RESEARCH DAY

LIGHTNING TALKS

Presentation #1	Hyperactivation of Visual Attention Brain Network in Evidence-Based Decisions: fMRI-CPCA Analysis of Delusions in Schizophrenia.
Clinical research	
Presenter	Saman Fouladirad, UBC Medical Student
Faculty Sponsor	Dr. Todd Woodward

Introduction: A "Jumping-to-conclusions" phenomenon has been documented in delusional patients with schizophrenia. This is a tendency for patients to make decisions based on little evidence due to the salience of a stimuli. This study aimed to identify the brain networks underlying hypersalience of evidence-hypothesis matches in delusional schizophrenia patients.

Methods: The study consisted of delusional (n=15) and non-delusional (n=15) schizophrenic patients completing a FISH task inside an fMRI scanner. The tasks consist of a central fish between two lakes containing different proportions of black and white fish and the participants had to choose which lake the central fish came from. Hypersalience condition is created when the color of the central fish is similar to the color of the majority of the fish in the lake that it's pointing to.

Results: Four brain networks were extracted from the analysis and ANOVA measures for network 1 (visual attention) revealed a significant difference between delusional and non-delusional patients in the hypersalience condition.

Conclusion: A possible explanation for these results is that delusional patients are unable to suppress visual attention network when there is a strong match between evidence and hypothesis.

Clinical relevance/implications: Implications of understanding the cognitive underpinnings of patients' decision-making include optimizing alternative forms of psychological therapeutic interventions. Implications of understanding the cognitive underpinnings of patients' decision making include optimizing alternative forms of psychological therapeutic interventions, such as cognitive behavioral therapy (CBT), and translation approaches including meta cognitive training (MCT) to improve the mental health of patients with schizophrenia, and adjustment to those networks using neuromodulation and neurostimulation.

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Faculty of Medicine

RESEARCH DAY

Presentation #2   Automated Alignment and Segmentation of Mouse Mesoscale Brain Images Using Machine Learning.

Basic research

Presenter   Donsheng Xiao

Faculty Sponsor   Dr. Timothy Murphy

Quantitative analysis of large scale brain images relies on accurate alignment and segmentation of regions of interest. Matching a reference atlas to the brain data are very labour- and time-intensive manual tasks and prevent high-throughput analysis. Furthermore, human error may occur when clicking the anatomical landmarks in different subjects. Machine learning-based alignment and segmentation approaches for brain images are gaining interest due to their self-learning and generalization ability when applied to large amounts of data. As machine learning architectures are becoming more mature, they gradually outperform previous state-of-the-art classical algorithms. Our aim is to develop an automated machine learning-based alignment and segmentation approaches for quantitative mouse mesoscale brain images. We first trained a deep learning model to identify specific landmarks (i.e. bregma, lamda) in a wide-field calcium imaging dataset from more than 200 transgenic mice. The model can then automatically label landmarks in a new dataset of calcium images with high accuracy. Furthermore, automated brain atlas segmentation onto the calcium images was then performed using a fully convolutional network based on previously labelled landmarks and sensory mapping (via visual/whisker/vibration stimulation). The model can be further optimized by training on a larger datasets and capable of processing large-scale brain images automatically under a few minutes. We propose to further demonstrate that our method significantly enhances the accuracy and robustness of alignment and segmentation of new data sets.

Presentation #3	Society View and Medical Students' Attitude Towards Psychiatry: International Cross-Sectional Study.
Clinical research	
Presenter	Mostafa Mamdouh, MD, PhD Candidate and Julie Elsner, MD, Research Assistant
Faculty Sponsor	Dr. Michael Krausz

Introduction: There is a universal scarcity of psychiatrists. Cultural aspects and their influence on medical students´ perception of psychiatry are important to consider as a cause since they might shape students´ views independently of academic frames.

Methods: In a cross-sectional design, data were obtained from undergraduate medical students at University of British Columbia (Canada), Charité University (Germany), Greifswald University (Germany), University of Pisana (Italy) and University of Zurich (Switzerland). Participants completed online survey composed of 37 questions covering the student's perspective on the social view towards psychiatry in 3 domains as: how society viewed psychiatry, how students viewed psychiatry and the effect of social acceptance on medical practice.

Results: The sample of n=1131 medical students were composed of 51.9% male students. 75% of students stated that, over the last ten years, the society's acceptance of psychiatry has increased. Italian students provided the smallest percentage of this opinion with statistical significance for location ($p \leq 0.001$). About 50 % of the students stated that they had seen physicians of other disciplines speaking disparagingly about psychiatry. Students from Switzerland reported the least experience of hearing negative comments with significant differences ($p \leq 0.001$).

Conclusions: The attitude towards psychiatry showed difference among various countries. The societal values seem to impact career choices and performance on medical practice.

The majority of students agreed that society's acceptance of psychiatry has consequences on the effectiveness of psychiatric practice. Future research should be done to investigate how to deal with the societal values.

RESEARCH DAY

Presentation #4   Creating a Mental Health Program for Vulnerable Youth living in Childcare
Institutions in India

Clinical research

Presenter   Priyanka Halli, Clinical Assistant Professor

India is home to 240 million adolescents and it is estimated that 170 million of them are vulnerable to or experiencing difficult circumstances. The most vulnerable of these children are housed in the estimated 9000 nationwide childcare institutions (CCIs). Recent media reports have put a spotlight on these homes for sexual abuse, physical abuse and neglect. There is also a lack of mental health care in these homes.

Objective: To determine the prevalence and severity of mental health symptoms of the girls living in CCIs. This was a cross sectional study of girls, age 11-18, living in 5 childcare institutions in Mumbai and Goa. We gathered demographic information and used a) Strengths and Difficulties Questionnaire (SDQ); b) Patient Health Questionnaire-9 (PHQ-9); and c) The Children's Global Assessment Scale (CGAS).

Results: On the PHQ, 17% of girls screened positively for moderate or severe level of depression and 40% reported thoughts they would be better off be dead. On the SDQ, 52% of the girls had a total difficulty score above 20 suggesting 52% need a referral to a child and adolescent mental health specialist for treatment.

Conclusion: Our findings reiterate a need for mental health care in childcare institutions in India. Following this study, we created a lay counsellor led 6 month intervention that taught the girls health promotion, emotional regulation and problem solving skills. Their caregivers were also trained in trauma informed care. We are currently analysing the data to determine if this intervention was acceptable and feasible.

RESEARCH DAY

Presentation #5	Traumatic Brain Injury in the Homeless and Marginally Housed: A Systematic Review and Meta-Analysis
Clinical research	
Presenter	Jacob L. Stubbs, BKin, PhD Student
Faculty Sponsor	Dr. William J. Panenka and Dr. William G. Honer
Authors	Jacob L. Stubbs, Allen E. Thornton, Jessica M. Sevick, Noah D. Silverberg, William G. Honer and William J. Panenka

Introduction: Recent research has suggested that traumatic brain injury (TBI) is common among homeless and marginally housed individuals, yet, no meta-analytic estimates of prevalence or systematic review of the impact of TBI on health outcomes has been conducted.

Methods: We conducted a meta-analysis (k=28 studies; n=20,711) to estimate the prevalence of lifetime TBI (any severity); the prevalence of moderate or severe TBI (>30 min. loss of consciousness); and the incidence of TBI. We then systematically reviewed all studies (k=38) that looked at associations between TBI and health or functioning-related outcomes.

Results: The lifetime prevalence of TBI in homeless and marginally housed individuals was 53.4% (95% CI: 47.6 – 59.1; 2.5-4 times the general population), and the lifetime prevalence of moderate or severe TBI was 27.3% (18.3 – 38.7; ~10 times the general population). 3.9% (0.59 – 21.5) of participants sustained TBI over a given year. TBI was broadly associated with poorer physical and mental health, higher mortality, and increased service use.

Conclusions: TBI is extremely common among homeless and marginally housed individuals, and represents an underappreciated yet potent factor that is associated with significant long-term impacts to health.

Relevance/implications: Screening for TBI is warranted these populations, and comprehensive prospective and longitudinal studies are needed.

Potential current or future clinical relevance: TBI is a powerful (and currently under recognized) factor that has wide-ranging impacts to the health of this vulnerable population. Though future studies are needed to clarify the full impact of TBI in this population, TBI may represent an important clinical consideration in the care of homeless and marginally housed individuals.

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Presentation #6	The Impact of Employment on Recovery among Individuals who are Homeless with Severe Mental Illness: Vancouver at Home/Chez Soi Trial
Clinical Research	
Presenter	Kiana Yazdani
Authors	Kiana Tazdani, Mohammadali Nikoo, Pegah Mortazavi, Maggie Wu, Taleen Chen, Fiona Choi, Skye Barbic, Kerry Jang, Michael Krausz

Introduction: Our objective was to assess the impact of employment history on recovery among individuals who were homeless and diagnosed with severe mental illness.

Methods: A sample of data were obtained from Vancouver At Home Study (VAH). Individuals were considered employed if they were working at either any casual or regular jobs in the past three months. Detailed chronological history of employment was assessed using Vocational Time Line Follow-Back (VTLFB), administered every 3 months in two years. Recovery was measured at baseline and after 24 months, using Recovery Assessment Scale (RAS) with focus on hope and determination. A multivariable regression model accounting for recency effect was fitted to examine the effect of weighted function of employment history during the follow-up on recovery after 24 months. Potential variables were adjusted for, either at baseline or throughout the follow- up using stepwise selection method.

