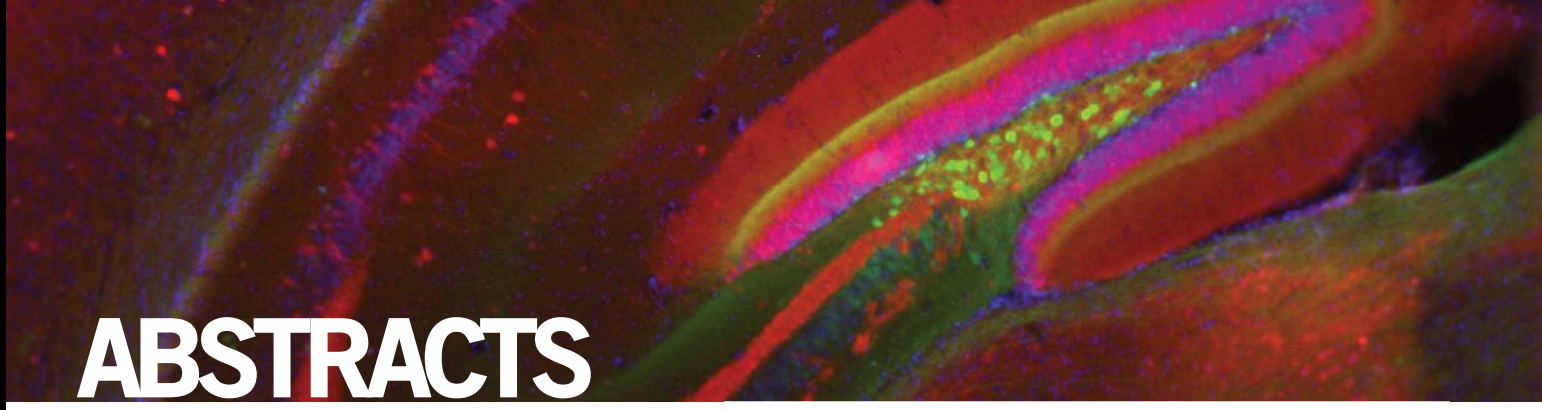


ABSTRACTS

INVESTIGATING PAOPA, A NEW POTENTIAL ANTIPSYCHOTIC FOR THE TREATMENT OF SCHIZOPHRENIA: AN *IN VIVO* MICRODIALYSIS STUDY

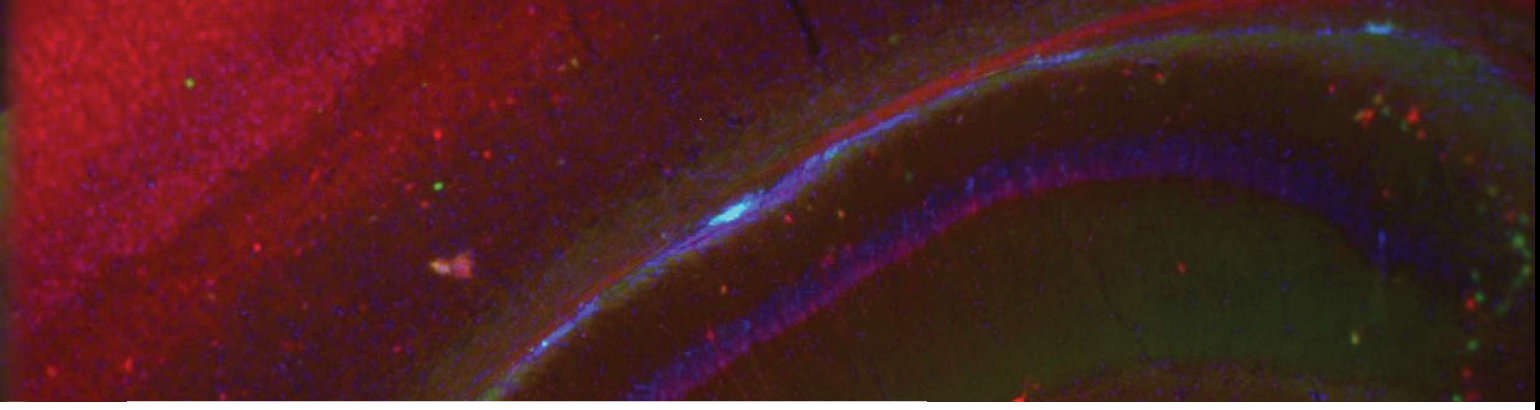
OMAR SHAWAF[1]
[1]McMaster Integrative Neuroscience Discovery & Study (MiNDS) Program

