42nd Annual Harvey Stancer Research Day
Thursday, June 16, 2016
Chestnut Conference Centre
Harvey Stancer Research Day Programme Committee 2016

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We are very appreciative of the Department of Psychiatry faculty members who contributed their time and expertise to the review and adjudication of the awards, and our sincere thanks to **Ms. Jennifer Wang** for this programme cover design.
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Dear Faculty and Students:

On behalf of the planning committee for Harvey Stancer Research Day for the Department of Psychiatry at the University of Toronto, I am delighted to welcome you to our 42nd Annual Harvey Stancer Research Day. The theme of this year’s Research Day is “Innovations in Mental Health Research and Health Care Delivery”. This theme emphasizes the importance of stimulating inquiry where new knowledge at the individual patient, provider and health system level can improve prevention and treatment of psychiatric illness, and enhance mental health and well-being.

It is a great honour to welcome Dr. Jürgen Unützer who will deliver the Trevor Young Lecture in Psychiatry Research entitled: “Achieving the Triple Aim: Can Collaborative Care Help Us Improve the Patient Experience, Improve Health Outcomes and Reduce Cost?”. Dr. Unützer is Professor and Chair of the Department of Psychiatry and Behavioural Sciences at the University of Washington in Seattle, Washington. He is an international expert in Psychiatry and Health Services Research, with expertise in designing, evaluating and implementing innovative models of mental health care, including a specific focus on the intersection between medical and behavioural health. He has over 200 scientific publications in this area, has received numerous awards and honours, and is the Director of the Advancing Integrated Mental Health Solutions (AIMS) Center that provides coaching and implementation support to help bring high quality mental health care to a broad range of settings.

Our Research Day will begin with the 2nd Annual Mentorship Breakfast, where our trainees have the opportunity to connect with seasoned researcher scientists in the Department. Over 30 trainees – graduate students, psychiatry residents and postdoctoral fellows – have signed up for the breakfast, and I wish to thank our faculty members who volunteered to make time to attend and act as mentors on this day. After the breakfast, we have a day packed with science that includes the Keynote Address by Dr. Unützer, 4 Plenary Presentations from Department Members who published high-impact manuscripts in 2015, and Poster and Oral Presentations. The submissions were of very high quality, and I look forward to hearing the presentations and viewing the posters. We will end our day with a Reception where the winners of the Graduate Student, Resident, Fellow and Early Career Investigator Awards will be announced, along with the winner of the Best Poster Presentation.

Our Plenary presentations comprise four papers selected as the top manuscripts published in the Department of Psychiatry in the past year. The selected manuscripts serve to demonstrate the breadth, depth and impact of the research being conducted in our department. Dr. Anne Wheeler will present the results of her innovative work that demonstrated the ability to use functional neuroimaging to identify neural signatures specific to Schizophrenia subtypes, bringing the field a step closer toward targeted treatments for this condition (published in JAMA Psychiatry). Dr. Tarek Rajji will present findings from an elegant study demonstrating the relationship between clozapine and its metabolite concentrations on cognitive function that will inform targeted treatment approaches to optimize cognition in the treatment of Schizophrenia (published in the American Journal of Psychiatry). Mr. Aaron Howe conducted a large meta-analysis of candidate genes in the search for etiological explanations of panic disorder, a common condition associated with significant distress and impairment for those affected (published in Molecular Psychiatry). Finally, our own Department Chair, Dr. Benoit Mulsant will present the findings of a large international multi-site randomized controlled trial demonstrating the efficacy and favorable risk-benefit ratio of aripiprazole augmentation in older adults with depression who do not respond to first-line treatment, a key study that fills a major gap in the evidence base for the treatment of late-life depression (published in The Lancet).

Thank you to the Department of Psychiatry for supporting this event, to our planning committee (Drs. Stephanie Ameis, Lucy Barker, Cindy-Lee Dennis, Benjamin Goldstein and Paul Kurdyak) and to the many faculty who donated their time to review submissions, chair sessions and help to select award winners. I would like to acknowledge the work of Lindsay Curtis, Howard Chow, Diane Granato and Leslie Smith without whom this event would not be possible. I would also like to mention Jenni Wang (UofT work study student) who designed this year’s event logo.

