



# 2021 Owerko Centre Conference

In the Beginning: How Early Experiences and Exposures Shape Lives

June 9, 2021

## ABSTRACT BOOKLET



Supported by generous donations through the Alberta Children's Hospital Foundation.

## 2021 Owerko Centre Conference Program

### *In the Beginning: How Early Experiences and Exposures Shape Lives*

9:00 – 9:10	Opening Remarks, Dr. Susan Graham, PhD, Director, Owerko Centre
9:10 – 10:10	<b>Keynote Speaker: Dr. Joanne Weinberg, PhD</b> Department of Cellular & Physiological Sciences, Faculty of Medicine, UBC <i>Prenatal alcohol exposure, fetal programming, and vulnerability over the life course: a translational approach</i>
10:10 – 10:20	Break
10:20 – 11:20	<b>3-minute Trainee Flash Talks</b> <ul style="list-style-type: none"><li>• <b>Paolo Pador</b>, Supervisor: Dr. Sheri Madigan, Dept. of Psychology <i>A meta-analysis on the global prevalence of depressive and anxiety symptoms in youth during COVID-19</i></li><li>• <b>Heidi O'Brien</b>, Supervisor: Dr. Carly McMorris, Dept. of School and Applied Child Psychology <i>Families Facing COVID: The association between perceived vulnerability for contracting COVID-19 and caregiver mental health of autistic individuals</i></li><li>• <b>Melissa Mueller</b>, Supervisor: Dr. Kelly Schwartz, Dept. of School and Applied Child Psychology <i>Unwarranted Hysteria of Screen Time Effects in Early Childhood</i></li><li>• <b>Daphne Nakhid</b>, Supervisor: Drs. Carly McMorris and Catherine Lebel, Depts. of School and Applied Child Psychology / Radiology <i>Brain volume and susceptibility differences in children with prenatal alcohol exposure</i></li><li>• <b>Bailin Xie</b>, Supervisor: Dr. Lianne Tomfohr-Madsen, Dept. of Psychology <i>Relationship Quality Predicts Mental Health in the Pregnancy During the COVID-19 Pandemic Cohort</i></li><li>• <b>Dr. Elnaz Mehrabani</b>, Supervisor: Dr. Gerald Giesbrecht, Dept. of Pediatrics <i>Pre-pregnancy obesity and childhood internalizing problems: Mediating role of prenatal systemic inflammation and moderating role of pre-pregnancy diet</i></li><li>• <b>Dr. Mezbah Uddin</b>, Supervisor: Dr. Tim Shutt, Dept. of Medical Genetics <i>Possible mechanism how ketone bodies may improve mitochondrial function in autism spectrum disorder</i></li><li>• <b>Dr. Xiaoqin Zhan</b>, Supervisor: Dr. Ray Turner, Dept. of Cell Biology and Anatomy <i>The use of a tat-conjugate FMRP fragment to treat Fragile X Syndrome</i></li></ul>
11:20 – 12:00	<b>Speakers:</b> <b>Dr. Ben Gibbard, MD</b> , Developmental Pediatrician, Associate Professor, Department of Pediatrics, University of Calgary; and <b>Christina Tortorelli, MA, RSW</b> , Assistant Professor Child Studies and Social Work, Health, Community and Education, Mount Royal University; and Associate Director, Calgary Region Children's Services <i>Understanding the Complexity of Adverse Exposures in the Lives of Children and Families</i>
12:00 – 12:45	Lunch break

12:45 – 1:45

**3-minute Trainee Flash Talks**

- **Queenie Li**, Supervisor: Dr. Lianne Tomfohr-Madsen, Dept. of Psychology  
*Associations between neighborhood factors, child sleep, and language development*
- **Kassondra Pedenko**, Supervisor: Dr. Catherine Lebel, Dept. of Radiology  
*The role of the extreme capsule and the uncinat fasciculus in reading and mental health*
- **Rachel Lacroix**, Supervisor: Dr. Deborah Kurrasch, Dept. of Medical Genetics  
*Impaired development of social and locomotor behaviours in zebrafish exposed to glyphosate embryonically*
- **Dion Kelly**, Supervisor: Dr. Adam Kirton, Dept. of Paediatrics  
*Building Blocks: Establishing baselines for pediatric brain-computer interfaces*
- **Kelsey Harkness**, Supervisor: Drs. Kara Murias and Signe Bray, Depts. of Paediatrics/Radiology  
*Exploring the effects of stimulant medication washout on function connectivity in children with autism spectrum disorder (ASD)*
- **Dr. Gillian England-Mason**, Supervisor: Dr. Deborah Dewey, Dept. of Pediatrics  
*Similar names, different results: consistency of the associations between prenatal exposure to phthalates and parent-ratings of behaviour problems in preschool children*
- **Dr. Pardis Pedram**, Supervisor: Dr. Paul D. Arnold, Dept. of Psychiatry  
*A candidate gene study of obsessive-compulsive and internalizing behaviours in childhood OCD*
- **Dr. Cristie Graziottin Noschang**, Supervisor: Dr. Deborah Kurrasch, Dept. of Medical Genetics  
*The effects of environment and sex on epileptogenesis in a mouse model of Dravet syndrome*

1:45 – 2:30

**Speaker: Dr. Deborah Kurrasch, PhD**

Departments of Medical Genetics, Biochemistry and Molecular Biology, UofC  
*Sensing maternal challenges in the developing rodent brain*

2:30 – 3:30

**Keynote Speaker: Dr. Michael Kobor, PhD**

Department of Medical Genetics, Faculty of Medicine, UBC  
*Epigenetic embedding of early life experiences - how environments get "under the skin"*

3:30 – 3:45

Closing Remarks, Dr. Susan Graham, PhD, Director, Owerko Centre

## Three Minute Trainee Flash Talk Presentation Abstracts

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### **Dr. Gillian England-Mason, PhD**

Postdoctoral Fellow, Supervisor: Dr. Deborah Dewey

Authors: Gillian England-Mason, Jonathan W. Martin, Amy MacDonald, David Kinniburgh, Gerald Giesbrecht, Nicole Letourneau, Deborah Dewey

#### ***Similar names, different results: consistency of the associations between prenatal exposure to phthalates and parent-ratings of behaviour problems in preschool children***

Background: Environmental health research has reported mixed findings on the associations between prenatal exposure to phthalates and parent-ratings of child behaviour. The objective of this study was to investigate some potential contributors to these research inconsistencies, by examining whether different standardized measures and analytical approaches impacted the consistency of associations.