Schizophrenia is a mental disorder that affects approximately 1% of the global population. The disorder is largely characterized into three main symptom groups: positive, negative, and cognitive. Conventional antipsychotic drugs (APDs) act as dopamine D2 receptor antagonists that compete with endogenous dopamine at the orthosteric binding site, thereby attempting to attenuate psychotic symptoms marked by striatal hyperdopaminergic signaling. Unfortunately, APDs are associated with adverse motor and metabolic side effects. In order to circumvent the challenges posed by the evolutionarily conserved nature of orthosteric sites when creating highly selective D2 receptor ligands, selective positive allosteric modulators (PAMs) are used. PAOPA, in addition to attenuating behavioural abnormalities in preclinical amphetamine-induced animal models of schizophrenia, has proven to be the most potent positive allosteric modulator of the dopamine D2 receptor. However, the mechanism through which PAOPA mediates its effects remains unclear. Three groups (n=14; n=3-5/group) of male Sprague Dawley rats received subcutaneous injections of d-amphetamine (1 mg/kg) following a 0.9% saline (1 mL/kg) or PAOPA (1 mg/kg) pre-treatment. Following treatment, *in vivo* striatal dialysate samples were collected using microdialysis to assess whether the behavioural changes measured in the locomotor test were associated with changes in dopamine levels. Interestingly, PAOPA pre-treatment attenuated the amphetamine-induced locomotor hyperactivity, confirming previous results which suggest D2 receptor internalization. PAOPA also reduced striatal dopamine dialysate levels overall, but not at the 20 or 40 minute interval. PAOPA treatment alone had no effect. This study presents further avenues of exploration for the potential development of PAOPA as a novel APD.

LPS-INDUCED BLOOD-BRAIN BARRIER DISRUPTION: ASSESSING LITHIUM'S MOLECULAR AND THERAPEUTIC EFFECTS

AARON EDWARD[1]**; JAY PATEL**[2]**; RITESH DAYA**[2]**; BENICIO FREY**[2,3,4]**; RAM MISHRA**[2,3]
[1]Molecular Biology and Genetics Co-op Program, McMaster University; [2]McMaster Integrative Neuroscience Discovery & Study (MiNDS) Program; [3]Department of Psychiatry & Behavioural Neurosciences, McMaster University; [4]Mood Disorders Program and Women's Health Concerns Clinic, St. Joseph's Hospital Hamilton

Bipolar disorder (BD) is a chronic and severely debilitating psychiatric illness that affects approximately 2% of the world population. While lithium compounds remain the hallmark mood-stabilizing agent for the treatment of BD, their exact mechanism of action is unknown. There is growing evidence suggesting that the inflammation of the blood-brain barrier (BBB), combined with the passage of pro-inflammatory cytokines into the central nervous system, is a contributing factor to the pathophysiology of a number of neuropsychiatric diseases, including BD. However, in the case of BD, the role of inflammation remains understudied. We tested lithium's ability to prevent inflammatory disruption in the BBB, implicating the role of inflammation in the pathophysiology of BD. In our study, we assessed if chronic pre-treatment with lithium was able to prevent BBB disruption in the Sprague Dawley rat. Lipopolysaccharide (LPS) was administered to induce an inflammatory response and subsequently disrupt the BBB 24 hours before sacrifice. Intravenous administration of sodium fluorescein (NF) was used to quantify the degree of BBB disruption. The results were compared to a group of sham-injected rats. Western blot analysis will also be completed on the tight junction proteins occludin and claudin-V to assess changes in BBB integrity. Through the NF assays, we were able to demonstrate that lithium partially prevents BBB disruption in several brain regions – including the prefrontal cortex, cortex, and striatum – and whole brain samples, as compared to LPS-only negative controls. The results suggest that lithium may have a therapeutic action in an animal model of BBB disruption. Our novel approach to studying BD through inflammation of the BBB will open new avenues for understanding BD's pathophysiology and will advance our understanding of lithium's therapeutic mood-stabilizing properties.