I hope you will enjoy this year’s Research Day and look forward to seeing you at the event (twitter #hsrd16).

Sincerely,

Simone Vigod, MD, MSc, FRCP
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Shirley Brown Clinician Scientist in Women’s Mental Health, Women’s College Research Institute
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Keynote Address

“Achieving the Triple Aim: Can Collaborative Care Help Us Improve the Patient Experience, Improve Health Outcomes and Reduce Cost?”

Presented by

Dr. Jürgen Unützer, MD, MPH, MA

Dr. Unützer is Chair of the Department of Psychiatry and Behavioral Sciences at the University of Washington and an internationally recognized psychiatrist and health services researcher.

His work focuses on innovative models that integrate mental health and general medical services and on translating research on evidence-based behavioral health interventions into effective clinical and public health practice.

He has over 250 scientific publications and is the recipient of numerous federal and foundation grants and awards for his research to improve the health and mental health of populations through patient-centered integrated mental health services.

Dr. Unützer directs the AIMS Center (Advancing Integrated Mental Health Solutions) (http://aims.uw.edu) which has worked with more than 1,000 primary care practices worldwide to test and implement evidence-based Collaborative Care for depression.

He works with national and international organizations dedicated to improving behavioral health care for diverse populations, has served as Senior Scientific Advisor to the World Health Organization and as an Advisor to the President’s New Freedom Commission on Mental Health, and holds adjunct appointments as Professor in the School of Public Health (Departments of Health Services and Global Health) and as Affiliate Investigator at the Group Health Research Institute in Seattle.

Dr. Unützer has advanced training in geriatric psychiatry, public policy and public health.
Plenary Presentation

Further Neuroimaging Evidence for the Deficit Subtype of Schizophrenia: A Cortical Connectomics Analysis

Dr. Anne Wheeler, The Hospital for Sick Children

Background: The clinical heterogeneity of Schizophrenia has hindered neurobiological investigations aimed at identifying neural correlates of the disorder.

Objective: To identify network-based biomarkers across the spectrum of impairment present in Schizophrenia by separately evaluating individuals with deficit and nondeficit subtypes of this disorder.

Methods: A university hospital network–based neuroimaging study was conducted between February 1, 2007, and February 28, 2012. Participants included patients with Schizophrenia (n = 128) and matched healthy controls (n = 130) from two academic centers and patients with bipolar I disorder (n = 39) and matched healthy controls (n = 43) from a third site. Patients with Schizophrenia at each site in the top quartile on the proxy scale for the deficit syndrome were classified as having deficit Schizophrenia and those in the bottom quartile were classified as having nondeficit Schizophrenia. Exposure All participants underwent magnetic resonance brain imaging.

Network-level properties of cortical thickness were assessed in each group. Interregional cortexwide coupling was compared among the groups, and graph theoretical approaches were used to assess network density and node degree, betweenness, closeness, and eigenvector centrality.

Results: Stronger frontoparietal and frontotemporal coupling was found in patients with deficit Schizophrenia compared with those with nondeficit Schizophrenia (17 of 1326 pairwise relationships were significantly different, P < .05; 5%false discovery rate) and in patients with deficit Schizophrenia compared with healthy controls (49 of 1326 pairwise relationships were significantly different, P < .05; 5%false discovery rate). Participants with nondeficit Schizophrenia and bipolar I disorder did not show significant differences in coupling relative to those in the control groups (for both comparisons, 0 of 1326 pairwise relationships were significantly different, P > .05; 5%false discovery rate). The networks formed from patients with deficit Schizophrenia demonstrated increased density of connections relative to controls and nondeficit patients (range, 0.07-0.45 in controls, 0.09-0.43 in the nondeficit group, and 0.18-0.67 in the deficit group). High centrality nodes were identified in the supramarginal, middle, and superior temporal and inferior frontal regions in deficit Schizophrenia networks based on ranking of four centrality metrics. High centrality regions were identified as those that ranked in the top 10 in 50% or more of the thresholded networks in three or more of the centrality measures. Network properties were similar in patients with deficit Schizophrenia from both study sites.