Methods: Participants included 351 mother-child pairs from the Alberta Pregnancy Outcomes and Nutrition (APrON) study. Maternal second trimester urine samples were analyzed for phthalates. Mothers completed the Behavior Assessment System for Children- Second Edition (BASC-2) and Child Behavior Checklist (CBCL) when children were 3-4 years old. Adjusted regressions examined associations between phthalate concentrations and child behaviour. To correct for urine dilution, primary analyses included creatinine as a covariate and secondary analyses used creatinine-adjusted phthalate concentrations.

Results: Primary analyses showed that higher prenatal phthalate concentrations were related to increased odds of scores falling into the borderline or clinical range on the Hyperactivity, Aggression, Anxiety, Depression, Withdrawal, Externalizing Problems, Internalizing Problems, and Behavioral Symptoms Index scales on the BASC-2 (ORs from 1.37 to 2.07), but only the Anxious/Depressed and Externalizing Problems scales on the CBCL (ORs from 1.80 to 3.28). Sex-stratified analyses showed that many associations were only significant for male children. Secondary analyses revealed unique associations.

Conclusion: Prenatal phthalate exposure was associated with preschool behavioral development; however, findings differed based on the parent-rating scale and analytical approach used. Future research is needed to better understand why differing methodologies impact the associations between prenatal phthalate concentrations and children, as behavior problems.

### **Kelsey Harkness**

PhD Student, Supervisors: Drs. Kara Murias and Signe Bray

Authors: Kelsey Harkness, Signe Bray, and Kara Murias

#### ***Exploring the effects of stimulant medication washout on function connectivity in children with autism spectrum disorder (ASD)***

Autism Spectrum Disorder (ASD) is characterized by a combination of social communication impairments and restrictive repetitive behaviours that is estimated to affect 1 in 66 children aged 5 to 17 in Canada. Co-occurring disorders are common in children with ASD, such as attention-deficit/hyperactivity disorder (ADHD). ADHD and attention deficits are often treated using long-term stimulant medication, which acts on the brain by increasing the availability of the neurotransmitter dopamine. Within research, a stimulant washout period is often used to simulate a stimulant naive condition. However, there is little evidence to suggest that the changes in functional connectivity (FC), due to stimulant use, are recovered to be similar to a naive condition following a washout period. Therefore, this study will explore the role of stimulant washout on FC in groups with and without ASD.

Participants were obtained from two databases; the adolescent brain and cognitive development (ABCD) database, and the autism brain imaging data exchange (ABIDE). ASD and medication status were obtained from a variety of questionnaires available through these databases. These participants were separated into the following groups: ASD on stimulants, ASD stimulant washout, ASD stimulant naive, non-ASD on stimulants, non-ASD stimulant washout, and non-ASD stimulant naive.

We will explore two questions from the data: 1) whether there are differences in FC between diagnostic groups within each of the stimulant conditions and 2) whether stimulant washout status plays a role in FC variation within diagnostic groups.

## **Dion Kelly**

PhD Student, Supervisor: Dr. Adam Kirton

Authors: Dion Kelly, Ephrem Zewdie, Adam Kirton

### ***Building Blocks: Establishing Baselines for Pediatric Brain-Computer Interfaces***

**Introduction:** Children with severe neurological disabilities may be intellectually normal and cognitively aware. Brain-computer interfaces (BCIs) may restore their ability to communicate and interact with their environment by translating brain signals into commands using electroencephalography (EEG). However, pediatric studies are limited. We have therefore established a clinical BCI program for children with disabilities. In order to gauge competency in pediatric patients, we aimed here to establish the ability of typically developing children to use EEG-based BCI systems.

**Methods:** Twenty-two neurotypical children ages 6-16 (mean age 11.36; 14 female) completed tasks in five different EEG-based BCI paradigms. Performance was assessed by accuracy scores for each paradigm. Potential factors affecting performance were evaluated.

**Results:** Children performed best on the visual P300 paradigm, where highest mean accuracies were achieved at medium frequency visual stimulation of 8 flashes per row/column (94%; 95% CI = 0.87, 1.01), although significant differences in performance were only observed below 4 flashes. Age affected performance on the auditory P300 paradigm ( $r^2 = 0.156$ ,  $p = 0.028$ ), while sex differences were observed in the motor imagery and 2-tactor vibrotactile paradigms ( $p = 0.006$ ). Only two participants were able to achieve accuracy scores greater than threshold (61%) for communication in the motor imagery paradigm (mean = 52.8%; 95% CI = 0.49, 0.56). One participant dropped out following the auditory paradigm, reporting extreme fatigue.

**Conclusion:** Many children can competently operate advanced BCI systems with accuracy scores comparable to established thresholds necessary for control. Performance likely varies by paradigm, algorithm, age and sex.

## **Rachel Lacroix**

Masters Student, Supervisor: Dr. Deborah Kurrasch

Authors: Rachel Lacroix, Deborah Kurrasch

### ***Impaired development of social and locomotor behaviours in zebrafish exposed to glyphosate embryonically***

Chemical exposure during prenatal brain development is thought to contribute to the etiology of neurodevelopmental disorders. Glyphosate is the active ingredient in commercial herbicides such as RoundUp™ and is the most widely used chemical in agriculture. Exposure to glyphosate prenatally is proposed to cause significant changes to developing brains; however, its exact effects have yet to be elucidated. Here, we hypothesize that environmentally relevant concentrations of glyphosate cause neural changes that lead to alterations in behaviours in larval and adult zebrafish. Embryonic zebrafish were exposed to glyphosate (0.001, 0.1 and 10 µg/L) from 10 to 48 hours post-fertilization (hpf), a time point that encompasses neurogenesis. The ZebraBox® recording chamber was used to monitor larval zebrafish (at 5, 7 and 10 days post-fertilization (dpf)), whereas the ZebraCube® was used to track adult (>3 months) behaviours in dark, light and light-dark flash conditions. Social behaviours of shoaling and numbers of contact were also examined. We found that exposure to environmentally relevant concentrations of glyphosate during zebrafish neurogenesis caused hypoactive swimming (2-fold decrease in distance travelled) upon low-dose exposure (0.001 µg/L) in larval zebrafish. We also observed changes in locomotion in zebrafish exposed to glyphosate embryonically when startled by a sudden change in light intensity, as a measure of anxious phenotypes. Startle assay results were recapitulated in adult fish, where zebrafish exposed embryonically to higher dose of glyphosate (10 µg/L) had a ~2-fold increase in locomotion. Our findings suggest that exposure to environmental concentrations of glyphosate during neurodevelopment alters the developing brain, leading to lasting changes in behaviour.