SPATIOTEMPORAL EXPRESSION OF AUTISM-RELATED AND FMRP TARGET GENES IN THE FMR1 KNOCK OUT MOUSE MODEL

DAIANA POGACEAN[1]; KATERINA LIACONIS[1]; JONATHAN LAI[1]; JANE A. FOSTER[1]
[1]Department of Psychiatry and Behavioural Neuroscience, St. Joseph's Healthcare

Autism Spectrum Disorder (ASD) is a neurodevelopmental disorder characterized by impaired social communication and repetitive behaviours. The Diagnostic and Statistical Manual of Mental Disorders (DSM-5) defines ASD as an umbrella term for the following four separate disorders: autistic disorder, Asperger disorder, childhood disintegrative disorder, and pervasive developmental disorder not otherwise specified. Currently, there is no empirical biological method to diagnose ASD patients. While advances have been made in understanding ASD, development of new treatments is limited. Fragile X Syndrome (FXS) has become pertinent to elucidating a biological understanding of ASD. FXS is the most common heritable single gene cause of ASD, and is caused by 200 or more CGG trinucleotide repeats in the Fragile X Mental Retardation 1 (*FMR1*) gene, which silences the function of the gene through epigenetic mechanisms. This thesis aims to identify the neurobiological underpinnings of Fragile X Syndrome as this serves as a gateway into understanding the complexity and heterogeneity of ASD. Using *in situ* hybridization, three genes are examined for their spatiotemporal expression across the hippocampus and somatosensory cortex (S1) brain regions. All samples were collected from wild type (WT) and fragile X mice during postnatal development. Target genes were selected to meet the following two criteria: 1) identified gene variants in ASD individuals and 2) known *FMR1* protein targets. Significant differences were observed in PTEN mRNA between WT and fragile X mice at postnatal day 21 in both the S1 and dentate gyrus brain regions. No significant differences were found between WT and fragile X mice for CHD8 and SYNGAP1 mRNA. This approach will further the ongoing analysis of the underlying biological basis of ASD, which is necessary for optimizing therapeutics in the future.

MOMMY MONITOR: THE DEVELOPMENT OF A MOBILE APP TO REDUCE THE ADVERSE MATERNAL HEALTH EXPERIENCES OF IMMIGRANT WOMEN IN CANADA

ELSIE AMOAKO[1]; AISHA LOFTERS[1,2]
[1]Institute of Health Policy, Management, and Evaluation, University of Toronto; [2]MD/Ph.D Program

Introduction: Research continues to show that immigrant women experience poorer birth outcomes compared to non-immigrant women in Canada. The main objectives of this study were to 1) explore the experiences of immigrant women with prenatal care, 2) determine the perceived relevance of topics taught in generic prenatal classes to immigrant women and 3) discuss the interplay between culture, perceived relevance, and use of prenatal care by immigrant women.

Methods: Qualitative, ethnographic, one-on-one semi-structured interviews were utilized to conduct a thematic analysis of participants' perspectives.

Results: The participants acknowledged the presence of prenatal care and services being provided by the healthcare system, though the majority did not attend prenatal classes. The immigrant women discussed a need for larger social support networks during and after pregnancy, as well as healthcare professionals who take initiative to understand their cultural values and needs on an individual level. The participants highly preferred midwifery as a form of prenatal care, and were not concerned with receiving competent care, but rather cultural sensitivity, relying on personal cultural networks.

Conclusion: Based on these findings, four final recommendations were made to provide a platform for the enhancement of prenatal care and services to reflect the needs of the immigrant women population. A mobile health application is being developed as a method of translating the knowledge produced through this study. Phase two of the study includes the development of the "Mommy Monitor" app in a mixed methods study which can be used by pregnant immigrant women in Canada. This app seeks to enhance surveillance, provide social networking access, peer counsellor support, as well as deliver a guideline for healthcare professionals to aid in implementing culturally sensitive healthcare.