2021-2022 Talent Development Successful Candidates Abstracts

Awardee: Sophia Atwells

Supervisor: Laurie Zawertailo

Title: Multi-modal MRI in daily e-cigarette users, daily smokers and healthy controls: functional and structural comparisons

Lay Abstract: Electronic cigarette (e-cigarette) use among young Canadians has reached epidemic proportions despite the unknown long-term health effects. E-cigarettes contain the highly addictive substance nicotine, which is also found in traditional tobacco cigarettes. Animal studies have examined how nicotine alters the developing brain, however, there are no such studies in humans. Therefore, determining the functional and structural impact of nicotine in the developing brain of regular daily e-cigarette users is of critical importance. Functional and structural changes in the brain can be visualized using brain imaging techniques called functional magnetic resonance imaging (fMRI) and quantitated MRI (qMRI). The proposed study will use both fMRI and qMRI to investigate and clinically measure the functional and structural changes in the brain of youth and young adults who use e-cigarettes on a regular daily basis, and compare the results to those who use tobacco cigarettes and those who do not use tobacco cigarettes nor e-cigarettes. The proposed study will be the first to provide evidence of brain alterations associated with daily e-cigarette use in youth and young adults. This is highly important since the human brain continues to develop until approximately age 25. Establishing brain changes specifically associated with e-cigarette use will: (i) contribute to the fields of addiction and mental health by potentially identifying cognitive dysfunction; (ii) help inform public health policy; and (iii) help develop treatment approaches for e-cigarette use cessation, thereby decreasing disability associated with addiction.

Awardee: Katrina Hui

Supervisor: Daniel Buchman

Title: Exploring Bias and Ethical Considerations of the Expansion of Artificial Intelligence Applications in Risk Assessments in Mental Health Care Through Natural Language Processing and Qualitative Interviews with Clinicians and Patients

Lay Abstract: Artificial intelligence (AI) provides opportunities to improve risk assessments to better predict patient violence, suicide, or readmission, which can help improve mental health care. However, there is growing concern that these tools may amplify existing inequities, such as

systemic racism, because the algorithms are trained on biased datasets. CAMH data demonstrates that Black inpatients are 44% more likely to be restrained than White patients, in keeping with data from other jurisdictions, and are also more likely to present with police (Dismantling Anti-Black Racism, 2021). This contributes to a disproportionate representation of Black people in the forensic system. In the Emergency Department (ED), patients are given a daily predictive risk score for violence, which informs care trajectories and restraint events. However, it is unclear whether other factors intersect with racialized status to influence risk assessments and contribute to inequities for marginalized populations. Such biases have serious consequences for the development of not only predictive models but ethical AI models that can improve patient care.

I aim to integrate unstructured and structured risk assessment data from electronic health records (EHRs) to identify biases and use findings to help create an ethics framework for applications of AI in mental health care. I will use natural language processing (NLP) to analyze sentiment in narrative clinical notes and determine if violence risk scores differ based on police involvement and sociodemographic factors. I will augment this analysis with qualitative interviews with clinicians and patients to contextualize involuntary admission, the lived experience of the ED, and perceptions of AI applications of mental health data. The findings will inform strategies to build fairer predictive models and decrease inequities in care, including discussions about ethical considerations for potential uses of AI in psychiatry for marginalized populations.

Awardee: Christopher Morrone

Supervisor: Wai Haung (Ho) Yu

Title: Mechanisms of sleeplessness and failed proteostasis interact and facilitate cognitive decline in Alzheimer's disease

Lay Abstract: Alzheimer's disease (AD) is the most common dementia in the elderly. AD causes memory loss and loss of executive function. People with AD develop toxic proteins that surround and are found inside brain cells, called neurons. Neurons are required for functions like thinking, learning and memory. Build-up of this pathology starts decades before AD is diagnosed, in a pre-dementia stage. In this pre-dementia stage, a process to breakdown and recycle proteins in neurons fails. Patients also have disturbed sleep, which increases toxic proteins and AD risk. In my research, I will examine the relationship between impaired sleep, memory and toxic protein recycling in AD.