## **Queenie Li**

Undergraduate Student, Supervisors: Dr. Lianne Tomfohr-Madsen & Anna MacKinnon

Authors: Queenie KW Li, Anna L MacKinnon, Susan Graham, Sheri Madigan, Suzanne Tough, Lianne Tomfohr-Madsen

### ***Associations between neighborhood factors, child sleep, and language development***

**Background:** Language ability is strongly related to valued child developmental outcomes including emotional functioning, social wellbeing, and academic achievement. Family-level socioeconomic status (SES) predicts child language ability, with children from disadvantaged homes trailing their affluent peers. It is unclear, however, whether neighborhood-level factors have a similar impact. Further, the mechanisms through which SES operates on language

development are not well understood. The current study investigated the association between neighbourhood factors and child language outcomes, and sleep as a potential mediator in the relationship.

Methodology: Multilevel Modeling (MLM) was conducted with data from the longitudinal All Our Families cohort study. A subsample of 2444 participants who provided postal codes in early pregnancy was included. Neighbourhood SES was determined using the census-based Vancouver Area Neighbourhood Deprivation Index (VANDIX). Neighbourhood disorder was assessed using community crime reports from local police services. Mothers reported their children's sleep duration (at 4 and 12 months postpartum) and language ability (at 5 years).

Results: MLM indicated that greater neighbourhood deprivation and disorder during pregnancy predicted worse child language outcomes at 5 years, even when controlling for family-level factors. Path analyses revealed an indirect effect of neighbourhood disorder through child sleep at 12 months, suggesting that sleep partially explains the relationship between certain neighbourhood factors and child language ability.

Conclusion: Neighbourhood-level factors can have significant effects on developmental outcomes, indicating that that child development should be considered within multiple systems of influence. Additionally, sleep as a mechanistic link between SES and child language ability warrants further study.

### **Melissa Mueller**

PhD Student, Supervisor: Dr. Kelly Schwartz

Authors: Melissa Mueller, Kelly Schwartz

### ***Unwarranted Hysteria of Screen Time Effects in Early Childhood***

Screen time is an ever-present topic in the media with stories using language such as, "dangerous," "overwhelming," and "delays" when discussing implications. Do we actually have research that supports the strong terminology spouted in the media? Since the popularization of the television, scientists have wondered about the impact of television on children's development. Although screen time, operationalized as the amount of time spent across different types of screens (e.g., television, smart phones, computers, etc.; Canadian Paediatric Society, 2017), is a pervasive part of a child's life, reliable estimates on cumulative screen time and its impact on various areas of child development is of critical importance to understand potential utility and risks.

The present study examined the relationship between average daily screen time and child development outcomes (i.e., separation anxiety, hyperactivity/impulsivity, emotional/anxiety disorders, physical aggression). Parental engagement was queried as a moderating variable in the analysis of secondary data from the All Our Families Study (AOF). Results showed that children in the AOF study were engaging in an average of 1.75 hours per day and this was statistically significantly related to all child development outcomes. It is important to note that parental engagement did not moderate any of the relationships and the effect sizes were all considered small. While these results suggest it is still important to limit, model, and monitor children's screen time, the effects are only a very small part of child's development when contextualized in an ecological systems theory and do not warrant the hysteria from media stories.

### **Daphne Nakhid**

PhD Student, Supervisors: Drs. Carly McMorris and Catherine Lebel

Authors: Nakhid D, Sun H, McMorris C.A., and Lebel C.

### ***Brain volume and susceptibility differences in children with prenatal alcohol exposure***

Background: Prenatal alcohol exposure (PAE) can have negative effects on neurodevelopment. The basal ganglia and limbic system play an important role in cognition, behaviour and emotions, and are commonly lower in volume in children with PAE. PAE lowers fetal brain iron, and iron is an essential micronutrient for neurodevelopment. Quantitative susceptibility mapping (QSM) is an MRI technique that measures tissue susceptibility, an indicator of iron. This study aimed to determine if susceptibility is altered in children with PAE.

Methods: Twenty children with PAE and 44 unexposed controls 7.5-15 years completed a QSM and T1-weighted MRI scan. Susceptibility and volume measurements of the caudate, putamen, pallidum, thalamus, amygdala, hippocampus, and nucleus accumbens were extracted using segmentations from Freesurfer. A series of ANCOVAs were conducted to compare volume and susceptibility between groups for each region of interest.

Results: The PAE group exhibited higher susceptibility in the thalamus ( $F=4.795$ ,  $p=0.032$ ) compared to unexposed controls. There was a trend of lower susceptibility in the hippocampus ( $F=3.965$ ,  $p=0.051$ ) in the PAE group compared to unexposed controls. The PAE group exhibited lower volume in the caudate (left:  $F=14.743$ ,  $p<.001$ ; right:  $F=15.789$ ,  $p<.001$ ), pallidum (left:  $F=13.349$ ,  $p<.001$ ; right:  $F=19.252$ ,  $p<.001$ ) and left putamen ( $F=9.024$ ,  $p=.004$ ).



Conclusions: These findings show altered susceptibility in children with PAE suggesting differences in brain iron levels. Altered susceptibility may underlie cognitive and behavioural difficulties that individuals with PAE experience. This study highlights the need to further understand the impact of iron on neurodevelopment in those with and without PAE.

**Dr. Cristie Graziottin Noschang, PhD**

Postdoctoral Fellow, Supervisor: Dr. Deborah Kurrasch

Authors: Cristie Noschang and Deborah Kurrasch

***The effects of environment and sex on epileptogenesis in a mouse model of Dravet syndrome***

Dravet syndrome is one of the more common epileptic encephalopathies that usually appears in the first year of life and is characterized by normal development before seizure onset. Although over 80% of children with Dravet have a disruption in Scn1a gene, environmental factors also contribute to disease onset and progression. Here, we tested the interplay between genetic and environmental factors that might contribute to Dravet disease progression and how sex influences this process. Genetically, we used male and female mice that harbour a mutation in Scn1a. To model an environmental challenge, we used heat since a warm bath or fever can trigger seizures in Dravet children. Three groups were generated for both sexes: control animals without the genetic disruption (e.g., Scn1a+/+); animals with the Scn1a genetic mutation (e.g., Scn1a+/-); animals with genetic disruption and exposed to heat (Scn1a+/- + heat). The electrical activity in the brain was recorded and analyzed for the frequency and amplitude of seizures. We observed sex differences in the number of seizures between these groups, with males showing that both genetic and environmental factor are necessary to trigger disease progression ( $p < 0.01$ ), while in females the genetic component alone was sufficient ( $p < 0.05$ ). Having a better understanding of the Gene x Environment x Sex interaction will contribute to identify health measures that might serve to prevent the disease progression in children with Dravet syndrome.

**Heidi O'Brien**

Masters Student, Supervisor: Dr. Carly McMorris

Authors: Heidi O'Brien, Jonathan Weiss, Connor Kerns, and Carly McMorris

***Families Facing COVID: The association between perceived vulnerability for contracting COVID-19 and caregiver mental health of autistic individuals***

Background: Individuals with neurodevelopmental conditions, including autism, are disproportionately impacted by COVID-19. Caregivers of children with autism report high levels of stress and anxiety, and unfortunately COVID-19 can exacerbate these.