Conclusions and relevance: Patients with Schizophrenia at one end of a spectrum show characteristic signatures of altered intracortical relationships compared with those at the other end of that spectrum, patients with bipolar I disorder, and healthy individuals. Cortical connectomic approaches can be used to reliably identify neural signatures in clinically heterogeneous groups of patients.

Plenary Presentation

**Prediction of Working Memory Performance in Schizophrenia by Plasma Ratio of Clozapine to N-Desmethylclozapine**

Dr. Tarek Rajji, Centre for Addiction and Mental Health

**Background:** Clozapine’s potent antagonism of muscarinic M1 receptors is thought to worsen working memory deficits associated with Schizophrenia. In contrast, its major metabolite, N-desmethylclozapine (NDMC), is thought to enhance working memory via its M1 receptor agonist activity. The authors hypothesized that the ratio of serumclozapine and NDMC concentrations would be inversely associated with working memory performance in Schizophrenia.

**Methods:** Thirty patients with Schizophrenia or schizoaffective disorder who were receiving clozapine monotherapy at bedtime completed the MATRICS Consensus Cognitive Battery (MCCB) on the day their blood was collected to assess concentrations of clozapine and NDMC as well as serum anticholinergic activity.

**Results:** The clozapine/NDMC ratio was significantly and negatively associated with working memory performance after controlling for age, gender, education, and symptom severity. No significant associations were found between individual clozapine and NDMC concentrations and working memory performance. Serum anticholinergic activity was significantly associated with clozapine concentration, but not with working memory performance or NDMC concentration. No significant associations were found between any pharmacological measure and performance on other MCCB cognitive domains.

**Conclusions:** This hypothesis-driven study confirms that clozapine/NDMC ratio is a strong predictor of working memory performance in patients with Schizophrenia. This finding suggests that manipulating the clozapine/NDMC ratio could enhance cognition in patients with Schizophrenia treated with clozapine. It also supports the study of procholinergic agents, such as M1 receptor-positive allosteric modulators, to enhance cognition in Schizophrenia.

Plenary Presentation

**Candidate Genes in Panic Disorder:**

Meta-Analyses of 23 Common Variants in Major Anxiogenic Pathways.

*Mr. Aaron Howe, Centre for Addiction and Mental Health*

**Background:** The utilization of molecular genetics approaches in examination of panic disorder (PD) has implicated several variants as potential susceptibility factors for panicogenesis. However, the identification of robust PD susceptibility genes has been complicated by phenotypic diversity, underpowered association studies and ancestry-specific effects.

**Methods:** In the present study, we performed a succinct review of case-control association studies published prior to April 2015. Meta-analyses were performed for candidate gene variants examined in at least three studies using the Cochrane Mantel-Haenszel fixed-effect model.

**Results:** Meta-analyses were performed on 23 variants in 20 PD candidate genes. Significant associations after correction for multiple testing were observed for three variants, TMEM132D rs7370927 (T allele: odds ratio (OR)=1.27, 95% confidence interval (CI): 1.15-1.40, P=2.49 × 10^-6), rs11060369 (CC genotype: OR=0.65, 95% CI: 0.53-0.79, P=1.81 × 10^-5) and COMT rs4680 (Val (G) allele: OR=1.27, 95% CI: 1.14-1.42, P=2.49 × 10^-5) in studies with samples of European ancestry. No significant associations were observed in the secondary analyses considering sex, agoraphobia comorbidity and studies with samples of Asian ancestry.

**Conclusions:** Although these findings highlight a few associations, PD likely involves genetic variation in a multitude of biological pathways that is diverse among populations. Future studies must incorporate larger sample sizes and genome-wide approaches to further quantify the observed genetic variation among populations and subphenotypes of PD.

Background: Treatment-resistant major depression is common and potentially life-threatening in elderly people, in whom little is known about the benefits and risks of augmentation pharmacotherapy. We aimed to assess whether aripiprazole is associated with a higher probability of remission than is placebo.