To test this, I will use a mouse model of AD with pathology and monitor changes in sleep and memory. I will correlate my results with inability to recycle toxic proteins. Four different ages will be used in these mice to understand the pre-dementia stage and AD progression. I will test

learning and memory, and measure awake and sleeping brain wave activity. Brain tissue will be tested for pathology and protein breakdown markers at each age in important brain regions for AD. Data from this work will be modelled by a computer algorithm. This will identify how loss of sleep and protein breakdown impact the risk for AD. I hypothesize that sleeplessness and protein recycling failure will come before behaviour deficits and predict disease progression.

My research will help explain the pre-dementia stage of AD. I expect sleeplessness and impaired protein recycling in neurons at young ages in AD mice. I expect learning and memory to become impaired at later ages. This work will help patients because doctors can identify the disease earlier and provide direct treatments. Future experiments will use my results to design AD treatments to improve sleep or increase the recycling of toxic proteins, potentially improving behaviour and neuron function.

Awardee: Alexia Polillo

Supervisor: Nicole Kozloff

Title: Delivering early psychosis intervention services during a pandemic: A mixed-methods analysis of factors associated with mode of delivery, digital equity, and associated outcomes

Lay Abstract: The COVID-19 pandemic has led early psychosis intervention (EPI) programs to rapidly implement virtual methods to continue delivering essential services. While virtual delivery can increase access to care, digital equity factors, including poverty and homelessness, may create barriers to virtual engagement. There is limited evidence on how different modes of service delivery can effectively meet the needs of youth with psychosis, particularly for those who are marginalized. “e-NAVIGATE” is a CIHR-funded study that is currently evaluating the implementation effectiveness of a virtual adaptation of the NAVIGATE model in CAMH’s EPI program. I will extend this work by using mixed methods to examine factors associated with different modes of EPI service delivery and time-to-disengagement from services during the pandemic. A chart review will examine how care is received throughout the pandemic, whether by remote or in-person methods. I will use logistic regression to inspect the association between mode of delivery and baseline demographic, clinical, and service use factors. Survival data analysis tools will be applied to associate time-to-disengagement with baseline factors and mode of delivery. I will also lead in-depth qualitative interviews with youth and families to explore their experiences with virtual EPI services, probing findings from the chart review. I will conduct an additional focus group with 5-7 clinicians to explore how modes of service delivery are determined and perceived effectiveness. Identifying what works and for whom in virtual delivery of EPI services will help ensure ongoing access to safe and equitable care.

Awardee: Annabel Sibalis

Supervisor: Brendan Andrade

Title: Deconstructing dysregulation: An examination of parent and child factors associated with the development of behavioural dysregulation in children

Lay Abstract: Behavioural dysregulation (BD) – aggression, impulsivity, and other behaviour harmful to oneself or others – is a core symptom of multiple mental disorders including attention-deficit/ hyperactivity disorder and disruptive behaviour disorders. BD is among the most common reasons for a child's referral to mental health services and a concerning risk factor for later delinquency, substance use disorders, and suicide. In order to improve life outcomes for children with BD and develop approaches to bolster children's ability to effectively self-regulate, it is necessary to determine its etiology.

Existing research and theory have linked executive functions (EF) – higher order cognitive skills such as attention, impulse control, and emotion regulation – to behavioural regulation. However, minimal research has examined specific mechanisms through which EF impacts BD, including investigating the role of parent factors such as parent EF and parenting behaviour. The current study addresses these gaps in knowledge.

This study will recruit clinically-referred children ages 6-12 with varying levels of BD and their parents, and typically-developing control children and parents. Computer tasks will be administered to children to measure EF (i.e., attention and impulse control). Emotion regulation will be measured by heart rate variability captured via a heart rate measurement system. Parents will complete questionnaires assessing parenting strategies and child BD symptoms, and will track child BD for two weeks after assessment.

By clarifying how BD develops and the key factors involved, this research will spark opportunities for novel clinical interventions for children with BD and their parents, improving developmental trajectories for children and decreasing the disability associated with BD.

Awardee: Anna Paula Silva

Supervisor: Vanessa Goncalves

Title: Analysis of mitochondrial DNA variants in youth diagnosed with schizophrenia and bipolar disorder.