Objectives: To fill this gap, the present study aimed to 1) identify caregivers reports of vulnerability to contract COVID-19, and 2) determine how perceived vulnerability is related to their mental health.

Method: 635 caregivers of autistic individuals across Canada participated, completing an online questionnaire between June and July 2020. Caregiver stress, anxiety and resiliency were measured using the Perceived Stress Scale (PSS), State Trait Anxiety Inventory (STAI) and Brief Resilient Coping Scale (BRCS), respectively. Caregivers were classified into two groups by report of vulnerability, to determine group differences on presented measures, using a T-Test.

Results: Caregivers were primarily female (60%) and married or common law (89%). Over half of respondents reported moderate levels of stress (84%), and high anxiety (68%), and just under half (49%) reported low resilient coping. Just under half of caregivers reported themselves being high risk or vulnerable to contracting COVID-19, and 41% reported their child as such. Group differences yield statistically significant results for parent and child vulnerability groups on anxiety ( $< .01$ ), ( $< .05$ ) and resilient coping ( $< .01$ ), ( $< .001$ ), respectively.

Conclusions: As expected, caregivers of autistic children are currently experiencing increased levels of burden. Perceived vulnerability groups report differing levels of anxiety and resilient coping, with no differing stress. Future research must focus on supporting caregivers of children with autism, especially as COVID-19 may exacerbate negative outcomes.

**Paolo Pador**

Undergraduate Student, Supervisor: Dr. Sheri Madigan

Authors: Paolo Pador, Nicole Racine, Jessica Cooke, Brae Ann MacArthur, Rachel Eirich, Jenney Zhu, Sheri Madigan

***A meta-analysis on the global prevalence of depressive and anxiety symptoms in youth during COVID-19***

Background: The global prevalence of youth mental illness symptoms has increased during the COVID-19 pandemic.

However, substantial variability currently exists regarding the prevalence rates of clinically significant depressive and anxiety symptoms.

**Objective:** The current meta-analysis aims to synthesize the current literature and provide more accurate estimates of the global prevalence of child and adolescent clinically significant depression and anxiety symptoms during COVID-19 and compare these rates to the estimates before the pandemic. The current study will also examine potential moderators that may explain the variation in rates across studies.

**Methods:** Databases were searched from January 1st, 2020 to February 16th, 2021. Studies were included if they were published in English; had quantitative data; and reported prevalence of clinically significant depression or anxiety in youth (<18 years). 3,100 non-duplicate titles/abstracts were retrieved, and 139 full-text articles were reviewed. Analysis was conducted March 8-22, 2021.

**Results:** 29 studies with 79,181 participants were included in random-effect meta-analyses. Pooled prevalence estimates of clinically significant depression (23.8%, 95%CI: 19.9, 28.1) and anxiety (19.0%, 95% CI: 15.5, 23.0) symptoms was found to have increased from pre-pandemic estimates. The rates were found to be higher in studies collected later in the pandemic and in girls.

**Conclusion:** During COVID-19, 1 in 4 and 1 in 5 youth are experiencing clinically significant depression and anxiety symptoms, respectively. The current prevalence doubles pre-pandemic estimates and appear to be increasing over time. Resources should be allocated to mental health care to reduce the incoming burden of COVID-19 related youth mental illness.

#### **Kassondra Pedenko**

Masters Student, Supervisor: Dr. Catherine Lebel

Authors: Kassondra Pedenko, Bryce Geeraert, Catherine Lebel

#### ***The role of the extreme capsule and the uncinate fasciculus in reading and mental health***

**Introduction:** Children with reading problems are at elevated risk for mental health problems. The neurological basis for this remains unclear. The extreme capsule (EmC) and uncinate fasciculus (UF) are implicated in both reading and mental health and are thus potential biomarkers for comorbid reading disorder and mental health.

**Methods:** 52 typically developing children (6-18y;10.30–±2.35y,27M/25F) underwent diffusion imaging. Some participants returned 2 and/or 4 years later, providing a total of 95 scans. The EmC and UF were segmented, and fractional anisotropy (FA) and mean diffusivity (MD) were calculated for each subject. Internalizing behaviours were assessed using the Behavioural Assessment System for Children (BASC-2) Parent Report. Reading comprehension and fluency were assessed using the Wechsler Individual Achievement Test (WIAT-3). Mixed effects models were used to test relationships between FA and MD in the EmC and UF with WIAT-3 and BASC-2 scores, including age and gender as covariates.

**Results:** Composite reading scores had a weak MD-gender interaction ( $P=0.054$ ) in the left EmC; in girls, higher MD was associated with higher WIAT-3 scores. MD in the right UF was weakly negatively associated with BASC-2 scores ( $P=0.064$ ). Age was significantly positively associated with FA in the left EmC ( $P=0.007$ ) and negatively associated with MD in the bilateral EmC ( $p<0.001$ ) and left UF ( $P=0.007$ ).

**Conclusion:** Trending relationships between MD and internalizing behaviour (right UF), and MD and gender-differentiated associations with reading (left EmC) suggest possible relationships, but larger samples are needed to verify this. Age-related changes in the bilateral EmC were identified for the first time.

#### **Dr. Pardis Pedram, PhD**

Postdoctoral Fellow, Supervisor: Dr. Paul D. Arnold

Authors: Pardis Pedram, SM Shaheen, Gregory L. Hanna, William Gehring, David Rosenberg, Yekeen Abu-Shiraz, Paul D. Arnold

#### ***A Candidate Gene Study of Obsessive-compulsive and Internalizing Behaviours in Childhood OCD***

Obsessive-Compulsive Behaviors (OCB) and Withdrawn-Depressed Behavior (WDB) are core features not only of obsessive-compulsive disorder (OCD) but also of other disorders such as autism, anorexia nervosa, anxiety and depression. These disorders were shown to share genetic risk in recent cross-disorder genomic studies. As part of a larger genetic study, we selected two single-nucleotide polymorphisms (SNPs) for association testing based on previous literature: Serotonin-2A-receptor (HTR2A-rs6314) and Alpha-2-adrenoceptor (ADRA2A-rs1800544) with OCB and also



WDB, two quantitative traits measured by the Child-Behavior-Checklist (CBCL), in a sample of children with psychiatric disorders (enriched for OCD) and controls.

At the outpatient clinic of the University of Michigan, 480 individuals (age=14.3±3.3 years) were recruited. Saliva DNA was extracted and genotyped using TaqMan® assays. OCB and WDB were assessed using the CBCL. Based on CBCL-OCB and CBCL-WDB scores, individuals were divided into three groups: Control (score=0), Low-Symptoms (score range:1-4) and High-Symptoms (scores ≥5).