Methods: We did a randomised, double-blind, placebo-controlled trial at three centres in the USA and Canada to test the efficacy and safety of aripiprazole augmentation for adults aged older than 60 years with treatment-resistant depression (Montgomery Asberg Depression Rating Scale [MADRS] score of ≥15). Patients who did not achieve remission during a pre-trial with venlafaxine extended-release (150–300 mg/day) were randomly assigned (1:1) to the addition of aripiprazole (target dose 10 mg [maximum 15 mg] daily) daily or placebo for 12 weeks. The computer-generated randomisation was done in blocks and stratified by site. Only the database administrator and research pharmacists had knowledge of treatment assignment. The primary endpoint was remission, defined as an MADRS score of 10 or less (and at least 2 points below the score at the start of the randomised phase) at both of the final two consecutive visits, analysed by intention to treat. This trial is registered with ClinicalTrials.gov, number NCT00892047.

Results: From July 20, 2009, to Dec 30, 2013, we recruited 468 eligible participants, 181 (39%) of whom did not remit and were randomly assigned to aripiprazole (n=91) or placebo (n=90). A greater proportion of participants in the aripiprazole group achieved remission than did those in the placebo group (40 [44%] vs 26 [29%] participants; odds ratio [OR] 2.0 [95% CI 1.1–3.7], p=0.03; number needed to treat [NNT] 6.6 [95% CI 3.5–81.8]). Akathisia was the most common adverse effect of aripiprazole (reported in 24 [26%] of 91 participants on aripiprazole vs 11 [12%] of 90 on placebo). Compared with placebo, aripiprazole was also associated with more Parkinsonism (15 [17%] of 86 vs two [2%] of 81 participants), but not with treatment-emergent suicidal ideation (13 [21%] of 61 vs 19 [29%] of 65 participants) or other measured safety variables.

Conclusions: In adults aged 60 years or older who do not achieve remission from depression with a first-line antidepressant, the addition of aripiprazole is effective in achieving and sustaining remission. Tolerability concerns include the potential for akathisia and Parkinsonism.

The Gut Microbiome in Schizophrenia and Metabolic Adverse Events from Antipsychotics: A Pilot Study

Sarah Kanji, Centre for Addiction and Mental Health
Trehani Foneska, Centre for Addiction and Mental Health;
Victoria Marshe, Centre for Addiction and Mental Health;
Venuja Siretnakumar, Centre for Addiction and Mental Health;
Margaret Hahn, Centre for Addiction and Mental Health;
Arun Tiwari, Centre for Addiction and Mental Health;
Valerie Taylor, Centre for Addiction and Mental Health;
Jane Foster, St Joseph's Hospital, Hamilton ON;
Daniel Mueller, Centre for Addiction and Mental Health.

Current evidence suggests that the Gut Microbiome (GMB) interacts with the nervous system and may play a role in mental illnesses such as Schizophrenia (SCZ). Antipsychotic treatment for SCZ is known to induce metabolic abnormalities in patients, but the exact mechanism is unclear. To date, no human studies have investigated the GMB in SCZ and their potential role in AP induced metabolic abnormalities.

1) to investigate GMB composition in SCZ patients compared to healthy individuals. 2) To examine the influence of AP treatment on GMB associated with metabolic disturbances.

We will recruit three groups of 25 subjects. Group A: Long term AP treated patients (for at least six months) with BMI between 18.5 and 29.9 taking either clozapine (CLZ), olanzapine (OLZ), risperidone (RIS) or aripiprazole (ARI). Group B: Healthy controls matched by BMI, age, sex and ethnicity to group A. Group C: Treatment naïve SCZ patients (BMI between 18.5-29.9) or patients newly switching to OLZ, RIS or ARI. Group C will be free of treatment for minimum 14 days prior to enrolment to minimize confounding factors of the GMB from previous AP exposure. Group A and B will be assessed at week 0 at which time stool samples, weight, inflammatory and metabolic markers will be collected. Group C will be assessed prospectively at weeks 0, 3 and 6 with the same measures collected. GMB will be extracted using bead-beating method of PowerFecal DNA isolation kits and characterized by sequencing 16S-rRNA genes from samples.

