ABSTRACTS

Brain-CODE – A Comprehensive Informatics Platform for Research Data Federation, Query and Analysis

Garth Smith and Brendan Behan, Ontario Brain Institute

The Ontario Brain Institute, in partnership with the Indoc Consortium and Baycrest, has built Brain-CODE – a comprehensive neuroinformatics platform for managing the acquisition, curation, integration and analysis of multi-dimensional data for over 240 researchers from over 40 research institutions. Brain-CODE's architecture is designed to incorporate and integrate a wide range of data management, curation and analysis tools. Clinical assessments in the form of clinician-administered and patient-reported outcomes are collected using REDCap and OpenClinica. Imaging and physiological measures (MRI, EEG, etc.) are managed using SPReD, an XNAT-based system. Brain-CODE also supports multiple omics modalities with the LabKey system serving as a repository for sample information, raw data files, processed data and associated metadata. Despite recent advances, research datasets largely exist in isolation with no practical avenue for sharing and pooling across data sources. Brain-CODE addresses this challenge through a data federation system utilizing a combination of data warehousing and NoSQL approaches to aggregate data across modalities and databases. This enables query and analysis capabilities which would otherwise require researchers to invest significant study-specific manual effort and technical resources. Brain-CODE's flexible and scalable architecture can suit a variety of research settings and has been recently deployed at the Centre for Addiction and Mental Health.

Big Data Variety and Veracity in Brain-Code: 80% Quality Curation and 20% Analysis

Stephen Strother, Professor, Medical Biophysics
and the ONDRI Investigators, University of Toronto

To illustrate Brain-CODE's data sharing and analytics I will describe the Neuroinformatics and Biostatistical (NIBS) platform within the Ontario Neurodegenerative Disease Research Initiative (ONDRI). The NIBS team is tasked with overseeing the quality control and curation of the 7 other data platforms (Clinical, Neuropsychological, Eye Tracking, Spectral Domain Optical Computed Tomography, Genomics, MRI Neuroimaging and Gait & Balance) for each of the five disease themes in ONDRI: Alzheimers Disease & Mild Cognitive Impairment (ADMCI), Parkinson's Disease (PD), Vascular Cognitive Impairment (VCI), Fronto-Temporal Dementia (FTD), Amyotrophic Lateral Sclerosis (ALS). With subplatform data types (e.g., MRI structural, PD/T2, functional resting state, diffusion tensor imaging, FLAIR, GRE-T2*) this results in over 80 distinct data sets to be aggregated, quality curated and released. I will illustrate the NIBS workflow with results from state-of-the-art multivariate outlier detection techniques (e.g., minimum covariance determinant). These combine quality curation and analysis approaches into a single iterative analytic step for each data set forming the core of the NIBS iterative workflow prior to data release and eventual data analysis.

Does the Mismatch Negativity Operate on conscious Stimulus Representations? Evidence from MEG and informational Masking

Andrew R. Dykstra, The Brain and Mind Institute, University of Western Ontario

The mismatch negativity, or MMN, is a change-related component of the auditory evoked response and one of the most oft-studied brain responses in neuroscience. Elicited by discriminable violations of acoustic regularity, the MMN is thought to reflect automatic, pre-attentive, and even pre-conscious change detection. We directly examined the pre-conscious notion of the MMN using informational masking and magnetoencephalography. Spectrally isolated and otherwise suprathreshold auditory oddball sequences were occasionally rendered inaudible by embedding them in random multi-tone masker "clouds". Despite identical stimulation/task contexts and a clear representation of all stimuli in auditory cortex, the MMN was only observed when the preceding regularity (that is, the standard stream) was consciously perceived. The results call into question the pre-conscious interpretation of MMN and raise the possibility that it might index partial awareness in the absence of overt behavior.

Dimensionality Reduction, Classification and its Application for Coma Prognosis

Narges Armanfard, McGill University (presented by Jim Reilly, McMaster University)

Dimensionality reduction is a very important component in data classification applications. It is well known that the performance of typical classifiers notably drops when the number of available observations is not adequate in comparison to the number of candidate features.

Feature selection approaches perform dimensionality reduction by selecting a subset of relevant features (from the available set of candidate features) that leads to an "optimal" characterization of different classes. Conventional feature selection algorithms select a single common feature set for characterizing all regions of the sample space. In fact, these methods assume that a single feature subset can optimally characterize sample space variations.

In this talk, I will present an alternative view to the traditional concept of a common feature set. I will discuss the novel concept of localized feature selection whereby each region of the sample space is associated with its own distinct optimized feature set, which may vary both in membership and size across the sample space. This allows the feature set to optimally adapt to local variations in the sample space. Furthermore, I will discuss relevant application automatic and continuous Mismatch Negativity (MMN) detection for coma outcome prediction.