Regression analysis adjusting for sex and age showed that allele G in ADRA2A-rs1800544 significantly increased the risk of having higher CBCL-OCB symptom level ( $p=0.03$ , OR=5.5, 95% CI=1.1 to 25.7). When individuals were classified as symptomatic and without-symptoms (based on obsessions, compulsions, lifetime-history of OCD and DSM5-OCD diagnosis) the risk of being symptomatic was not increased by these two SNPs.

In conclusion, this study provides evidence that ADRA2A may be associated with obsessive-compulsive behaviors. Sample recruitment in the current study is growing actively and will be used to validate the current findings in a larger population. Additionally, a genome-wide association study will be conducted on these traits.

#### **Dr. Mezbah Uddin, PhD**

Postdoctoral Fellow, Supervisor: Dr. Timothy Shutt

Authors: Golam Mezbah Uddin; Rasha Sabouny; Govinda Sharma; Iman Al Khatib; Timothy Shutt

#### ***Possible mechanism how ketone bodies may improve mitochondrial function in autism spectrum disorder***

While evidence suggests that mitochondrial dysfunction contributes to Autism Spectrum Disorder (ASD), the mechanism is poorly understood. Our previous work showed that the ketogenic diet (KD) improves mitochondrial function and ASD behaviours in mouse. Our current work investigates how the KD improves mitochondrial function, in particular mitochondrial dynamic changes, which is determined by fission and fusion events. Importantly, as fragmented mitochondria are often linked to mitochondrial dysfunction, targeting mitochondrial fission and fusion is gaining traction as a therapeutic approach for a growing list of neurological disorders.  $\beta$ -hydroxybutyrate (BHB) is a key metabolite proposed to mediate the beneficial effects of the KD. Notably, the use of BHB as an energy source is proposed to elevate nicotinamide adenine dinucleotide (NAD<sup>+</sup>), which may begin to explain some of the benefits of the KD. NAD<sup>+</sup> is an important metabolic cofactor that activates the sirtuin enzymes (SIRT6). Critically, previous work shows that SIRT6 deacetylate and activate mitochondrial fusion proteins. Thus, our goal is to investigate if BHB increases NAD<sup>+</sup> to promote mitochondrial fusion.

We show that supplementation with BHB significantly increases the NAD<sup>+</sup> pool and leads to mitochondrial elongation in cultured cells. Furthermore, the SIRT6 inhibitor sirtinol prevents the mitochondrial elongation induced by BHB, while the SIRT6 activator SIRT6 alone is sufficient to promote mitochondrial elongation. Thus, SIRT6 play a key role in mediating BHB-mediated mitochondrial elongation.

We conclude, that the KD improves mitochondrial function by boosting NAD<sup>+</sup> and activating SIRT6, revealing a novel mechanism to improve mitochondrial function that may be applicable to ASD.

#### **Dr. Elnaz Vaghef Mehrabani, PhD**

Postdoctoral Fellow, Supervisor: Dr. Gerald Giesbrecht

Authors: Elnaz Vaghef Mehrabani, Megan Jarman, Rhonda C. Bell, Catherine J. Field, Gerald F. Giesbrecht

#### ***Pre-pregnancy obesity and childhood internalizing problems: Mediating role of prenatal systemic inflammation and moderating role of pre-pregnancy diet***

Background: Childhood internalizing problems are a growing health issue in Canada. Maternal pre-pregnancy obesity (p-OB) and excessive gestational weight gain (EGWG) might predispose children to internalizing problems by increasing prenatal systemic inflammation. Pre-pregnancy anti-inflammatory diet could prevent these effects. We aim to investigate whether prenatal systemic inflammation mediates the association between maternal p-OB/EGWG and internalizing problems at ages 3, 5, and 8 years, and if a healthy pre-pregnancy diet can moderate this association.

Methods: We will use data from the Alberta Pregnancy Outcomes and Nutrition (APrON) study ( $n=2200$ ). We will use pre-pregnancy dietary data (food frequency questionnaire; FFQ) to calculate Mediterranean diet score (MDS; a proxy of an anti-inflammatory diet) and dietary inflammatory index (DII; an index of the inflammatory potential of diet); prenatal

systemic inflammation (C reactive protein; CRP), and childhood internalizing problems (Child behavior checklist; CBCL) data at 3, 5, and 8 years. We will test mediator/moderator models in MPlus.

Results: We expect to find an association between prenatal body mass index (BMI) and gestational weight gain (GWG), and childhood CBCL total/sub- scores. Mediator/moderator analyzes might also show that higher prenatal CRP connects prenatal BMI and GWG to childhood CBCL total/sub- scores, and that higher MDS and lower DII scores pre-pregnancy can buffer these associations.

Conclusions: If we find a moderating role for the pre-pregnancy diet and a mediating role for the prenatal inflammation in the association between p-OB/EGWG and childhood internalizing problems, designing dietary interventions to manage maternal weight and systemic inflammation will gain more importance.

#### **Bailin Xie**

PhD Student, Supervisor: Dr. Lianne Tomfohr-Madsen

Authors: Elisabeth Bailin Xie, Charlie Rioux, Joshua W. Madsen, Catherine Lebel, Gerald F. Giesbrecht, Lianne Tomfohr-Madsen

#### ***Relationship Quality Predicts Mental Health in the Pregnancy During the COVID-19 Pandemic Cohort***

Objective: The current study aimed to explore the longitudinal association between relationship satisfaction and depression and anxiety among pregnant individuals during the COVID-19 pandemic.

Background: Mental health problems are concerning high among pregnant women during the COVID-19 pandemic, which poses long-term risks for maternal and child well-being. Relationship quality is robustly linked to psychopathology and protects against mental health problems during pregnancy. During the COVID-19 pandemic, couples are spending more time together and may experience increased stressors, highlighting the importance of investigating the association between relationship satisfaction and mental health problems.

Method: Pregnant mothers (n = 1842) were surveyed monthly (April-July 2020) after the onset of the COVID-19 pandemic. Depression and anxiety symptoms, and relationship satisfaction were self-reported. Cross-lagged panel models were conducted to examine bidirectional associations between relationship satisfaction and mental health symptoms over time.

Results: Relationship satisfaction was significantly correlated with depression and anxiety at all time points.

Longitudinally, relationship satisfaction predicted later depression and anxiety symptoms, but depressive and anxiety symptoms did not predict later relationship satisfaction. Specifically, lower relationship satisfaction in April 2020 predicted higher depressive and anxiety symptoms in May 2020. Lower relationship satisfaction in May 2020 also predicted higher depressive and anxiety symptoms in June 2020.