We have received REB approval in March 2016 and will provide an update at the HSRD meeting.
Poster Presentation #2 (Adult Psychiatry and Health Systems)

A Study of the Effectiveness for an Early Psychosis Intervention Population of Compensatory and Restorative Cognitive Interventions: Preliminary Findings

Genevieve Hayden, Centre for Addiction and Mental Health
Yarissa Herman, Centre for Addiction and Mental Health;
Gursharan Virdee, Centre for Addiction and Mental Health;
Christopher Bowie, Centre for Addiction and Mental Health, Queens University;
April Collins, Centre for Addiction and Mental Health;
Joy-Ann Perry, Centre for Addiction and Mental Health, UofT, Dept. of Occ.Science and Occupational Therapy;
Cecilia Manicatide, Centre for Addiction and Mental Health;
Raquel Williams, Centre for Addiction and Mental Health, UofT, Dept. of Occ.Science and Occupational Therapy;
Tony George, Centre for Addiction and Mental Health, University of Toronto, Department of Psychiatry;
Dawn Velligan, University of Texas, Department of Psychiatry;
Sean Kidd, Centre for Addiction and Mental Health, University of Toronto, Department of Psychiatry.

The purpose of the study is to compare the effectiveness of compensatory and restorative cognitive interventions for young individuals diagnosed with Schizophrenia. Cognitive Adaption Training (CAT) the compensatory intervention being examined and Action Based Cognitive Remediation is the restorative intervention. This first phase of investigation will be followed by a second that will examine these two interventions combined.

Through a randomized trial we have compared the impacts of Cognitive Adaption Training (CAT) and Action-Based Cognitive Remediation (ABCR). We recruited 16 participants between the ages of 16-34 who have been diagnosed with Schizophrenia. For each intervention there is four months of specialist-delivered treatment followed by five months of maintenance by case managers with baseline, four month, and nine month evaluations conducted. The evaluations include measures of cognitive functioning, symptomology, and community functioning.

Preliminary findings are examined through Wilcoxon Signed Rank and t-Tests to compare cognitive functioning, symptomology, and community participation from baseline to post specialist-delivered treatment (4 months) and between interventions and effect sizes are examined using Cohen’s d.

This comparative design is the first of its kind to be conducted to the best of our knowledge and moves forward the literature on the relative effectiveness of cognitive interventions for Schizophrenia and how they might be optimized.
To objectively evaluate different facets of the motivational system using a battery of computerized tasks in patients with Schizophrenia and healthy controls.

Thirty-one patients with Schizophrenia and 26 controls participated in this study. All participants underwent clinical characterization and were administered computerized tasks to evaluate hedonic capacity, reward learning, reward and effort valuation, and goal-directed decision making using the International Affective Pleasure System (IAPS), the Probabilistic Selection Task (PST) task, the Kirby Delay Discounting task, the Effort Expenditure for Rewards Task (EEfRT), and the Multitasking in the City Test (MCT), respectively.

Compared to controls, patients required significantly more training to learn reinforcement contingencies on the PRL ($t = 2.814, p = 0.007$); expended significantly less effort on high reward - high certainty trials on the EEfRT ($t = -2.377, p = 0.021$); and completed goal-oriented tasks significantly slower and less efficiently on the MCT ($t = 2.904, p = 0.005$). However, patients did not demonstrate impaired hedonic capacity. Furthermore, the MCT was significantly correlated with the PRL ($r = 0.299$, $p = 0.048$) and EEfRT tasks ($r = -0.313$, $p = 0.019$). As well, clinical measures of amotivation were significantly related to poorer task performance.

Preliminary data suggest that despite intact reward sensitivity, patients demonstrate impaired reward learning, effort valuation and goal-directed decision making. These findings highlight the need to conceptualize and examine motivation as a multi-faceted system rather than a one-dimensional construct. Furthermore, given the prevalence of motivational deficits in Schizophrenia, as well as its negative impact on functional outcomes, a more comprehensive analysis is needed to delineate specific deficits across the discrete facets of motivation.
Becoming a parent precipitates changes in new mothers’ psychological and social domains. Previous literature has focused exclusively on pregnancy and the early postpartum, but parenting is an evolving process, necessitating adaptation to changing circumstances. We extend previous literature and investigate the changes in the postpartum from 3 to 18 months that occur in maternal attitudes.