Disappearing Into Nothingness: Graphs, Shapes, and Advanced Analysis Techniques Applied to Understanding Disorders of Consciousness

Martin M. Monti, Department of Psychology, UCLA

In the past 20 years, research on disorders of consciousness -- including coma, the vegetative state, and the minimally conscious state -- has reshaped much of our understanding of how to detect consciousness and how to conceptualize loss and recovery of consciousness after severe brain injury. Yet, to date, still little is known about why some brains can support the emergence of a conscious state and others cannot, and why some recover consciousness after a period of unawareness and others do not. In this presentation I will provide an overview of the latest research attempting to disentangle these issues. In particular, I will focus on work employing advanced analytical techniques on neuroimaging data in order to relate specific structural and functional measurements to level of consciousness, as well as longitudinal designs attempting to capture the relationship between the evolution of the pathological processes triggered by severe brain injury and measures outcome.

Predicting Treatment Outcomes in Psychiatry with Machine Learning

Bo "Cloud" Cao, Department of Psychiatry, The University of Alberta

This talk will illustrate two cases of machine learning applications in treatment outcomes predictions of psychiatric disorders.

In the first study, by using a machine learning algorithm and the functional connections of the superior temporal cortex, we successfully identified the first-episode drug-naïve (FEDN) schizophrenia patients (accuracy 78.6%) and predict their responses to antipsychotic treatment (accuracy 82.5%) at an individual level. The functional connections (FC) were derived using the mutual information and the correlations, between the blood-oxygen-level dependent signals of the superior temporal cortex and other cortical regions acquired with the resting-state functional magnetic resonance imaging. We also found that the mutual information and correlation FC was informative in identifying individual FEDN schizophrenia and prediction of treatment response, respectively.

The second study used machine learning to predict response to the electroconvulsive therapy (ECT). ECT is one of the most effective treatments for major depression disorder (MDD). ECT can induce neurogenesis and synaptogenesis in hippocampus, which contains distinct subfields. It is unclear which subfields are affected by ECT and whether we predict the future treatment response to ECT by using volumetric information of hippocampal subfields at baseline. By using a state-of-the-art hippocampal segmentation algorithm, we found that ECT induced volume increases in specific subfields. We applied a machine learning algorithm to the hippocampal subfield volumes at baseline and were able to predict the change in depressive symptoms ($r = 0.81$; within remitters, $r = 0.93$). Receiver operating characteristic analysis also showed robust prediction of remission with an area under the curve of 0.90.

The approach used in these two studies may be generalized to predictions of treatment outcomes in other mental disorders. Future interdisciplinary collaborations will be crucial for better treatment outcome predictions in psychiatry.

Predicting Mood Disorders in a Cohort of Bipolar Offspring

Ives Cavalcante Passos, Department of Psychiatry, Federal University, Brazil

In the present study, we explore several methods, including machine learning techniques, to predict which individuals will develop mood disorders in a cohort of high-risk offspring of bipolar parents. Method: High-risk offspring age 30 or older who had passed the peak period of risk were selected from an ongoing Canadian longitudinal high-risk study. We divided participants into 2 groups: offspring who developed major mood episodes and those who did not by last assessment. Predictive analyses with

logistic regression and machine learning techniques (neural network and random forest) were performed. Results: A total of 79 high-risk offspring age 30 years and older were included. Female sex, perceived neglect by mother, and high emotionality were significantly associated with the development of mood disorders in the logistic regression model. In the predictive analyses, the logistic regression model had an area under the receiver operating characteristic (ROC) curve (AUC) of 0.72 (95% CI: 0.60-0.83), while the artificial neural network model had an AUC of 0.80 (0.70-0.90) and the random forest model had an AUC of 0.77 (0.66-0.87). Balanced accuracy for the logistic regression, artificial neural network and random forest models were 64%, 71% and 72% respectively. Conclusion: Risk for mood disorders among offspring of bipolar parents can be estimated at an individual level by incorporating both demographic and clinical variables readily available to clinicians. Future studies should examine the performance of these methods in independent and larger datasets and its subsequent utility in facilitating selection of interventions to prevent mood disorders.