Results: Data were captured on 372 individuals who were primarily males (71.24%) and single, never married (71.27%). Mean age of participants were 41 (SD: 10.40). During the follow-up, 66.94% of the participants had no history of employment and only 0.54% of the participants had consistent employment history for the full duration of the follow-up. Individuals with consistent history of paid work for the full period of the follow-up had significantly higher mean RAS score [7.94 (95% CI: 1.43, 14.45) p = 0.0169] versus individuals with no absolute employment history. Participants' mean RAS score increased more if they had consistent employment history in second year of follow-up [5.75 (95% CI: 1.04, 10.47) p = 0.0169] compared to participants with consistent employment history in first year of follow-up [2.21 (95% CI: 0.39, 4.01) p = 0.0169].

Presentation #7	Multimodal Hippocampal Imaging in Patients with Depression Undergoing Repetitive Transcranial Magnetic Stimulation
Clinical Research	
Presenter	David Long, UBC Resident
Faculty Sponsor	Dr. Fidel Vila-Rodriguez

Introduction: Repetitive transcranial magnetic stimulation (rTMS) is an effective neurostimulation treatment for treatment-resistant depression (TRD). The hippocampus is a structure important for episodic memory and emotion regulation. Structural changes in the hippocampus have been observed in depression. Hippocampal structure or biochemistry could potentially serve as a biomarker of rTMS treatment response.

Methods: 59 patients with TRD underwent intermittent theta-burst or 10 Hz left dorsolateral rTMS at a UBC clinic. Patients additionally underwent structural MRI as well as MR spectroscopy of the left hippocampus, assessing concentrations of N-acetyl-aspartate, creatine, choline, glutamate/glutamine and myoinositol.

Results: Baseline total hippocampal volume did not differ between responders and non-responders ($p=0.50$). Change in hippocampal volume from pre- to post-treatment was not associated with treatment response ($p=0.91$). Baseline hippocampal concentrations of the 5 metabolites were not significantly different between rTMS responders and non-responders ($p=0.98, 0.68, 0.45, 0.82, 0.31$). Changes in concentration of the 5 metabolites from pre- to post-treatment were not associated with treatment response ($p=0.329, 0.734, 0.443, 0.269, 0.659$).

Implications: Structural and biochemical features of the hippocampus did not predict or correlate with rTMS treatment response. Further study is necessary to determine alternative biomarkers for rTMS treatment in depression.

Clinical Relevance: The structure and biochemistry of the hippocampus is often investigated in depression, and some studies report changes in the hippocampus which predict or correlate with treatment response. This work is a negative replication of these studies with a larger sample size and suggests alternative directions for biomarker research in depression.

Presentation #8   Variability in Cognitive Function in Treatment-Resistant Depression

Clinical Research

Presenter   Elizabeth Gregory, Masters Student

Faculty Sponsor   Dr. Ivan Torres

Introduction: Cognitive impairment is common in major depressive disorder; however, not all patients exhibit cognitive impairments and contributing factors are unclear. The present study examined cognitive impairments in patients with treatment-resistant depression.

Methods: Moderate to severely treatment-resistant depressed patients (TRD) were compared to demographically-matched healthy volunteers (HV) in verbal memory, attentional shifting, inhibitory control, verbal fluency, and verbal working memory. Cluster analysis was used to identify subsets of the TRD sample based on cognitive functioning.

Results: TRD were impaired in domains of verbal memory, attentional shifting, and inhibitory control. The cluster analysis revealed two groups: a cognitively impaired (CI) group showed a generalized deficit in all cognitive domains, while a cognitively unimpaired (CU) group showed a specific deficit in attentional shifting. A logistic binomial regression of the two groups revealed significant contributing demographic characteristics, which were (1) older age, (2) lower premorbid IQ, and (3) benzodiazepine dose in CI TRD.

Conclusions : Age, lower premorbid IQ, and use of benzodiazepines increased the likelihood of cognitive impairment in TRD patients.

Relevance/Implications: Inter-individual variation in neurocognitive impairment in MDD may be masking the presence of generalized deficits in a subset of patients. Further research is needed to characterize the timeline of cognitive impairment in depression.

Clinical Relevance: Understanding what factors increase the likelihood of cognitive impairment in TRD may help clinicians identify at-risk patients. The finding that benzodiazepine is a predictor of cognitive impairment may have important implications in clinical practice.

RESEARCH DAY

Presentation #9	Light Therapy for Patients with Bipolar Depression: Systematic Review and Meta-Analysis of Randomized Controlled Trials
Clinical Research	
Presenter	Minnie Teng, Work Learn Student
Faculty Sponsor	Dr. Raymond W. Lam

Introduction: Light therapy is an evidence-based treatment for seasonal and nonseasonal major depressive disorder but there are fewer studies in bipolar disorder (BD). Hence, we examined the effects of light therapy treatment on depressive episodes in BD.

Methods: In this systematic review and meta-analysis, we searched MEDLINE, Embase, Web of Science, PsychInfo, and ClinicalTrials.gov from inception to Dec 31, 2018 for randomized, double-blind, placebo-controlled trials of light therapy in patients with bipolar depression. The primary outcome was change in clinician-rated depressive symptom score; secondary outcomes were clinical response, clinical remission, and treatment-emergent mood switches. We used pooled random-effects models, and conducted sensitivity analysis with less robust studies removed.

Results: We identified seven trials representing 241 patients with bipolar depression. Light therapy was associated with a moderate and significant improvement in clinician-rated depressive symptom score (standardized mean differences 0.400 [95% CI 0.141–0.660], p=0.003). Additionally, clinical response and remission rates corroborated with this finding where the odds ratio for clinical response was 2.530 [1.473-4.346], p=0.001 and for clinical remission it was 3.562 [1.599-7.937], p=0.002.

Conclusion/Implications: Light therapy may be an effective non-pharmacologic treatment for bipolar depression.

Potential Clinical Relevance: Numerous studies have examined the effectiveness of pharmaceutical interventions to treat depressive episodes in Bipolar Disorder (BD). Clinical trials have focused primarily on symptom assessment and relatively few trials include non-pharmaceutical interventions. Light therapy is a non-pharmaceutical intervention that may be effective for treating depressive episodes in patients with BD.

Presentation #10   Brief Illness Perception Questionnaire in Patients with Treatment Resistant Depression: A Patient-Centered Perspective

Clinical Research

Presenter   Renata Barbosa Menezes, Graduate Student

Faculty Sponsor   Dr. Fidel Vila-Rodriguez

Introduction: Studies show that illness perception may be associated with adherence to treatment and outcome prediction. The brief illness perception questionnaire is a validated self-rated instrument aiming at measuring dimensions of perception. This study's objective was to characterize different dimensions of illness perception using BIPQ in patients with treatment resistant depression (TRD) receiving repetitive transcranial magnetic stimulation (rTMS).

Methods: 62 patients enrolled in an RCT for rTMS in TRD were assessed with the BIPQ, Sheehan Productivity Scale (SPS) and Hamilton Rating Scale for Depression (HRSD-17) at baseline and at the end of rTMS treatment.

Results: Dimensions with highest means were concern (8.8), emotional response (8.78), and consequences (8.67). The two most important ranked causes were "life stressors" (27%), "genetics" (27%) and "trauma" (16%). Higher frequency in perceived symptoms was associated with HRSD-17 improvement and more missed days of school/work. The level of impact perceived in their lives was associated with disruption in social/leisure activities, while higher concern was correlated with disturbance in family/home responsibilities.

Conclusion: Experiencing TRD strongly impacts function. Perceived causes match the conceptualization based on biopsychosocial model.

Relevance/Implications: BIPQ provides information about patients' perceptions. This can help physicians pre-assess patients to optimize appointment toward a goal-oriented approach.

Continued

Presentation #10	Brief Illness Perception Questionnaire in Patients with Treatment Resistant Depression: A Patient-Centered Perspective
Clinical Research	
Presenter	Renata Barbosa Menezes, Graduate Student
Faculty Sponsor	Dr. Fidel Vila-Rodriguez

Potential Clinical Relevance: BIPQ is a self-applied, quick-to-use tool that can be utilized to identify patient characteristics that can be targeted and addressed in a psychiatric setting. This can help clinicians optimize appointment time, thus improving patients' quality of life.

Presentation #11   Exendin-4, a GLP-1 Receptor Agonist, improves Alzheimer-Associated
Phenotypes

Basic Research

Presenter   Yun Zhang, Post-doctoral Fellow

Faculty Sponsor   Dr. Weihong Song

Abstract: Alzheimer's disease (AD) is the most common neurodegenerative disorder leading to dementia. Its pathological hallmarks include extracellular neuritic plaque, intracellular neurofibrillary tangles and neuronal death. However, its etiology is still not clear. Growing evidence suggests the role of impaired insulin signalling and cerebral glucose metabolism in AD pathogenesis. AD has been considered as type 3 diabetes that exclusively occurs in the brain. Glucagon-like peptide-1 (GLP-1) is an endogenous peptide of 30 amino acids that plays a critical role in glucose homeostasis by regulation of insulin secretion. GLP-1 exerts its insulinotropic activity via binding to a specific G-protein coupled receptor (GLP-1R). We now identified that exendin-4, a long-lasting GLP-1R agonist, significantly increased the activity of AMP-activated protein kinase (AMPK), which decreased BACE1 gene transcription and expression, resulting in the reduction of BACE1-mediated cleavage of the β-amyloid precursor protein (APP) and Aβ production. Furthermore, we found that treatment with exendin-4 reduced Aβ neurotoxicity and tau phosphorylation and significantly improved cognitive deficits in transgenic AD model mice. Take together, our findings suggest that GLP-1 affects Alzheimer's pathogenesis and may be an effective therapeutic target for AD treatment.

Potential Clinical Relevance: This study provides novel insights into the role of GLP-1 in neurodegeneration and its pharmaceutical potential for Alzheimer's treatment.