Using the Childbearing Attitudes Questionnaire, we collected data on mothers’ ratings of maternal worries, self-efficacy, mother-infant bonding, relationship with the partner, and interest in sex (n =171 women). Data were analyzed with a latent growth curve.

Results demonstrate stability in all maternal attitudes after 3 months postpartum. Further, different maternal attitudes are affected by different variables. Maternal worries and self-efficacy are associated with parity, postpartum depression, and child temperament. Interestingly, a negative evaluation of the relationship with the partner was only associated with breast-feeding status, while interest in sex was associated with parity, Socio-Economic Status (SES), and depressive symptoms.

Despite general stability, different maternal attitudes relate to different sets of variables. These patterns of attitudes in relation to relevant variables are discussed in terms of the literature on self-efficacy and gender roles, with important implications for clinical interventions.
Antipsychotic Use In Ontario: Trends And Predictors

Tanya Hauck, Centre for Addiction and Mental Health
Cindy Lau, Institute for Clinical Evaluative Sciences;
Karen Tu, Institute for Clinical Evaluative Sciences, Department of Family and Community Medicine;
Paul Kurdyak, Department of Psychiatry, Institute for Clinical Evaluative Sciences.

Antipsychotic prescriptions were identified by the American Psychiatric Association as a target for Choosing Wisely. Increasing off-label use of antipsychotics is concerning, considering the high risk of adverse events. The purpose of our research is to understand trends and predictors of antipsychotic prescriptions in Ontario.

This study involves chart abstraction and data collection from more than 300,000 primary care charts as well as linkage to administrative data. A subset of charts was abstracted for mental health diagnoses, such as depression and ADHD. Charts contained prescriptions provided by primary care physicians. All charts were linked to administrative data including physician billings and laboratory tests. Logistic regression was used to determine predictors of treatment.

In a youth population with a diagnosis of ADHD, antipsychotics were prescribed to 11.9% of patients with the diagnosis versus 0.9% of patients without the diagnosis. Psychiatric consultation predicted antipsychotic prescriptions (OR=3.85, 95% CI 2.11, 7.02) in this population, whereas antidepressant prescriptions were predicted by age (OR 1.14 95% CI 1.07, 1.21), diagnoses of depression and anxiety (OR 18.4 95% CI 8.03, 42.1), and also psychiatric consultation (OR 2.04 95% CI 1.16, 3.58).

Work so far indicates that antipsychotics are highly prescribed in some subsets of the population, even with limited evidence for their use. Future work will study prevalence in adults and also study other factors such as simultaneous use of multiple antipsychotics and the prevalence of metabolic monitoring in patients with antipsychotic prescriptions (using OHIP linked laboratory data).
**Poster Presentation #7 (Adult Psychiatry and Health Systems)**

**Using Mental Health Telemetry (MHT) to Predict Relapse and Re-hospitalization in Mood Disorders**

David Kreindler, Sunnybrook Health Sciences Centre  
Anthony Levitt, Sunnybrook Health Sciences Centre, University of Toronto;  
Charles Lumsden, University of Toronto;  
Nicholas Woolridge, University of Toronto Mississauga;  
Shauna Eisen, Sunnybrook Health Sciences Centre;  
Felicia (Yue) Zhang, Sunnybrook Health Sciences Centre, Princeton University;  
Tasmia Hai, Sunnybrook Health Sciences Centre, Baycrest

MHT/PATH uses cell phones to collect self-report data on symptoms of illness and then makes it available to clinicians in real time. We hypothesized that MHT/PATH would be well tolerated and could be used to reduce re-hospitalization in patients with diagnosed mood disorders by improving the quality of information available to clinicians when making clinical decisions.

We offered MHT to two cohorts of patients followed by psychiatrists at Sunnybrook Health Sciences Centre: a series of patients being discharged from an inpatient unit with recurrent mood disorders, and outpatients with bipolar disorder. Recruits were randomized 2:1 to MHT use or treatment-as-usual (TAU) arms. Those in the MHT arm were asked to complete daily symptom ratings questionnaires over a six-month period; their clinicians were provided with access to patients’ telemetry. Both groups followed up with their clinicians as usual, and completed every-two-month mood rating and quality of life paper questionnaires.