Using Structural MRI to Identify Bipolar Disorders – 13 Site Machine Learning Study in 3020 Individuals from the ENIGMA Bipolar Disorders Working Group

Tomas Hajek, Department of Psychiatry, Dalhousie University

Bipolar disorders (BD) are among the leading causes of morbidity and disability. Objective biological markers, such as those based on brain imaging, could aid in clinical management of BD. Machine learning (ML) brings neuroimaging analyses to individual subject level and may potentially allow for their diagnostic use. However, fair and optimal application of ML requires large, multi-site datasets. We applied ML (support vector machines) to MRI data (regional cortical thickness, surface area, subcortical volumes) from 853 BD and 2167 control participants from 13 cohorts in the ENIGMA consortium. We attempted to differentiate BD from control participants, investigated different data handling strategies and studied the neuroimaging/clinical features most important for classification. Individual site accuracies ranged from 45.23%- 81.07%. Aggregate subject-level analyses yielded the highest accuracy (65.23%, 95%CI=63.47- 67.00, ROC-AUC=71.49%, 95%CI=69.39-73.59), followed by leave-one-site-out cross- validation (58.67%, 95%CI=56.70-60.63). Meta-analysis of individual site accuracies did not provide above chance results. There was substantial agreement between the regions that contributed to identification of BD participants in the best performing site and in the aggregate dataset (Cohen's Kappa=0.83, 95%CI=0.829-0.831). Treatment with anticonvulsants and age were associated with greater odds of correct classification. Although short of the 80% clinically relevant threshold, the results are promising and provide a fair and realistic estimate of classification performance, which can be achieved in a large, ecologically valid, multi-site sample of BD participants based on regional neurostructural

measures. Furthermore, the significant classification in different samples was based on plausible and similar neuroanatomical features. Future multi-site studies should move towards sharing of raw/voxelwise neuroimaging data.

The Importance of Point Process Models to Quantify the Electroencephalogram

Jose C. Principe, Computational NeuroEngineering Lab, University of Florida

The EEG is the most applied signal in neurology, however the methodologies to quantify its properties are still based on assumptions that do not fit its temporal characteristics (stationarity). This talk will propose a transient generative model for the EEG and will discuss its advantages, applications, and technical difficulties. We will also briefly present examples of its potential use to quantify brain state.

Perception as Prediction: Using Neural Network Architectures to Study Brain Perceptual Inference

Sylvain Baillet, Neurology and Neurosurgery; Biomedical Engineering and Computer Science; School of Computer Science, McGill University

A difficult research question in systems neuroscience is the elucidation of mechanisms of directed communication in brain networks: How do sensory inputs perturb the ongoing activity of the brain? How are input signals relayed downstream in brain networks via bottom-up signaling? What is the top-down influence of higher-order brain circuits on sensory perception? We recently proposed a model with predictions that bottom-up signaling and top-down modulations in hierarchical brain networks could be enabled by polyrhythmic and interdependent oscillatory brain activity. This mechanistic framework implements a form of contextual predictive inference of input signals to brain systems. In essence, the theoretical implications are to verify the principles of perceptual inference, which predict that the large spontaneous, resting brain activity during wakefulness (25% of whole-body metabolism) constantly implements the self's representation of the environment

From this framework, we will present our work with Peter Donhauser, who recently proposed a neural network architecture that models brain predictions generated during speech listening about upcoming speech sounds and words. The approach enables the functional separation of uncertainty-related from error-related neural activity captured with scalp electrophysiology, in ecological speech listening situations.

Neurotechnology and Data Mining in Advancing Treatment Options and Prescription for Depression

Faranak Farzan, Simon Fraser University

Major depressive disorder affects 350 million people worldwide and its prevalence (13%) peaks in youth 15 to 24 years of age. Antidepressants are the first line of treatments for depression. While antidepressants can treat 60-70% of individuals diagnosed with depression, majority of patients fail to respond to initial interventions, and some youth even experience increased suicidal thoughts with serotonergic antidepressants. Electroconvulsive therapy is the most effective treatment for treatment-resistant depression but is rarely used due to stigma and side effects. The failure in matching patients with the best treatment is in part due the heterogeneity of response to each antidepressant modality and lack of an objective treatment selection methodology. This talk reviews how neuromodulation and neuroimaging technologies can be used in combination to develop novel therapeutic and diagnostic solutions for treatment of depression.

Toward Brain Computer Interfacing: Algorithms for On-line Differentiation of Neuroelectric Activities

Klaus-Robert Müller, ML Group, TU Berlin, and MPII, Saarbrücken and
Dept of Brain and Cognitive Engineering, Korea University

Brain Computer Interfacing (BCI) aims at making use of brain signals for e.g. the control of objects, spelling, gaming and so on. This talk will first provide a brief overview of Brain Computer Interface from a machine learning and signal processing perspective. In particular it shows the wealth, the complexity and the difficulties of the data available, a truly enormous challenge: In real-time a multi-variate very strongly noise contaminated data stream is to be processed and neuroelectric activities are to be accurately differentiated in real time.

Finally, I report in more detail about the Berlin Brain Computer (BBCI) Interface that is based on EEG signals and take the audience all the way from the measured signal, the preprocessing and filtering, the classification to the respective application. BCI as a new channel for man-machine communication is discussed in a clinical setting and for gaming.