Presentation #12   Parental "Awareness to Act": Role of Psychiatric Genetic Counseling for 22q11 Deletion Syndrome

Clinical Research

Presenter   Prescilla Carrion, Clinical Associate Professor

Introduction: People with 22q11 deletion syndrome (22q11DS) have a 30% chance to develop a psychotic disorder. Early intervention leads to the best long-term outcomes, but evidence suggests that mental health (MH) services are underused by people with 22q11DS. We provided psychiatric genetic counselling (PGC) to parents of children with 22q11DS and qualitatively explored its effects on: awareness of psychiatric risk, use of strategies to protect their child's MH, attitudes towards treatments/services, and self-efficacy in recognizing/managing emerging MH problems.

Methods: Fourteen parents of children diagnosed with 22q11DS were interviewed 1-month post-PGC. Grounded theory analysis was used to generate the theoretical framework describing the process/outcomes of PGC.

Results: Before PGC, parents described how they faced barriers (e.g. lacking anticipatory guidance) that stalled their process of building awareness of MH problems associated with 22q11DS, resulting in them "carrying the burden" of identifying emerging symptoms. PGC facilitated for them an "awareness to act" in ways to protect and/or manage their child's MH.

Conclusion: Parents felt equipped with helpful "tools" (e.g. stress-reduction strategies) and awareness that MH problems are manageable.

Relevance/Implications: PGC helps empower parents to engage in protective behaviours to reduce risk for MH problems and promote improved outcomes for their child with 22q11DS.

Potential Clinical Relevance: Mental health problems are common amongst this population, and are inadequately treated. PGC for parents, through increasing awareness of the risk of mental health problems, risk-reduction strategies, therapies and treatments, could be an effective strategy for reducing the risk of psychiatric problems and improving outcomes amongst youth with 22q11DS.

Presentation #13   Isolating the Effects of Mild Traumatic Brain Injury on Reaction Time

Clinical Research

Presenter   Lisa Zhang, MD Candidate 2021

Faculty Sponsor   Dr. William Panenka

Introduction: The simple clinical test of reaction time (RT_{clin}) provides an objective measurement in assessing mild traumatic brain injury (mTBI). Current RT_{clin} literature is limited to comparing mTBI patients with healthy controls, overlooking the effects general trauma may have. Therefore, to further isolate the specific effects of head injury on RT_{clin}, we compared RT_{clin} values to trauma controls (TC).

Methods: mTBI (n=41) and TC patients (n=50) enrolled from Vancouver General Hospital completed RT_{clin} assessments within 24 hours of injury. T-tests were done to compare RT_{clin} values between groups, and subgroups such as those triaged to computerized tomography (CT).

Results: Mean RT_{clin} of the mTBI group (.193 msec) differed from that of the TC group (.180 msec) (p=.057). There was a significant difference between the values of mTBI patients triaged to CT (.197 msec) and TC patients (p=0.009).

Conclusion: RT_{clin} appears to be significantly delayed due to specific to mTBI mechanisms and not general trauma. The delay is more significant in patients with more cause for clinical concern (CT subgroup).

Relevance/Implications RT_{clin} is a specific, objective and easily implementable measurement for mTBI, having the potential to be a simple but powerful diagnostic tool in acute care assessment.

Potential Clinical Relevance: RT_{clin} has been proven to be a sensitive tool in mTBI assessment. It is easy to administer and economical, making it feasible to implement in many acute care settings. This study shows that the delays in RT_{clin} are specific to mTBI patients, which indicates its potential as a diagnostic measure.

RESEARCH DAY

Presentation #14	Childhood Trauma and Substance Use in relation to Psychiatric Diagnoses in those with Concurrent Disorders
Clinical research	
Presenter	Wen Qian Zhang, Graduate Student
Faculty Sponsor	Dr. Christian Schütz

Introduction: The Burnaby Center for Mental Health and Addictions (BCMHA) is a tertiary care center for people with severe concurrent mental illnesses and substance use disorders. Previous data suggest that this population suffers from alarming rates of psychotic disorders as well as high rates of childhood trauma much greater than the general population. To investigate the interaction between childhood trauma and substance use in relation to psychiatric diagnoses later in life, we surveyed patients at the BCMHA.

Methods: Inpatients (n=161) completed a battery of self-report questionnaires related to substance use (Maudsley's Addiction Profile) and childhood trauma (Childhood Trauma Questionnaire). Psychiatric diagnoses were drawn from review of patients' medical charts.

Results: Descriptive statistics will be conducted to summarize rates of childhood trauma, psychiatric diagnoses, and substance use. Additionally, multiple logistic regressions will be conducted to examine the interaction between substance use and childhood trauma in predicting psychiatric diagnoses.

Conclusion: Childhood trauma is common among people with severe concurrent disorders, as is psychosis disorders. Treatment efforts should include trauma informed practices.

Potential Current or Future Clinical Relevance: People with severe concurrent disorders are among the most vulnerable PWUD, so developing a better understanding of their experience with childhood trauma in relation to their current psychiatric diagnoses. It can inform treatment approaches.

Presentation #15	Gradual Induction of Buprenorphine-Naloxone in Patients treated with existing Opioid Agonist Therapy – the Microdosing Technique
Clinical Research	
Presenter	Jay Ching-Chieh Wang, MD
Authors	Jay Ching-Chieh Wang, MD, Nicole Cowen, BSN, Manal Tanyous CCFP

Introduction: Current guideline recommends that patients with opioid use disorder (OUD) treated with opioid agonist therapy (OAT) who wish to transition to buprenorphine-naloxone need to taper the existing OAT. This process exposes patients to the risk precipitated withdrawals. Developing an induction protocol that minimizes such risks is clinically significant. This case series illustrates such a method: the microdosing technique (MT).

Methods: Two patients with OUD that were initiated on buprenorphine-naloxone without tapering existing OATs. Clinical Opioid Withdrawal Scales were utilized to document the degree of opioid withdrawal during the induction process.

Results: The first patient presented with OUD and a maintenance dose of methadone 170 mg po once daily who suffered from continued craving and on-going illicit street opioid use. The second patient presented with OUD and a maintenance dose of slow-release oral morphine 1100mg po once daily which he was unable to taper due to significant withdrawal symptoms. Both patients tolerated the buprenorphine-naloxone MT induction process and achieved maintenance doses of buprenorphine-naloxone.

Conclusion: In OUD patients treated with OAT, buprenorphine can be initiated without tapering the existing OAT.

Current & Future Clinical Relevance: There is limited data to support and guide the transition from non-buprenorphine-naloxone OAT to buprenorphine-naloxone. This case series will contribute to support the feasibility of transitioning without taper and potentially establish clinical guidance for addiction psychiatrists and other clinicians that work with patients with OUD.

RESEARCH DAY

Presentation #16	e-Mental Health Access, Literacy, and Interest among Patients with Substance Use and Mental Health Disorders
Clinical Research	
Presenter	Kiana Yazdani, MSc Experimental Medicine, James Wong, MSc Experimental Medicine and Andy Man Yeung Tai, MSc Neuroscience
Faculty sponsor?	

Introduction: We aimed to identify rates of technology access, literacy, and interest among patients at the Burnaby Center for Mental Health and Addiction (BCMHA), a tertiary care center for patients with concurrent disorders.

Methods: We conducted brief interviews with patients at BCMHA. The survey included questions about patients' computer literacy, their access to digital devices at home and at BCMHA, and their interest in e-mental health services implemented in 6 their future treatment plans.

Results: 174 participants completed the survey. They were primarily male (71%) and white (52.1%). Their mean age in years (SD) and mean years of education (SD) were 36.51 (10.5) and 12 (5) respectively. 88.39% of participants were familiar with what a smartphone is. 92.90% of the participants were familiar with what the Internet is. 57.33% and 60% of participants had access to a smartphone and the internet at home respectively. 79.74% of participants were interested in integrating computers/smartphones for the management of their health in the future. Conclusion: Given the level of access, literacy, and interest, our results support the feasibility of implementing e-mental health services in this patient population.

Our results support the feasibility of implementing e-mental health services for patients with concurrent disorders. The integration of e-mental health interventions in inpatient psychiatric care has the potential to positively affect treatment outcomes, reduce rates of relapse and readmittance, and decrease the overall costs of the treatment system.

Presentation #17	Patterns of Substance Use among Participants in an Opiate Substitution Treatment Clinical Trial in Iran
Clinical Research	
Presenter	Mohammadali Nikoo, PGY1 Psychiatry Resident, PhD Candidate and Kiana Kianpoor, Research Assistant
Faculty Sponsor	Dr. Michael Krausz

Introduction: Iran is an interesting area to investigate the patterns of substance use due to its proximity to the major opium production sites and less stigmatized use of opium.

Methods: Data were obtained from 204 participants in opium trial, a phase 3 multi-center, parallel-group, double-blind, non-inferiority randomized clinical trial in Iran. Participants with opioid use disorder were randomized to receive either methadone or opium tincture. Recruitment centers were four private outpatient medication-assisted treatment clinics located in three major cities and one rural center in Iran.

Results: The three most commonly used substance during lifetime were opium (80%), methadone (67%), and Shireh/Sukhteh (58%). Polysubstance use was reported by 96 (47%) participants. Urban centers reported significantly higher heroin and methamphetamine use and a significantly lower prevalence of opium than rural centers. Moreover, participants in urban areas demonstrated a higher risk profile with a higher number of overdoses in the past (12% vs. 0, p=0.01). Rural and urban participants were different in terms of socioeconomic factors, such as employment and lifetime incarceration.

Conclusions: From an international perspective, Iran has a unique substance use profile, such as high opium use as the substance of choice among individuals with opioid use disorder.