Conclusion: This study suggests that poor relationship satisfaction is linked to subsequent elevations in prenatal depressive and anxiety symptoms during the COVID-19 pandemic. Relationship enhancement interventions during pregnancy may be a means of improving the mental health of pregnant mothers during times of prolonged psychological distress.

#### **Dr. Xiaoqin Zhan**

Research Associate, Supervisor: Dr. Ray Turner

Authors: Zhan X, Douglas P, Schriemer D, Morrissey S, Turner RW

#### ***The use of a tat-conjugate FMRP fragment to treat Fragile X Syndrome***

Introduction: Fragile X Syndrome is a neurodevelopmental disorder that is closely related to Autism Spectrum Disorder. In patients, the FMRP protein is missing, a key protein that is expressed in almost all types of neurons and binds to mRNAs to regulate protein translation through its active domains. We hypothesize that by reintroducing the active domain of FMRP protein into FMRP KO mice, the dysregulated protein expressions can be corrected.

Method: We constructed an FMRP-N-tat protein by tagging the tat sequence to the N terminus domain of FMRP protein. With or without injection of the FMRP-N-tat, we then studied the protein expression profile of adult wild type and FMRP KO mice in frontal cortex and cerebellum with TMT labelling followed by mass spectrometry.

Result: 181 out of a total 5825 proteins identified showed significant up or down regulation by more than 50% in the adult FMRP KO compared to WT mice. Among them, 23% proteins were corrected to the normal level. In cerebellum, 38% proteins were significantly restored. These restored proteins are closely related to the core functions disrupted in the Fragile X Syndrome or Autism Spectrum Disorder, such as synapse maturation, protein metabolism and hyperactivity.

Conclusion: The high-throughput method confirmed that a single treatment of FMRP-N-tat restores a subset of protein level in both frontal cortex and cerebellum, even at adult age. This FMRP-N-tat could be a potential therapeutic treatment for Fragile X Syndrome patients and restore at least partial disrupted functions in adult patients.

## Non-presenting Trainee Abstracts Submitted

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### **Alida Anderson**

Undergraduate Student, Supervisor: Dr. Deborah Dewey

Authors: Alida Anderson, Rhonda Bell, Nicole Letourneau, Deborah Dewey, Bonnie J. Kaplan, David W. Johnston, Gerald F. Giesbrecht, Nalini Singhal, Maeve OíBeirne, Lisa Gagnon, Catherine Field, Anna Farmer, Laki Goonewardene, Linda McCargar, Francois Bernier, Marja Cantell, Linda Misha Eliasziw, Libbe Kooistra, Donna Manca, Jonathan Martin, Victor Pop, and Catherine Lebel.

#### ***The association of pre-pregnancy BMI, gestational weight gain, and cognitive outcomes of offspring at 3-4 years of age***

Background Previous studies have found a negative association between pre-pregnancy obesity and child cognition at various ages. Additionally, a possible link between gestational weight gain (GWG) and child cognitive outcomes has been proposed. The association between pre-pregnancy BMI, GWG and child cognition may be more complicated, as GWG may be a possible moderator in this relationship. This study aimed to understand the relationship between pre-pregnancy BMI, GWG, child intelligence and executive function as well as the combined effect of pre-pregnancy BMI and GWG on these cognitive outcomes at age 3-4.

Methods Using the APrON data, 379 mother-child pairs with information available for maternal pre-pregnancy BMI, GWG, and child outcomes of intelligence and executive function were included. Multivariable regression analyses were used to test the association between pre-pregnancy BMI, GWG, and child outcomes.

Results: Pre-pregnancy BMI was found to be a significant predictor of child intelligence and executive function, but found no such association between GWG and child outcomes were found. When the model was adjusted for interactions between pre-pregnancy BMI and GWG, pre-pregnancy BMI was no longer significantly associated with child intelligence and overall executive function, although no significant interaction between pre-pregnancy BMI and GWG was found. There was a significant interaction between pre-pregnancy BMI and GWG classification and certain subscales of the outcome measures indicating that GWG may moderate different aspects of child intelligence and executive functioning.

Conclusion: Findings from this study underpin the complex relationship between pre-pregnancy BMI, GWG and child intelligence and executive function.

### **Lilit Antonyan**

PhD Student, Supervisor: Dr. Paul Arnold

Authors: Lilit Antonyan, S-M Shaheen, David R. Rosenberg, Gregory L. Hanna, Paul D. Arnold

#### ***Genetic Variants and Imaging Endophenotypes of Obsessive-Compulsive Behaviors***

Background: Obsessive-compulsive disorder(OCD) is a common mental health disorder that involves persistent intrusive thoughts and/or repetitive behaviors[DSM-5,2013]. We focus on OC behaviors(OCB) measured via the Child-Behavior Checklist OC-Subscale(CBCL-OCS) which is highly heritable in pediatric twin studies[Hudziak,2004]. The involvement of the cortico-striato-thalamo-cortical model in pathophysiology of OCB has been shown[Pauls,2014]. The goal is to identify genetic variants associated with OCB and imaging endophenotypes and determine the relationship between brain activity and childhood OCB.

Methods: Genotyping analysis was performed on non-related pediatric subjects. Four different genome-wide arrays were used. Quality control(QC) and genome-wide association study(GWAS) was carried out using the PLINK software[Purcell,2007]. CBCL-OCS total score (0-16) was considered as a quantitative trait. Further, imaging analysis was conducted to identify putative neuroimaging endophenotypes, including cortical thickness(3-dimensional T1- and T2-weighted structural scans), and regional task-related hyperactivity(functional MRI).

Results: After QC, 627 samples with corresponding CBCL-OCS scores, and ~2million single nucleotide variants(SNV) passed the QC filters. Although none of the genetic variants passed the p-value threshold for genome-wide

significance( $p < 5 \times 10^{-8}$ ), a number of markers were observed to be close to significance. The top ranked loci associated with CBCL-OCS scores as quantitative traits were identified. Imaging analyses are in progress.

Conclusion: Quantitative GWAS was performed. The sample size, low for GWAS, is likely the main reason of the markers not passing stringent p-value significance threshold and genotyping more participants will address this. This is a unique study that will be the largest to date to report genetic markers, and imaging endophenotypes of OCB susceptibility in pediatric-clinic-based population.

#### **Richard Besney**

Masters Student, Supervisor: Dr. Carly McMorris

Authors: Richard Besney, Kari Duerksen, Megan Ames, Carly McMorris

#### ***A Systematic Review of Peer Mentorship Programs for Autistic Adults in Post-Secondary Settings***

Background: There is an increasing number of autistic individuals attending postsecondary; however, graduation rates remain low, with 39% of autistic students matriculating within 8 years of study, versus 60% of the total student populace within 6 years. This is despite autistic students having strengths which lend themselves to success in academia. The failure of post-secondary institutions to support the individual needs of these students is thought to be one contributing factor. A promising approach is the emergence of peer mentorship programs designed to provide individualized, one-on-one support for autistic students.

