the Santa Fe Institute. Bassett is most well-known for blending neural and systems engineering to identify fundamental mechanisms of cognition and disease in human brain networks. Bassett is currently writing a book for MIT Press entitled Curious Minds, with co-author Perry Zurn Professor of Philosophy at American University. Bassett received a B.S. in physics from Penn State University and a Ph.D. in physics from the University of Cambridge, UK as a Churchill Scholar, and as an NIH Health Sciences Scholar. Following a postdoctoral position at UC Santa Barbara, Bassett was a Junior Research Fellow at the Sage Center for the Study of the Mind. Bassett has received multiple prestigious awards, including American Psychological Association's 'Rising Star' (2012), Alfred P Sloan Research Fellow (2014), MacArthur Fellow Genius Grant (2014), Early Academic Achievement Award from the IEEE Engineering in Medicine and Biology Society (2015), Harvard Higher Education Leader (2015), Office of Naval Research Young Investigator (2015), National Science Foundation CAREER (2016), Popular Science Brilliant 10 (2016), Lagrange Prize in Complex Systems Science (2017), Erdos-Renyi Prize in Network Science (2018), OHBM Young Investigator Award (2020), AIMBE College of Fellows (2020). Bassett is the author of more than 300 peer-reviewed publications, which have garnered over 25,000 citations, as well as numerous book chapters and teaching materials. Bassett is the founding director of the Penn Network Visualization Program, a combined undergraduate art internship and K-12 outreach program bridging network science and the visual arts. Bassett's work has been supported by the National Science Foundation, the National Institutes of Health, the Army Research Office, the Army Research Laboratory, the Office of Naval Research, the Department of Defense, the Alfred P Sloan Foundation, the John D and Catherine T MacArthur Foundation, the Paul Allen Foundation, the ISI Foundation, and the Center for Curiosity.

Abstract: Connectomics in Epilepsy: The Why and Wherefore

In this talk, I will take a step back from the exciting research findings presented throughout the day, and ask the question of why we are pursuing connecomics in epilepsy, and where the field might be going next. I will argue that we are seeking mechanisms of the disease, and that connectomes have a key role to play in understanding those mechanisms. Drawing on recent work in philosophy of science, I will discuss what a mechanism is, and what it is not. I will walk through distinct components of mechanisms and highlight where connectomes become central. I'll describe how network science can be used to understand the organization of a connectome, and to build network models with descriptive, explanatory, and predictive validity. I will acknowledge that connectomes are not mechanisms, and that pathways are not causings. I will conclude by underscoring the key challenge to build out connectomes into mechanistic network models.

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