Potential current/future clinical relevance of this work: This study highlights the differences in substance use profiles in various jurisdictions indicating the need for taking into account regional and contextual factors when planning treatments for specific populations.

Presentation #18	The Use of Artificial Intelligence in Predicting Fatal Opioid Overdoses – Key Informant Survey of Physicians
Clinical Research	
Presenter	James Wong, MSc Experimental Medicine, Kiana Yazdani, MSc Experimental Medicine, and Andy Man Yeung Tai, MSc Neuroscience
Faculty Sponsor	Dr. Michael Krausz

Introduction: In April 2016, B.C. declared a public health emergency under the Public Health Act in response to increasing overdoses and deaths in the province. Methods like artificial intelligence (AI) have the capability to predict health outcomes based on risk factors in diseases and disorders, but there is limited knowledge on their potential to predict fatal opioid overdoses. We aimed to understand the clinical opinions of physicians on the role of AI in predicting fatal opioid overdoses.

Methods: This key informant survey was delivered online through Qualtrics and included questions on: appropriate variables to include in an AI tool, its feasibility development, its potential applications, and outcome measures for assessing its performance.

Results: 11 physicians completed the survey. 'Recent opioid overdose history' was rated as an 'extremely important' variable by the majority of respondents. Most agree that Canada has sufficient data to develop an AI tool, but state that the availability and validity of data and selection of variables would be major challenges.

Conclusions: The majority of respondents agreed that it is feasible to create such a tool. The results gave insight into the appropriate variables to be included and the tool's potential implementation in a variety of settings.

The majority of respondents agree that it is feasible to create a fatal opioid overdose prediction AI tool. The results give insight into the appropriate variables to be included, the possible challenges in the tool's development, and the tool's potential implementation in a variety of settings for future use.

Presentation #19	Side Effects Characterization & Trajectories in rTMS Treatment for Depression: HFL (10 hz) vs. iTBS Protocols

Clinical Research

Presenter	Afifa Humaira, Research Coordinator
Faculty Sponsor	Dr. Fidel Vila-Rodriguez

Introduction: Repetitive Transcranial Magnetic Stimulation (rTMS) is a first-line treatment for treatment-resistant depression (TRD). Newer rTMS protocols are being developed and it is extremely important to characterize their side effect profile and trajectories

Methods: 62 patients were randomized to receive either HFL 10 Hz or iTBS. Side effects were systematically assessed each treatment day for immediate rTMS side effects using a Likert scale. Linear mixed-effects modelling and General Estimating Equation were used to test for main effects of time, clinical outcomes, or sex.

Results: Pain at stimulation site, headache, and fatigue were the most frequent side effects. All three showed a significant decrease over time. Patients who received iTBS reported 0.96 higher severity of pain than those who received HFL (p=0.009). Patients who received iTBS reported 0.88 less severe fatigue than those who received HFL (p=0.013). Responders reported 0.8 less severe pain (p=0.04) and 0.4 less severe headache (p=0.02) than non-responders. Pain and headache scores decrease at a slower rate overtime. Drop out rates were low (9.7%) and similar in both groups.

Conclusions: rTMS was well tolerated with low drop out rates. The most common side effects showed a clear decreasing trajectory over time consistent with tolerance phenomenon.

Relevance/Implications: Patient centered outcomes such as side effects characteristics and trajectories are essential to inform clinical practice.

Potential Current or Future Clinical Relevance: The result of this project is important for clinicians in deciding which rTMS protocol to administer to their patients in terms of their side effects tolerability, especially since it has been shown that both protocols have similar efficacy. We could also use this data to see if side effects can predict clinical outcomes of rTMS treatment.

Presentation #20	Mental Health outcomes in Medication-Assisted Substitution Treatment for Opioid Use Disorder: A Systematic Review
Clinical Research	
Presenter	Kimia Ziafat, Undergraduate Student
Faculty Sponsor	Dr. Michael Krausz

Introduction: There is a dearth of systematic evidence on the effectiveness of opioid agonists in improving mental health in opioid use disorder.

Methods: Randomized clinical trials were included in the review if they compared opioid agonists with each other or a placebo in substitution treatment of opioid use disorder and reported at least one mental health outcome using a validated measure. Studies primarily focused on adjunctive or comprehensive psychiatric interventions were excluded. In September 2018, we did a systematic literature search, the protocol for which can be found at (https://www.crd.york.ac.uk/prospero/, CRD42018109375).

Results: Of the total 6034 citations retrieved, 27 published studies were initially included in the review. Studies varied considerably regarding dropout rates, dosing, psychosocial services, duration, and severity of opioid use disorder. Most studies had moderate-high risk of bias and provided either none or insufficient data to make a meta-analysis possible. Overall, it appears that opioid agonists improve mental health more prominently compared to placebo/waitlist; however, it is unclear if a particular agonist is superior to another. Meta-analysis on some of the studies is currently in process.

Conclusions: There is a shortage of robust evidence on the effectiveness of opioid agonists for mental symptoms in opioid use disorder.

Relevance and Implications: Considering the extent of mental health problems in the opioid-dependent population, this review can help shed light on the level of available evidence and effectiveness of the different available substitution treatments in improving mental health in this population.

RESEARCH DAY

ORAL PRESENTATIONS

Presentation #1   Investigation of Genetics and Machine-Learning Based Autism Gene and Variant Prioritization Methods

Basic Research

Presenter   Margot Gunning, Graduate Student

Faculty Sponsor   Dr. Paul Pavlidis

Introduction: Machine learning (ML) algorithms that incorporate 'gene networks' have been proposed to supplement genetics approaches to identify genes associated with autism risk. However, previous work in our lab has raised questions about the utility of ML methods for this type of task. Therefore, I conducted a computational evaluation of ASD gene prioritization methods.

Methods: I used high-confidence ASD genes, including genes identified recently using genetics approaches, to evaluate performance of eight prioritization methods, including 5 ML approaches, and to evaluate "generic" features that help uncover sources of biases in predictors.

Results: While the ML methods have moderate overlap in their high-priority predictions, they perform poorly at recovering known ASD genes compared to genetics approaches. Furthermore, the ML methods have substantial bias in their prioritizations. A generic genic feature, the haploinsufficiency score (pLI), performed comparably to sophisticated ML methods.

Conclusion / Implications: The poor performance of the ML methods suggests a substantial challenge in providing useful prioritization above that provided by direct genetic analysis. To this end, we are developing a modified ML method that builds on genetics prioritizations in a more direct manner than past approaches.

Clinical Relevance: ASD is a major mental health issue, and improved methods for identifying relevant genes are needed. By leveraging useful orthogonal biological data in a way that negates their biases toward highly studied and non-specific genes, we can better reprioritize novel ASD candidate genes for experimental and clinical study.

RESEARCH DAY

Presentation #2	Using Machine-Learning and Data from STAR*D and CAN-BIND to Predict Antidepressant Response
Clinical Research	
Presenter	John-Jose Nunez, UBC Psychiatry Resident
Faculty Sponsor	Dr. Raymond W. Lam

Introduction: Antidepressant monotherapy remains the first-line treatment for major depressive disorder (Kennedy et al., 2016). However, a number of patients will not initially respond. Predicting a patient's risk for non-response based on clinical symptom and episode features represents an exciting application of modern machine learning. In current work, sensitivity and specificity remain below 70% (Chekroud et al., 2016). Our study aims to replicate and improve on these prior methods, and externally validate our models using data from CAN-BIND (Lam et al., 2016).

Methods: We replicate and adopt Nie et al's recent 2018 methodology to predict initial antidepressant response, and externally validated with the CAN-BIND-1 clinical features database (Nie, Vairavan, Narayan, Ye, & Li, 2018). We then attempt to improve their results by different modalities such as feature selection and new predictive models, including kernel-regression, an ensemble of the Nie paper's methods, and deep learning.

Results: Results generally replicate prior work, though consistently underperform by a small margin, likely due to a different dataset being used. New techniques trialed may outperform current results if this is corrected.

Conclusion: New machine-learning models may improve prediction of antidepressant non-responders using clinical data. CAN-BIND is a valid dataset for external validation.

Potential Clinical Relevance: Though in its early stages, machine-learning, artificial intelligence, and big data approaches will likely eventually be used in clinical psychiatric practice. This project seeks to advance one such possible clinical application – predicting anti-depressant response – and so will show those at Research Day what the future may hold.

RESEARCH DAY

Presentation #3	Automated Tracking and Electrophysiology: Combining Data for Comprehensive Analysis
Basic Research	
Presenter	Adrian Lindsay, Graduate Student
Faculty Sponsor	Dr. Jeremy Seamans

Abstract: Many researchers rely on recorded video of experimental animals, to perform tracking of an animal's location or for analyses of individual limb movements, and it is often important to know how these movements relate to physiological variables that are being tracked concurrently. For example, an experimenter may be interested in determining how changes in heartrate or neuron firing relate to a rodent's location in an enclosure or the position of limbs or overall behaviour (e.g. rearing, freezing, exploratory or anxious behaviour). Recent work in computer vision has produced complex neural network models that are remarkably effective at identifying and locating arbitrary features in an image. These tools are open source and can be adapted for specific tasks through incremental architecture changes and retraining. Here, we combine automated tracking of detailed rat movement and behaviour with simultaneously recorded electrophysiology data and heartrate monitoring to enable comprehensive analysis of behaviour in concert with multiple-single-unit tetrode recordings in several different experimental tasks (ranging from more complex paradigms of anxiety-related and other behaviours, as well as classic fear/appetitive tasks).

Potential Clinical Relevance: A critical benefit is the ability to pair data gathered from brain areas of interest with behaviour. Both to increase our understanding of how these behaviours are associated with activity in the brain but also as a more general tool to identify and track relevant behaviours in an experimental context.