Methods: A systematic review was conducted that described existing peer mentorship programs for autistic students in post-secondary education, as well as their effectiveness. Nine unique programs that were evaluated in 11 peer-reviewed articles were revealed.

Results: Most programs involved both individual peer mentor meetings and group meetings. Positive outcomes, some of which included social skills, academic performance, and a sense of belonging were reported. The importance of the peer-mentor relationship was also a common theme. Program evidence was mostly qualitative, small in sample size, and there was considerable heterogeneity in the design, delivery, and goals of these programs, as well as the evaluation methodology used.

Conclusions: Peer mentorship programs are a promising means of addressing the needs gap of autistic students, with a variety of positive and diverse outcomes reported. Making statements about the overall effectiveness of peer mentorship programs is challenging due to heterogeneous program design and goals. Further research is needed to quantify program effectiveness and conduct program comparisons.

#### **Makayla Freeman**

Undergraduate Student, Supervisor: Dr. Lianne Tomfohr-Madsen

Authors: MacKinnon A. L., Freeman M, Tomfohr-Madsen L, & Tough S.

#### ***Maternal Adverse Childhood Experiences and Risk of Child Atopic Diseases at 5-Years Old: A Longitudinal Follow-Up Study***

Background: Adverse childhood experiences (ACEs) are linked to negative health outcomes and intergenerational transmission of risk to child health outcomes. Previous findings from the All Our Families (AOF) prospective cohort study showed a relationship between mothers' history of childhood abuse and subsequent reports of asthma and allergy among their children at two years old. Asthma is the most common noncommunicable disease in Canadian children and atopic disease presents a significant health concern that impacts quality of life and increases risk for the development of other chronic diseases.

Objectives: The current follow-up study investigated the relationship between maternal history of ACEs and child atopic disease, including asthma, allergy, and atopic dermatitis (eczema), assessed when children were five years old. The role of maternal history of atopy as well as symptoms of anxiety and depression during pregnancy were investigated as potential mediators.

Methods: Archival analyses of AOF maternal report data ( $n=3387$ ) was conducted using logistic regression and counterfactually based indirect effects in Mplus.

Results: Maternal history of ACEs were associated with increased risk of child allergy at five years in adjusted and unadjusted models. Exploratory analyses showed a significant indirect effect of ACEs through maternal history of atopy on child asthma, allergy, and eczema at five years. There were no significant indirect effects through maternal symptoms of depression and anxiety.

Conclusions: Maternal history of ACEs, combined with maternal history of atopy, may elevate the risk of child atopy. This presents an opportunity for early intervention for children at risk of developing atopic disease.

**Preeti Kar**

PhD Student, Supervisor: Dr. Catherine Lebel

Authors: Preeti Kar, Jess E. Reynolds, Melody N. Grohs, W. Ben Gibbard, Carly McMorris, Christina Tortorelli, Catherine Lebel

***Longitudinal white matter development in young children with prenatal alcohol exposure***

Introduction: Prenatal alcohol exposure (PAE) is associated with widespread neurological alterations.

Previous cross-sectional PAE research has shown discrepant findings related to white matter connectivity in young children compared to older children which may indicate altered trajectories of development. This study investigated white matter development in young children with PAE.

Methods: 54 children with PAE (27M) and 90 unexposed children (45M) underwent diffusion tensor imaging between 2-7 years to acquire 122 PAE and 202 control datasets. Image processing and tractography was completed to delineate 10 white matter tracts. For the whole brain and each tract, fractional anisotropy (FA) and mean diffusivity (MD) were calculated to measure myelination/axon diameter/density. Linear mixed effects model included age, sex, group and a group-age interaction.

Results: For FA, significant main effects of group showed higher FA in the corpus callosum and lower FA in the fornix for the PAE group, compared to controls. For MD, significant main effects of group and group-age interactions were present in the corpus callosum, inferior fronto-occipital fasciculus, inferior longitudinal fasciculus, and uncinate fasciculus, where children with PAE had slower decreases of MD across ages compared to controls.

Discussion: Findings show altered white matter development trajectories in young children with PAE, who underwent less change over time than controls. This trajectory connects previous cross-sectional findings in younger and older children with PAE, suggesting reduced brain plasticity in these tracts. This aligns with previous work showing altered trajectories in similar tracts which may underlie cognitive and behavioral impairments associated with PAE.

**Madison Long**

PhD Student, Supervisor: Dr. Catherine Lebel

Authors: Long M, Reynolds J, Zheng J, Huo Y, Landmen B, Ramadass K, Lebel C.

***Sex differences in gray matter volume development: an analysis of 116 regional trajectories***

Introduction: Sex differences in brain structure are well-documented in older children and adolescents, suggesting greater proportional gray matter volume in girls. However, developmental sex differences in gray matter volume are unclear in early childhood, a time of substantial brain change. Here, we characterized sex effects in development of cortical and subcortical gray matter volume in young children.

Methods: We used T1-weighted MRI to analyze 116 gray matter volumes in a longitudinal sample of 130 neurotypical children aged 2-8 years (437 scans, mean=3.4 scans/subject). Images were acquired on a 3T GE MR750w scanner at the Alberta Children's Hospital. We tested different developmental trajectories (ie. linear, quadratic, or cubic) for each of 116 brain regions with sex main effects and interactions.

Results: 51% of regions followed a quadratic pattern, 31% linear, 2.5% cubic, and 15.5% showed no significant change with age. Most regional trajectories (53.5%) showed a main effect of sex with boys having larger volumes than girls. However, when regions were normalized by intracranial volume, girls had larger subcortical volumes than boys. In models with significant sex by age interactions, absolute trajectories tended to be steeper for boys (6/8 regions) while normalized trajectories were more dynamic for girls (4/7 regions).

Significance: Most gray matter regions showed quadratic trajectories during early childhood. Boys had larger absolute cortical volumes, subcortical regions were proportionally larger in girls, and developmental sex differences varied by region. Sex differences in brain development may explain differential susceptibility of girls and boys to developmental and mental health disorders.

**Dr. Anna MacKinnon, PhD**

Postdoctoral Fellow, Supervisor: Dr. Lianne Tomfohr-Madsen

Authors: Anna L. MacKinnon, Katherine Silang, Kailey Penner, Maureen Zalewski Regnier, Lianne Tomfohr-Madsen, Leslie E. Roos

## ***Promoting Mental Health in Parents of Young Children using eHealth Interventions: A Systematic Review and Meta-Analysis***

Background: eHealth interventions offer an accessible option for parents struggling with stress and mental health problems, and are urgently needed given the increased barriers to in-person services during the COVID-19 pandemic. This study aimed to systematically review and meta-analyze the effect of eHealth interventions on parent stress and mental health outcomes, and identify family- and program-level factors that may moderate treatment effects.