Lay Abstract: Mitochondria are the main energy source for neurons and other brain cells and play crucial roles in various neural processes, such as neurogenesis, neuroplasticity, and neurotransmission. Moreover, the dysfunction in this organelle may alter critical neuronal processes underlying abnormal brain development and cognitive impairment in psychosis. Several clinical, genetic, and neuroimaging studies implicate mitochondrial dysfunction to play a crucial role in the pathophysiology of schizophrenia (SCZ) and bipolar disorder (BD). The present study aims to investigate the association between common and rare variants of mitochondrial DNA (mtDNA), with the severity of clinical outcomes, brain imaging measures, and medication response in youth diagnosed with SCZ and BD. Our sample size is 512 individuals and genetic (mtDNA whole genome sequences), clinical (cognitive scores for speed of processing and attention) and imaging data (fractional anisotropy and cortical thickness) were already collected. This study will provide a set of mitochondrial genetic variants that can be used in future tests for early screening of patients at risk for more severe course of psychosis or better response to drug treatment.

Awardee: Victor Tang

Supervisor: Daphne Voineskos

Title: Repetitive Transcranial Magnetic Stimulation for Suicidality in Concurrent Major Depressive Disorder and Alcohol Use Disorder

Lay Abstract: Major Depressive Disorder (MDD) and Alcohol Use Disorder (AUD) are leading causes of disability in Canada and patients are frequently affected by both conditions. Each disorder is associated with an increased risk for suicide, with an even greater risk when in combination. Unfortunately, current antidepressant medications have little to no efficacy in patients with AUD, and there are few established treatments for suicidality. The development of an effective intervention for suicidality in this high-risk population remains a major therapeutic challenge and opportunity. Repetitive transcranial magnetic stimulation (rTMS) is a brain treatment that uses magnetic pulses to non-invasively modulate a region called the dorsolateral prefrontal cortex (DLPFC). It is widely accepted as an effective therapy for difficult to treat MDD, and there is now emerging evidence showing efficacy in reducing suicidality. These findings are extremely promising given that the DLPFC has been implicated in the pathophysiology of suicidality through cognitive control of negative emotion. A new rTMS technique called theta burst stimulation (TBS) has recently been developed to decrease the daily treatment length to 1/10th of the time. Clinical trials comparing TBS to standard rTMS have found equivalent efficacy in treating MDD. We propose to conduct the first clinical trial of TBS to the DLPFC to treat suicidality in patients with both MDD and AUD. We hypothesize that a 4-week course of TBS will improve symptoms of suicidality and may also benefit symptoms of

depression and alcohol craving and consumption. rTMS has proven its efficacy, safety, and tolerability over decades of research for MDD, and TBS has been shown to be a form of rTMS that is much more efficient and cost-effective for the healthcare system. This study will explore the potential of TBS to be a safe and effective treatment modality for reducing suicidality in this highly vulnerable and complex patient population.

Awardee: Kazunari Yoshida

Supervisor: Daniel Mueller

Title: Investigating the genomic overlap between antipsychotic-induced weight gain and antipsychotic efficacy in schizophrenia

Lay Abstract: Antipsychotic drugs are widely used for treatment of schizophrenia and for other psychiatric disorders. Despite their established efficacy, they are associated with antipsychotic-induced weight gain (AIWG), a common and problematic side effect. Numerous studies have reported a positive correlation between AIWG and antipsychotic treatment response, although the underlying molecular mechanisms of AIWG and antipsychotic efficacy are not fully understood. Notably, genetic factors are known to be associated with both AIWG and antipsychotic efficacy. With the advent of novel technologies allowing to estimate the effects of multiple genetic risk variants (i.e. polygenic risk scores; PRS), contributing to the risk for AIWG, we now have a promising tool to investigate the overlap of the genetic liability to AIWG and antipsychotic efficacy.

To close this critical research gap in understanding the molecular genetics of both AIWG and treatment efficacy, my project will answer the following questions: (1) Are there overlapping genetic factors for AIWG and antipsychotic efficacy? (2) Is there a correlation between PRSs for AIWG, antipsychotic efficacy, and related metabolic outcomes (e.g., diabetes and hyperlipidemia)? (3) Can AIWG and antipsychotic efficacy be predicted using state-of-the-art machine learning algorithms integrating clinical and genetic factors? To answer these questions, I will use a large, well-characterized sample of individuals prospectively assessed for AIWG and antipsychotic efficacy (N=345). I will validate my findings in independent samples available through large public biobank samples (e.g., UK biobank). This study will lead to the development of a tool that will capture patients at risk of developing weight gain and benefiting from antipsychotic treatment. This tool will improve pharmacotherapy, and contribute to bringing precision medicine to the clinic.