RESEARCH DAY

Presentation #4	miR-204 Attenuates Memory Deficits in a Mouse Model of Alzheimer's Disease
Basic Research	
Presenter	Xiaolei Zhu, Visiting Associate Professor
Faculty Sponsor	Dr. Weihong Song

Introduction: Deposition of amyloid β protein (Aβ) in the brain is a key neuropathological hallmark of Alzheimer's disease (AD). miRNAs have been shown to contribute to the accumulation of Aβ and the pathogenies of AD. However, the mechanism underlying the effect of miRNA on AD remains elusive.

Methods: The miRNA Microarray was performed using the hippocampus of 6-month old APPswe/PS1dE9 (APP/PS1) mice and their wild-type littermates, and the results were verified by qPCR. The miR-204 overexpression lentivirus (lenti-204) was injected into the bilateral hippocampus of APP/PS1 mice via infusion cannulae. The memory function was examined by Morris water maze. The amyloid load was determined by immuofluorescence assay (IFA) and ELISA. The potential targets of miR-204 were predicted by Targetscan, and confirmed by luciferease assay and Western blotting.

Results: miR-204 was significantly downregulated in AD mouse brains and miR-204 overexpression attenuated spatial memory deficits in APP/PS1 mice. In addition, lenti-204 treatment inhibit the expression of presenilin 1 (PSEN1) and decreased amyloid plaques loads in the hippocampus. NADPH oxidase 4 (Nox4) was identified as a direct target of miR-204, and inhibition of Nox4 by GLX351322 protected neuronal cells against Aβ induced neuronal cell death.

Conclusions: miR-204 inhibits the level of NOX4 and attenuates memory deficits in APP/PS1 mice.

Potential Clinical Relevance: miR-204 is a potential target for the treatment of AD.

Presentation #5   Victimization among Women and Men Experiencing Homelessness and Mental Illness: Implications for Policy and Practice

Clinical Research

Presenter   Karen Petersen, Post-doctoral Fellow

Faculty Sponsor   Dr. Tonia Nicholls

Introduction: Evidence suggests that the rates and patterns of victimization among mentally ill women experiencing homelessness are distinct to men. Moreover, few studies have considered the objective (prevalence/frequency) and subjective (meanings/perceptions) experiences of victimization by gender in this population.

Methods: The At Home/Chez Soi study was a Canadian multi-site mixed-methods randomized controlled trial that examined the effectiveness of Housing First interventions. This analysis considers qualitative and quantitative experiences of victimization between women and men using data collected at baseline.

Results: Women experienced significantly higher rates of victimization than men for assault, robbery, and sexual assault. Several variables associated with victimization were similar for women and men across a range of health service, crisis, and justice system contacts. Thematic analysis of qualitative data also revealed several similar themes that demonstrate multiple forms of trauma and structural violence among both women and men throughout their lives.

Conclusion, Relevance/Implications: Quantitative research reveals high rates of victimization and trauma among both men and women who are homeless and mentally ill; however empirical and qualitative examinations suggest potentially important gender-specific clinical implications. Women are at particularly high risk for experiencing diverse forms of serious victimization highlighting the importance of gender-sensitive and trauma-informed services.

Potential Current or Future Clinical Relevance: A deeper understanding of the synergistic effects of gender and other socio-structural factors that impact victimization among individuals who are homeless and mentally ill is essential to guide responsive policy and practice.

RESEARCH DAY

Presentation #6   Medial Temporal Cortical Changes in Response to Yoga and Aerobic Exercise in Early Psychosis Patients.

Clinical Research

Presenter   Melissa Woodward, Graduate Student

Faculty Sponsor   Dr. Donna Lang

Introduction: Exercise is known to induce changes in hippocampal volume in psychosis patients, but its ability to impact cortical regions remains equivocal. Psychosis patients are observed to have neuroanatomical deficits in the medial temporal cortex and these reductions are associated with increased positive symptom severity.

Methods: In a cohort of 52 female first-episode psychosis patients from Hong Kong, we investigated the effects of a twelve-week exercise intervention (yoga, aerobic or waitlist group) on cortical grey matter. Clinical assessments and structural MRI were completed at the beginning and end of the intervention.

Results: Neuroanatomical increases were observed in the entorhinal and fusiform temporal gyrus for patients who completed the aerobic intervention. Increases in fusiform and parahippocampal temporal gyri were associated with increased hippocampal volume. For the aerobic group, decreasing psychosis symptom severity was associated with increases in the entorhinal and fusiform temporal gyri. Reduction in severity of depression was associated with increases in the fusiform gyrus.

Conclusions: These findings demonstrate the potential for neuroremediation beyond the hippocampus and indicate that these changes may be associated with improvements in physical fitness and clinical symptoms. Relevance/Implications: Psychosis patients may benefit from exercise interventions, particularly aerobic exercise, as a safe, cost-effective adjunct treatment.

Clinical Relevance: Aerobic exercise interventions for first-episode psychosis patients may confer a variety of benefits including neuroanatomical remediation and reductions in clinical symptom severity, as well as the ability to counteract the negative cardiovascular impact of antipsychotic medication.

RESEARCH DAY

BASIC POSTERS

Poster #1   Characterising Dendritic Chloride Entry in Cytotoxic Edema using Fluorescence Lifetime Imaging

Basic research

Presenter   Nicholas Weilinger, Post-doctoral Fellow

Faculty Sponsor   Dr. Brian MacVicar

Introduction: Chloride (Cl-) flux controls cell volume by altering cytosolic tonicity. As such, intracellular [Cl-]i is tightly constrained within the neuronal plasmalemma to defend cell volume, as increases in [Cl-]i has been reported as the principal driver of osmotic water entry in cellular swelling (cytotoxic edema). We are using fluorescent lifetime imaging (FLIM) to ask how subcellular [Cl-]i is influenced by excitotoxic activity to glean insights into the mechanisms of Cl- influx and edema.

Methods: Layer 4 pyramidal neurons were whole-cell patch-filled with the Cl- sensitive dye MQAE and imaged using FLIM, enabling us to map shifts in [Cl-]i and commensurate changes in dendritic volume with NMDA application (to trigger edema).

Results: Patched neurons maintained dendritic (but not somatic) [Cl-]i at baseline levels by homeostatic function of the K+/Cl- cotransporter (KCC2). Depolarisation increased [Cl-]i and was exacerbated by blocking KCC2 with furosemide. In contrast to depolarisation alone, NMDA-triggered excitotoxicity elicited massive Cl- entry upwards of 80mM from rest (~10mM) and dendritic swelling/beading. Under these conditions, localised [Cl-]i heterogeneities were observed along dendritic shafts/spines, with severe beading occurring in regions where [Cl-]i was highest.

Conclusion: We conclude that dendritic [Cl-]i is stabilised at rest in patched neurons and is overwhelmed by NMDA activation, revealing distinct Cl- microdomains that couple directly to membrane beading in edema.

Clinical Relevance: Edema is the leading cause of death in stroke victims with severe infarctions, with over 14,000 reported deaths in 2009 (in Canada, www.statcan.gc.ca). Uncovering the membrane conduit(s) of Cl- entry at the cellular level holds considerable promise to inform novel treatments of brain swelling.

Poster #2   Activity Dependent Neuroprotection in the Acute Phase after Stroke

Basic research

Presenter   Matilde Balbi, Post-doctoral Fellow

Faculty Sponsor   Dr. Timothy Murphy

Introduction: Stroke represents a leading cause of death and disability worldwide. Optogenetic stimulation used to enhance stroke recovery has shown potential benefits when applied weeks after injury. However, benefits of acute brain stimulation have not been reported. Changes in gamma oscillations (20–50 Hz) have been observed in several neurological disorders but the relationship between gamma oscillations and cellular pathologies is unclear. We investigated the effect of the gamma-wave modulation in the acute phase – within 1 hr – after stroke

Methods: We combined optogenetics in conjunction with laser speckle imaging, electrophysiology and behavioral tasks. Transgenic VGAT-ChR2 mice with a transcranial chronic window were subjected to photothrombotic stroke while awake in the target area of somatomotor cortex.

Results: Optogenetic stimulation at 40 Hz ipsilateral to the stroke side resulted in a significantly higher increase in blood flow in the first week following stroke ($p= 0.0148$). Stroke area and stroke volume were significantly reduced in mice that received the stimulation ($p= 0.0010$; $p= 0.0249$). Assessment of motor function showed a significant improvement over time in mice that received stimulation ($p< 0.0001$; Group x time effect: $p <0.0001$).

Conclusion: In this study, we describe the beneficial effects of acute, 40 Hz brain stimulation at gamma range: reduced lesion volume and improved motor function after stroke.

Clinical Relevance: Understanding intrinsic mechanisms of neuroprotection of the brain may reveal potential strategies for intervention after stroke. These natural occurring processes may be enabled by non-invasive brain stimulation allowing therefore, for intervention in the acute phase after stroke.

RESEARCH DAY

Poster #3	Microglial Metabolic Flexibility Regulates Immune Function and Neuronal Activity
Basic research	
Presenter	Elisa York, Graduate Student
Authors	Elisa York, Louis-Philippe Bernier, Jingfei Zhang, Hyun B. Choi, Jeffrey M. LeDue, Brian A. MacVicar
Faculty Sponsor	Dr. Brian MacVicar

Introduction: Microglial immune surveillance is critical for maintaining brain health. However, during immune activation, microglia also contribute to altered brain function, neurotoxicity, and degeneration. In peripheral immune cells, activating stimuli increase glycolysis, while anti-inflammatory polarization enhances oxidative phosphorylation. Therefore, we investigated whether microglia also become dependent on glycolysis following an immune challenge, and whether blocking the glycolytic pathway reduces pro-inflammatory responses.