Methods: A comprehensive search of PsycINFO, Medline, CINAHL, Cochrane and Embase databases was conducted from inception to July 2020. English-language controlled and open trials were included if they reported: (a) administration of an eHealth intervention, and (b) stress or mental health outcomes such as self-report or clinical diagnosis of anxiety and depression, among (c) parents of children who were aged 1-5 years old. Risk of bias was assessed using the NIH Study Quality Assessment Tools. Random-effects meta-analyses of standardized mean differences were conducted and meta-regressions tested potential moderators.

Results: 38 studies were included (N = 4,360 participants), from 13 countries (47.4% USA). Meta-analyses indicated eHealth interventions were associated with better self-reported mental health among parents (overall standardized mean difference = .368, 95% CI: .228, .509), regardless of study design (k = 30 controlled, k = 8 pre-post) and across most outcomes (k = 17 anxiety, k = 19 depression, k = 12 parenting stress), with small to medium effect sizes. No significant family- or program-level moderators emerged.

Discussion: Despite the different types and targets, eHealth interventions offer a promising and accessible option to promote mental health among parents of young children.

### **Shefali Rai**

Masters Student, Supervisor: Dr. Signe Bray

Authors: Shefali Rai, Kirk Graff, Dr. Signe Bray

## ***Precise patterns of reliability in functional brain networks***

Introduction: Functional MRI (fMRI) provides insight on the organization of the human brain. Using fMRI we can study functional connectivity (FC), described as the correlation of neural activity between two separate brain regions(1). To advance research and associate FC to behavioural traits, we first need reliable estimates of FC(2,3). The aim of this study is to characterize relationships between anatomical and network variation in signal properties (mainly temporal signal-to-noise ratio) and how this relates to FC reliability.

Methods: This study used the Midnight Scan Club dataset, for which resting-state fMRI data were collected from 10 individuals for a total of 300 minutes per participant(4). Data was processed using an in-house custom pipeline, Freesurfer, Ciftify, and Infomap. Ultimately, FC reliability was compared with tSNR on a network-wise group averaged level.

Results: Similar to previous work(3,5), we found that frontal (FPN) and default mode networks (DMN) have the highest reliability, while the somatomotor and limbic networks displayed lower reliability. Interestingly, tSNR had a non-linear relationship with reliability. Below  $r=0.8$ , reliability increases with tSNR; however, above  $r=0.8$ , reliability has a small negative relationship with tSNR ( $\beta=-1.15 \times 10^{-4}$ ;  $p<0.001$ ). The limbic network exhibited both low tSNR and low reliability, whereas the DMN and FPN networks had the highest reliability, yet moderate tSNR.

Conclusions: Using data from densely sampled individuals, we showed a non-linear relationship between reliability and tSNR. A fulsome understanding of how and why FC reliability varies across the brain can support the progression of developmental and behavioural fMRI studies.

### **Katherine Silang**

Masters Student, Supervisor: Dr. Lianne Tomfohr-Madsen

Authors: Katherine Silang, Pooja R. Sohal, Katherine Bright, Jennifer Leason, Leslie Roos, Catherine Lebel, Gerald Giesbrecht, Lianne M. Tomfohr-Madsen

## ***eHealth Interventions for Treatment of Depression, Anxiety and Insomnia during Pregnancy: A Systematic Review and Meta-Analysis***

Background: Pregnancy is associated with an increased risk for developing depression, anxiety and insomnia. eHealth interventions provide a promising treatment option to individuals who may prefer a more accessible alternative to face-to-face interventions. The objective of this systematic review and meta-analysis was to determine the effectiveness

of eHealth interventions to prevent and treat depression, anxiety and insomnia during pregnancy. Secondary aims of the study were to identify demographic and intervention moderators of effectiveness.

Methods: Five databases (PsycINFO, Medline, CINAHL, Embase, Cochrane) were searched from inception to May 2020. Terms related to eHealth, pregnancy, randomized controlled trials, depression, anxiety, and insomnia were included. RCTs were included if they reported (a) an eHealth intervention for (b) the prevention or treatment of depression, anxiety or insomnia (c) in pregnant women or partners. Study screening, data extraction and quality assessment were conducted independently by two reviewers. Random effects meta-analyses of intervention outcome pooled effect sizes were conducted to determine the effect of eHealth interventions on prenatal mental health. Meta-regression analyses were conducted to identify potential moderators.

Results: The results indicated that during pregnancy, eHealth interventions showed small to moderate effect sizes for preventing and treating anxiety and depression and a large effect size for treating insomnia symptoms. No significant moderators were detected.

Conclusion: eHealth interventions are an effective mean of treating anxiety, depression and insomnia during pregnancy. However, further research and intervention development is necessary to increase the clinical significance of the effects.

### **Joyce Singh**

Undergraduate Student, Supervisor: Dr. Kathleen Chaput

Authors: Singh J, Scime NV, Chaput KH

### ***Exploring the association between Caesarean delivery and breastfeeding difficulties in a prospective cohort: The Happy Baby Study***

Background. The World Health Organization recommends that women breastfeed their infants exclusively from birth to six months and non-exclusively up to two years. Caesarean delivery is associated with earlier breastfeeding cessation compared to vaginal delivery, but differences in breastfeeding difficulties by mode of delivery have not been examined. Our objective was to explore the relationship between Caesarean delivery and types of breastfeeding difficulties experienced by mothers of full-term infants.

Methods: We used cross-sectional data from the Happy Baby Study, a prospective cohort study of adult women in Calgary, Alberta who delivered healthy, singleton infants (N=418). Women completed self-report questionnaires during delivery hospitalization. Mode of delivery was defined as vaginal or Caesarean birth. Breastfeeding difficulties were measured using the Breastfeeding Experiences Scale, and operationalized with binary variables for presence of various types of maternal (i.e., physical, supply, social) and infant (i.e., latch, temperament) difficulties. We used logistic regression modelling to estimate adjusted odds ratios (AORs) and 95% confidence intervals (CIs), controlling for potential confounders.

Results: The majority of women had postsecondary education, high-income, and were White, Canadian-born, and married/common law. Overall, 37.1% had a Caesarean delivery and 58.4% experienced a breastfeeding difficulty. Of the difficulties studied, Caesarean delivery was significantly associated with low milk supply (AOR=1.76, 95% CI=1.18-2.64) and infant temperament difficulties (AOR=1.36, 95% CI=1.04-1.79).

Conclusion: Mothers who delivered by Caesarean have higher odds of experiencing low milk supply and infant temperament difficulties than women who delivered vaginally. Additional research on whether difficulties persist after hospital discharge and influence later breastfeeding outcomes is warranted.