Methods and Results: Here, we establish the use of fluorescence lifetime imaging (FLIM) of endogenous NAD(P)H to investigate the metabolic state of microglia and neuropil in acute hippocampal slices. While neuropil energy rapidly declines in conditions of 0 mM glucose, microglia appear metabolically flexible and are able to maintain oxidative phosphorylation. This unique NAD(P)H FLIM signal in microglia suggests that they are capable of utilizing alternative metabolic sources. To investigate whether the relative activity of glycolysis and oxidative phosphorylation pathways regulate microglial immune activation states, we used lipopolysaccharide (LPS) stimulation of TLR4 receptors in microglial cultures. This treatment increased production of the pro-inflammatory cytokine, interleukin-1b (IL-1b), which was blocked by the glycolysis inhibitor 2-deoxy-D-glucose. This glycolysis-dependent microglial activation affects neuronal function, as in hippocampal field recordings, LPS-induced IL-1b release impairs long term potentiation. This effect can be rescued by either the IL-1b receptor antagonist or by decreasing glycolysis.

Conclusion and Significance: These results suggest a link between inflammation and cognitive deficit, and implicate cellular metabolism as a potential mediator of microglial immune function.

RESEARCH DAY

Poster #4	Neuroprotective Effect of Signma-1 Receptor on Synaptic Function & Calcium Handling in Huntington Disease
Basic research	
Presenter	Wissam B. Nassarallah, Graduate Student
Authors	Wissam B. Nassrallah, James P. Mackay, Amy Smith-Dijak and Lynn A. Raymond
Faculty Sponsor	Dr. Lynn A. Raymond

Introduction: Huntington disease (HD) is a monogenic disorder with autosomal dominant inheritance. In HD patients, neurons involved in motor function degenerate leading to motor and cognitive problems. Synaptic function and Ca^{2+} handling is abnormal in HD. One level of Ca^{2+} regulation is at the endoplasmic reticulum (ER), known to be involved in synapse-to-nuclear communication. I hypothesize that this mechanism is altered in HD. Sigma-1 Receptors (S1Rs) are proteins located on the ER that play an important role in Ca^{2+} regulation and thus gene transcription. Interestingly, activating S1Rs has been shown to normalize this Ca^{2+} handling and restore synaptic function in HD mouse models. The goal of this project is to determine the link between S1Rs, Ca^{2+} handling, Ca^{2+}-dependent gene expression, and synaptic function.

Methods: Electrophysiology, pharmacology, imaging, and the YAC128 HD mouse model were used.

Results: Our data shows that elements of synaptic dysfunction, such as impaired homeostatic synaptic plasticity, in YAC128 cortical cultures are rescued by a S1R agonist. Ca^{2+} imaging also suggests impairments in nuclear signaling in YAC128 spiny projection neurons in corticostriatal co-cultures.

Conclusion and Relevance/Implications: This project will help us understand the complex pathogenesis of HD and elucidate the roles of key therapeutic targets, toward developing disease-modifying treatments.

Poster #5	In Vivo Striatal Neural Activity during Motor Skill Learning in Huntington's Disease Mice
Basic research	
Presenter	Ellen T. Koch, PhD Candidate
Faculty Sponsor	Dr. Lynn A. Raymond

Introduction: Huntington's disease (HD) is a genetic neurodegenerative disorder characterized by motor, cognitive and psychiatric deficits. The dorsal striatum is the major site of neurodegeneration in HD. HD patients and animal models display deficits in striatum-dependent learning, such as motor skill learning. The YAC128 mouse model of HD shows deficits in the accelerating rotarod task. These mice also display aberrant cortico-striatal signalling, including changes to glutamate release and deficits in cortico-striatal plasticity. The contribution of these signalling changes to motor skill learning deficits in vivo has never been tested.

Methods: We combined the accelerating rotarod task with GCaMP7f imaging using fiber photometry to correlate activity in striatal neurons with task performance and motor learning. We also measured GCaMP7f activity of mice in an open field to assess anxiety-like behaviour and locomotor activity.

Results: We found that population activity in dorsal striatum increases during rotarod performance, and returns to a low level afterwards. Over training, the amplitude of population activity during rotarod performance reduces as mice become more proficient. We also found that activity in the striatum is correlated with movement in an open field.

Conclusion: This research will contribute to our understanding of the changes to striatal signalling that may cause motor, cognitive and psychiatric symptoms in HD.

Clinical Relevance/Implications: By measuring neural activity in vivo, we can detect aberrant neural activity in HD mice that correlate with deficits in motor skill learning. This could lead to identification of therapeutic targets for HD that rescue these changes to neural signalling and the corresponding behavioural deficits.

RESEARCH DAY

Poster #6	Dynamics of in Vivo Cortical Network Activity and Local Field Potentials in a Huntington Disease Mouse Model
Basic research	
Presenter	Marja Sepers, Research associate
Faculty Sponsor	Dr. Lynn A. Raymond

Huntington's disease (HD) is a hereditary neurodegenerative disease characterized by profound degeneration of the striatum and cortex, with patients showing progressively disordered movement and cognition. Although the striatum is well studied in HD models, fewer studies have examined cortical neuron function in HD and in particular in vivo cortical network connectivity. Preliminary in vivo data from our labs with mesoscopic imaging using voltage-sensitive dyes (VSDs) showed a more extensive spread of evoked sensory signals across the cortical surface in YAC128 HD mice. To further examine mHtt-induced changes in the cortex, here we used tetrodes chronically implanted across various cortical areas in 6 month-old YAC128 vs. wild-type mice to measure local field potential (LFP) oscillations. Consistent with the VSD imaging experiments, our preliminary data suggest that YAC128 mice show an augmented response to evoked sensory input by limb stimulation. In multiple cortical areas instantaneous LFP power remained elevated in YAC128 longer than wild-type, particularly in beta frequencies. We also repeatedly tested awake-behaving mice and used video analysis to differentiate between behavioural states. The work presented here extends our knowledge of the impact of mHtt beyond ex vivo studies of individual neurons to the function of the intact cortical network in HD.

This work is of potential clinical relevance because mechanisms of cortical network dysfunction determined in a Huntington's mouse model could help determine underlying mechanisms of cognitive dysfunction in patients.

Poster #7	fMRI Analysis of Functional Brain Connectivity in Two Language Tasks in Schizophrenia
Basic research	
Presenter	Chantal Percival, Undergraduate Student/Research Assistant
Faculty Sponsor	Dr. Todd Woodward

Introduction: Schizophrenia is often considered a disorder of connectivity of large-scale brain networks. The current investigation examined functional brain networks underlying two language experiments in healthy controls and schizophrenia patients.

Methods: In semantic association, participants indicated which potential semantic match word was most related to a prompt word. In the thought generating task (TGT), participants either mentally generated or listened to a definition of a noun. Functional brain networks and their associated hemodynamic responses were determined with fMRI Constrained Principal Component Analysis (fMRI-CPCA).

Results: Functional brain networks included the external volitional attention network, response network, default mode network, language and cognitive evaluation network, and auditory network. Schizophrenia patients demonstrated hyperactivity in the external volitional attention network in TGT. Patients with recent hallucinations indicated hyperactivity when presented with external auditory stimuli.

Conclusion: Results suggest that schizophrenia patients require additional cognitive resources to pay attention to presented visual stimuli, and that hyperactivity in auditory brain networks is related to a lack of control exerted over auditory stimuli.

Relevance/Implications: Identification of functional brain networks with fMRI increases understanding of functional connectivity in schizophrenia patients. Merging language datasets allows for comparison and differentiation between brain networks and corresponding cognitive processes. Due to the limited efficacy of both pharmaceuticals and cognitive therapy for schizophrenia, there is a need to both improve current treatment options as well as investigate effective alternatives, one such being neuromodulation. Our understanding of functional brain networks by virtue of fMRI will influence neuromodulation methods.

RESEARCH DAY

Poster #8   A Role for Brain Pericytes in Cerebrovascular Regeneration after Stroke

Basic research

Presenter   Louis-Philippe Bernier, Post-doctoral Fellow

Faculty Sponsor   Dr. Brian MacVicar

Brain pericytes of the neurovascular unit are critical for the developmental maturation of cerebral blood vessels and for the integrity of the blood-brain barrier (BBB). Pericytes are perivascular mural cells that share similarities with mesenchymal progenitors (MP), a cellular pool critical in supporting peripheral tissue regeneration. However, the identity of brain MPs and their role in injury response is unclear. Using a new transgenic MP reporter mouse, we identify pericytes and perivascular fibroblasts as the two major brain MP populations and show that after stroke, both cell populations enter the cell cycle to support cerebrovascular regeneration. Following stroke, brain MPs proliferate and migrate into the infarct region where they accumulate inside a border of reactive astrocytes. The activated MP-astrocyte interface forms an angiogenic zone that progressively migrates into the ischemic core, thereby supporting a wave of tissue revascularization. Within a few weeks vessels with an intact BBB and normal perivascular MP localization are found perfusing the previously ischemic cortical area. Using single-cell and population RNA sequencing, we identify distinct transcriptional signatures of stroke-associated pericyte and perivascular fibroblast subpopulations indicating the unique roles of both MP pools in trauma recovery. Brain pericytes and perivascular fibroblasts in the adult brain represent major progenitor populations that can modify their phenotype to contribute to the regeneration of cerebral blood vessels following injury in a process that recapitulates their role in developmental vasculogenesis.

RESEARCH DAY

Poster #9   Targeting NFκB Signaling by Puerarin for Alzheimer's Disease

Basic research

Presenter   Lina Gao, Post-doctoral Fellow

Faculty Sponsor   Dr. Weihong Song

Alzheimer's disease (AD) is the most common neurodegenerative disorder leading to dementia without effective disease-modifying treatments. Our previous studies have shown that nuclear factor κB (NFκB) is increased in AD brains and inhibition of NFκB signaling reduced AD-associated phenotypes. Puerarin, an extract from the Chinese herb Gegen, has been identified as a strong NFκB inhibitor. However, it is not clear whether puerarin has any effect on NFκB signaling-mediated AD pathogenesis. In this study, effect of puerarin on amyloid precursor protein (APP) processing was detected by Western blot in vitro. BACE1 transcription, translation and enzyme activity were tested by RT-PCR, Western blot and luciferase assay, respectively. Effect of puerarin on NFκB promoter activity was measured by luciferase assay. We found that puerarin treatment significantly inhibits APP processing, resulting in decreased APP C-terminal fragment production in both wild type and Swedish mutant APP stable cell lines. Puerarin works as a strong BACE1 inhibitor, decreasing its mRNA, protein expression and enzyme activity. Furthermore, puerarin treatment remarkably inhibited NFκB promoter activity in LPS-induced BV2 cells. Further investigation of puerarin targeting NFκB signaling pathway is needed. Our results will provide novel insights into the pharmaceutical potential for AD prevention and treatment.

Poster #10	Hypoxia Regulates CNTNAP2 Gene Expression
Basic research	
Presenter	Qing Zhang, PhD Candidate
Faculty Sponsor	Dr. Weihong Song

Introduction: Contactin-associated protein-like 2 (CNTNAP2) plays important roles in neuronal network formation. CNTNAP2 rs802571 is a locus for susceptibility to late-onset Alzheimer's disease (AD), and abnormal CNTNAP2 expression has been found in the hippocampus of AD patients. However, it remains elusive how CNTNAP2 is regulated at the transcriptional level.

Methods: In this study, we cloned a 2949 bp 5'-flanking region of the human CNTNAP2 gene. Thirteen deletion fragments of its 5'-flanking region were cloned. Luciferase assay was performed to examine the transcriptional activation.

Results: The transcriptional start site was mapped between -524 to -472 upstream of translational start site. The fragment -524 to -81 bp had the minimum promoter activity required for transcription. There were five 5'-RCGTG hypoxia-responsive elements (HRE) in the human CNTNAP2 gene promoter. The activity of CNTNAP2 promoter was increased to 270% when treated with hypoxia (1% O_2). Co-transfection with hypoxia-inducible factor 1 subunit α (HIF-1 α) expression plasmid significantly increased the CNTNAP2 promoter activity to 133%.

Conclusion: This is the first study defining the promoter region of human CNTNAP2 gene. Our results demonstrated that CNTNAP2 is tightly regulated by hypoxia at the transcriptional level.

Implications: Our study suggests a novel role of hypoxia regulating CNTNAP2 gene expression in contributing to AD pathogenesis.

RESEARCH DAY

Poster #11	Upregulation of MIF as a Defense Mechanism and a Biomarker of Alzheimer's Disease
Basic research	
Presenter	Fang Cai, Research Associate
Faculty Sponsor	Dr. Weihong Song

Abstract: Macrophage migration inhibitory factor (MIF) is a pro-inflammatory cytokine. Chronic inflammation induced by amyloid β proteins (Aβ) is one prominent neuropathological feature in Alzheimer's disease (AD) brain. We found MIF expression was upregulated in the brain of AD patients and AD model mice. Elevated MIF concentration also detected in the cerebrospinal fluid of AD patients but not the patients suffering from mild cognitive impairment and vascular dementia. Reduced MIF expression impaired learning and memory in the AD model mice and MIF expression largely associated with Aβ deposits and microglia. The binding assay revealed a direct association between MIF and Aβ oligomers. Neurons instead of glial cells were responsible for the secretion of MIF upon stimulation by Aβ oligomers. In addition, overexpression of MIF significantly protected neuronal cells from Aβ-induced cytotoxicity. Our study suggests that neuronal secretion of MIF may serve as a defense mechanism to compensate for declined cognitive function in AD, and increased MIF level could be a potential AD biomarker.

RESEARCH DAY

Poster #12	Regulation of IAPP Transcription by Spliced XBP1
Basic research	
Presenter	Susan Lin, Master Student
Faculty Sponsor	Dr. Weihong Song

Introduction: A major risk factor for Alzheimer's disease (AD) is type II diabetes mellitus (T2DM). Extracellular amyloid plaques found in AD brains are comprised of brain-derived amyloid β as well as pancreas-derived islet amyloid polypeptide (IAPP). IAPP is a component of the islet amyloid found in T2DM patients and its aggregation is cytotoxic. The mechanisms underlying IAPP aggregation include IAPP overexpression and endoplasmic reticulum (ER) stress.

Methods: To study IAPP transcription, a 1618 base pair 5' flanking region of the human IAPP promoter was cloned along with deletion constructs. Promoter-reporter assays were used to determine IAPP promoter activity in response to ER stress.

Results: The IAPP promoter and its deletion constructs were active in β- and non-β-cell lines. Tunicamycin-induced ER stress enhanced IAPP promoter activity, transcript levels, and protein levels in β-cells via activating X-box binding protein 1 (XBP1) splicing. The binding site of spliced XBP1 was elucidated, and abolishing this binding site by mutagenesis diminished the effects of ER stress on IAPP transcriptional activity.

Conclusion/Relevance: Our study uncovers a link between ER stress, XBP1 splicing, and IAPP at the transcriptional level and provides insight into the role of ER stress in IAPP cytotoxicity during T2DM and ultimately, AD.

Clinical Relevance: Studying how IAPP expression and/or release is altered during stress provides a strong context and solid basis for understanding the role of IAPP in AD pathogenesis; in turn, we gain greater insight in its therapeutic potential for treatment of the disease.

RESEARCH DAY

Poster #13   The role of HIP1R in Alzheimer's Disease-Associated Cognitive Deficits

Basic research

Presenter   Lin Peng, Post-doctoral Fellow

Faculty Sponsor   Dr. Weihong Song

Alzheimer's disease (AD) is the leading cause of dementia in the elderly. Accumulative evidence has shown that hippocampal dendritic spine loss and altered synaptic plasticity play a major role in AD-associated cognitive deficits. However, the underlying mechanism is unclear. Our previous study revealed that the expression of huntingtin interacting protein 1 related protein (HIP1R) was decreased in brains of AD model mice. We also found that HIP1R regulated spine density, size and excitatory synaptic transmission in cultured hippocampal neurons. In addition, similar spine changes were observed by disturbing the interaction of HIP1R with cortical actin binding protein (Cortactin). These results suggest that HIP1R may be important for synaptic function and cognitive function through its interaction with Cortactin in AD. Further study is under way to explore the mechanism of HIP1R's protective effects on AD-associated synaptic dysfunction and cognitive deficits.

RESEARCH DAY

CLINICAL POSTERS

Poster #1	Exploratory Pilot Study on the Influence of Race and Ethnicity in Pediatric OCD: Examination of a Canadian Tertiary Care Clinical Sample
Clinical research	
Presenter	Joanne Wang, Medical Student
Faculty Sponsor	Dr. Evelyn Stewart

Introduction: Clinical correlates between race and OCD, especially within the pediatric population, are poorly explored. We aim to determine whether race and ethnicity may influence OCD characteristics, clinical course, and family functioning.

Methods: Participants presented to BC Children's Hospital provincial OCD program between 2011-2018, including Asians (N=35) and Caucasians (N=183). Upon consent to registry, clinician-, parent- and child-reported measures were used to capture: symptom type, severity and family environment. Descriptive and comparative analyses were conducted via SPSS. Post-hoc analyses compared an independent mixed-Asian/Caucasian group in significant variables.

Results: Asians reported significantly higher symmetry obsession prevalence, later ages for: OCD onset, treatment offered, and received, and are less likely to receive treatments offered prior to our program ($p < .05$). Asian parents reported significantly poorer cohesion and higher blame in family functioning ($p < .05$). Mixed ethnicity youths' results lie mostly between Caucasian and Asian subgroups. No group differences were identified with respect to gender, socioeconomic status, OCD severity, comorbidities, and delay to diagnosis and treatment ($p > .05$).

Conclusion: Notable distinctions between Caucasian and Asian subgroups of OCD-affected youth presenting to a tertiary care facility has been identified. Replication in a larger independent cohort is warranted to expand upon further understanding.

Relevance/implications: Careful consideration should be given to family dynamics and description of treatments to address any ethnic concerns and minimize stigma.

Continued

Poster #1	Exploratory Pilot Study on the Influence of Race and Ethnicity in Pediatric OCD: Examination of a Canadian Tertiary Care Clinical Sample
Clinical research	
Presenter	Joanne Wang, Medical Student
Faculty Sponsor	Dr. Evelyn Stewart

Clinical Relevance: As poorer family dynamics predicts non-response to CBT, attention should be given to Asian youths to maximize therapy effectiveness. Cultural concerns should be considered when describing treatment options to minimize stigma. Education on deviation from normal childhood development could potentially allow for more accurate parent-reported onset age, leading to earlier diagnosis and treatment.

RESEARCH DAY

Poster #2	Predicting Recurrence in Bipolar Disorder: A Pilot Study Using a Machine Learning Technique
Clinical research	
Presenter	Jairo Vinícius Pinto, Post-doctoral Fellow
Faculty Sponsor	Dr. Lakshmi N. Yatham

Introduction: Bipolar disorder (BD) is a highly recurrent and disabling condition. Prediction of recurrence in BD is especially important since this would help guide treatment decisions. Therefore, we aimed to predict recurrence using a machine-learning approach.

Methods: A sample of 170 subjects with BD were included and clinically followed for one year. A set of clinical and sociodemographic data were used to build a model to predict recurrence within 12 months after the first assessment. We tuned the elastic net regularisation algorithm, a classification model that utilises penalties, using the training dataset through 10-fold cross-validation, and the performance of the model was estimated by its ability in classifying the subjects of the testing dataset.

Results: The algorithm identified the subjects with recurrence with an accuracy of 78% (sensitivity: 78.9%, specificity: 77.3%, balanced accuracy: 78.1%, kappa: 0.56). The selected predictors were baseline HAMD and CGI scores, current use of lithium and age, in order of coefficients magnitude. Only lithium showed a negative coefficient.

Conclusion: The model achieved good accuracy to predict recurrence in one year using clinically relevant variables. It is possible to hypothesise that predictive models based on machine learning will help to make critical clinical decisions in the future.

Potential Current or Future Clinical Relevance: Our model achieved good accuracy using clinically relevant and pragmatic variables. Although it is a pilot study, our result suggests that predictive models based on machine learning techniques possibly will support important clinical decisions in the future, such as prognosis orientation and selection of treatment options for BD.

RESEARCH DAY

Poster #3	Does Experiencing Care as Collaborative Enhance Inpatient Eating Disorders Treatment Outcome?
Clinical research	
Presenter	Lindsay Samson, Graduate Student and Nadia Maiolino, Resident
Authors	Lindsay Samson, Nadia Maiolino, Josie Geller, Suja Srikameswaran
Faculty Sponsor	Dr. Josie Geller

Introduction: Inpatient eating disorders treatment is costly and resource intensive. Evidence suggests that collaborative care produces higher levels of patient motivation to change, a predictor of better outcome. Unfortunately, given that mandatory treatment components are central to effective inpatient care, fostering a collaborative environment can be challenging. This study examined whether experience of care as collaborative contributed directly to better outcome and explored whether collaborative care was associated with the manner in which mandatory treatment components (i.e., weight gain, abstinence from use of compensatory strategies) were delivered.

Methods: Inpatients (N = 146) completed measures of readiness for change, eating disorder and psychiatric symptoms, and quality of life, pre and post-treatment. At post, they also completed measures of collaborative care and the extent to which mandatory treatment components were implemented with a sound rationale, consistent, advance warning, and the provision of choices.

Results: Experiencing care as collaborative was associated with improvements in nearly all symptom domains. Collaboration ratings were also associated with the manner in which mandatory treatment components were implemented.

Conclusions: Findings add to the growing literature that enhancing patient collaboration and autonomy on inpatient units is associated with best outcomes, and may be fostered by the delivery of mandatory treatment components.

RESEARCH DAY

Poster #4	The CanTBI Study: The Creation of a National Database and Biobank for Traumatic Brain Injuries
Clinical research	
Presenter	Martina Knappett, Louise Meddings and Simarpreet Pattar
Authors	Lindsay Samson, Nadia Maiolino, Josie Geller, Suja Srikameswaran
Faculty Sponsor	Dr. William Panenka

Effective treatment of traumatic brain injury (TBI) remains one of the greatest unmet needs in public health. Greater than 1.5 million Canadians are currently living with a variety of somatic, cognitive, and psychological symptoms. Researchers collaborating on the Canadian Traumatic Brain Injury (CanTBI) Study aim to create a large, high quality database on TBI in order to establish more precise methods for TBI diagnosis and prognosis. This multi-centre, longitudinal study intends to recruit 450 TBI and 150 trauma control (TC) patients from seven hospitals across the nation. All participants have experienced TBI or an orthopaedic injury (not involving the head or neck) within 24 hours, and are asked to provide a blood sample for the biobank. Subjects are then followed up with at 2 weeks, 3 months, 6 months, and 12 months post-injury.

The local study team at Vancouver General Hospital aims to recruit 60 TBI and 30 TC participants from the CanTBI patient population to complete additional psychiatric assessments, neurocognitive testing, and advanced imaging techniques to create a comprehensive clinical, imaging, genomic, and proteomic dataset. We hypothesize this highly integrated and widely accessible database will act as a catalyst for TBI clinical trials and contribute to improved TBI patient classification.
Future Clinical Significance:

We hypothesize this highly integrated and widely accessible database will act as a catalyst for TBI clinical trials. Furthering our knowledge of the predictors of recovery will allow physicians to refine their management of these patients in order to minimize costs and maximize treatment effectiveness.

RESEARCH DAY

Poster #5   Exploring Staff Supported Community Outings in a Forensic Psychiatric Sample

Clinical research

Presenter   Karen Petersen, Post-doctoral Fellow

Faculty Sponsor   Dr. Tonia Nicholls

Introduction: Staff Supported Community Outings (SSCOs) are designed to support safe forensic psychiatric patient re-integration into the community. They allow patients to maintain family ties, access community resources (e.g., transit skills, grocery shopping, fitness), and develop vocational and leisure skills. There is currently a dearth of evidence examining the rehabilitative efficacy of short-term community access in a forensic population.

Methods: We employed a cross-sectional design in which we examined all SSCOs in one Canadian forensic psychiatric hospital for a one-year period (January 1, 2017 - December 31, 2017).

Results: Most patients attending SSCOs were male with a primary diagnosis in the schizophrenia spectrum. A large number of SSCOs occurred during the one-year period, including 87 Assessment SSCOs in which two staff escort one patient on a short outing to assess their readiness to attend further SSCOs. Of particular interest, there were no significant adverse events (e.g. violence, AWOL) on any SSCO during the one-year period.

Conclusion, Relevance/Implications: The results can help address misconceptions about the risks associated with community access by patients given that there were no significant adverse events. In addition, results contribute to the international dearth of literature regarding the utility and safety (patient, staff, public) of SSCOs.

Potential Current or Future Clinical Relevance: Skill development that generalizes to the social environment and contributes to community re-integration is relevant to the recovery of mentally ill individuals who have become entangled in the criminal justice system. These findings provide additional evidence of the rehabilitative efficacy of short-term community access in the forensic psychiatric population.

Poster #6	Metabolic and Genetic Explorations in Refractory Schizophrenia Project – Chromosomal Variants in 1st 25 cases
Clinical research	
Presenter	Robert Stowe, MD
Authors	Robert Stowe, Monica Hrynchak, Agata Minor, Christine Tyson, Prescilla Carrion, Ashley DeGraaf, Pedram Lagaei, Olga Leonova, Mahesh Menon, Ivan Torres, Veerle Willaeys, Randall White, Clara Westwell-Roper, Clare Beasley and William Honer

Introduction: Chromosomal copy number variants (CNVs) are the most potent genetic contributors to schizophrenia risk. Data on the first 25 MAGERs research project patients with treatment-resistant psychosis (TRP) are presented.

Methods: High resolution SNP chromosomal microarray (CMA), identified CNVs containing ≥ 25 probes, curated for reliability and frequency in the Database of Genomic Variants (DGV); ClinGen and DECIPHER overlap; gene content; and database/literature review.

Results: Participants had severe psychosis on admission (mean PANSS Total Score of 88.1) Family histories revealed remarkable genetic loading for major psychiatric illness. Using ACMG clinical guidelines, CNVs were clinically reported in 36% of patients and in 24%, potentially related to schizophrenia), including pathogenic CNVs in 8% With size filters relaxed to ≥ 25 markers, 44% without clinical CNVs had ≥ 1 exonic research CNV, and 24% had CNVs involving introns with prominent regulatory features, implicating novel as well as established risk genes involved in axonal and neuritic outgrowth, chromatin modification, neurotransmitter function, cortical development, synaptic function and plasticity, and immunological functions

Conclusion: The diagnostic yield of CMA in TRP is significant, particularly when smaller variants are considered. In total, 32%‑58% of participants carried CNVs likely to play a pathogenic role in their psychosis.

Relevance/Implications: CMA is recommended as a diagnostic modality in TRP cases.

RESEARCH DAY

Poster #7	A Multivariate fMRI Investigation of Functional Networks Associated with Thermal Pain
Clinical research	
Presenter	Matteo Damascelli
Faculty Sponsor	Dr. Todd Woodward

Introduction: Pain is an aversive psychological state—created and modified in the brain. Imaging research has identified several key regions associated with pain processing and regulation. However, the functional networks involved have not been comprehensively described.

Methods: To this end, we applied constrained principal component analysis (CPCA) on an open-source functional magnetic resonance imaging (fMRI) dataset, where 33 healthy participants were administered thermal stimuli and increased or decreased their pain by self-regulation. Effects of self-regulation and stimulus temperature on hemodynamic responses were investigated.

Results: Three networks emerged: a sensorimotor response network, a frontoparietal cognitive-evaluation network, and the default mode network (DMN). Hemodynamic responses in all networks were modulated by an interaction between regulation and temperature, but overall activity was regulation-dependent in the DM and response networks, and temperature-dependent in the attention and response networks.

Conclusion: From this, we conclude that the sensorimotor response network generates a pain-induced response, the cognitive-evaluation network underlies attention to pain stimuli, and the DMN engages in pain regulation.

Relevance/Implications: Applying a similar research paradigm to chronic pain populations may reveal new functional reorganizations at the network-level. Ultimately, this may have implications for the development of treatments based on neuro-modulation, behavioural therapy, or combinations of the two.

Future clinical relevance: This research serves as a point of comparison for similar analyses applied to chronic pain patient data. This may lead to an understanding of how these networks behave differently in chronic pain and how they can be targeted to enhance existing treatments or provide alternatives.