Recruitment and retention rates in this study were lower than in previous MHT-based studies. Retention rates were poor in the TAU arm. Re-hospitalization rates were rare. Key barriers to uptake identified by participants and prospective participants included (i) data not being usable by participants and (ii) availability to Sunnybrook patients only.

This study was the first attempt at a pragmatic study of MHT. Although the uptake rate was substantially lower that in prior studies, MHT was highly useful for a select sub-population, with positive qualitative feedback from users. Subsequent developments in core technology have responded to PATH-MOD participant feedback.
Individuals with coronary artery disease (CAD) are at an increased risk for depression. Diets low in omega-3 fatty acids (FAs) and depression have been vastly explored; however, less is known about linoleic acid (LA), an omega-6 FA. Evaluation of dietary habits and LA intake is crucial to determine if a relationship exists with depression for disease management.

Eligibility criteria included patients with stable CAD and enrolment in a cardiac rehabilitation program. Patients were required to complete food diaries for 3 consecutive days at baseline. Age, gender, weight and depressive symptoms (Center for Epidemiologic Studies Depression (CES-D)) were also collected. Food intake was quantified using Nutritionist Pro software.

Ninety-nine patients (mean ± SD age = 64.2 ± 7.5, weight = 84.0 ± 14.9kg, CES-D overall = 11.6 ± 11.0, gender = 77% male) were included. A backward linear regression model showed an increased consumption of foods with LA was significantly associated with higher total CES-D scores (r = 0.47, p < 0.003). Age, weight, diabetes, platelet inhibitor use and history of depression were controlled for. There was no significant association between EPA and DHA (omega-3 FAs) intake and CES-D scores.

These findings demonstrate a diet high in LA is associated with an increased risk of depressive symptoms in this population. Given the role of LA in promoting inflammation, intake of food high in omega-6 FAs may be a modifiable factor in alleviating depressive symptoms.
Depression is highly prevalent in individuals with coronary artery disease (CAD), and increases risk of future cardiac events and mortality. Ceramides, a family of sphingolipid species, have been implicated in the pathophysiology of CAD and the ceramide species C18:0 and C20:0 may be particularly important in depression due to their pro-inflammatory and pro-apoptotic characteristics. This study assessed the association of ceramide concentrations and depressive symptoms in CAD subjects.

Depressive symptoms were assessed using the depression subscale of the self-reported Hospital Anxiety and Depression Scale (HADS-D). Ceramide concentrations were measured from fasting blood plasma samples using high performance liquid chromatography coupled electrospray ionization tandem mass spectrometry (LC/MS/MS). Linear regression models assessed the association between log-transformed concentrations of C18:0 and C20:0 and HADS-D scores adjusting for age, gender, body mass index (BMI), HbA1c, and anxiety. Seven other ceramide species were also explored as predictors of depressive symptoms.

117 CAD patients (mean (SD) age = 64±6, 85% male, mean BMI = 29±5) were included. Higher C18:0 (β = 0.174, p = 0.02) concentration and C20:0 (β = 0.162, p = 0.03) concentration were significantly associated with higher HADS-D scores. In exploratory analysis, higher C16:0 (β = 0.184, p = 0.02) concentration was also significantly associated with higher HADS-D scores.

Ceramides C18:0, C20:0, and C16:0, were found to be associated with depression symptom severity in a population of CAD patients. The potential role of ceramides in depression should be further examined in CAD patients as well as in other populations.
Individuals with Schizophrenia have high rates of Diabetes and receive poor care. Little is known about what determines the Diabetes care quality within this population.

To investigate the factors which impact Diabetes care quality in patients with Schizophrenia.

A retrospective cohort study of Ontario administrative health records in individuals aged 18 or older with Schizophrenia and Diabetes on April 1, 2011. Patients were divided into groups depending on how many of the three guideline-concordant diabetes care procedures they received in a two-year period. Optimal care was defined as having all three of the following in a two-year period: 4 HbA1C tests, 1 eye test and 1 cholesterol test. Demographic, clinical and service utilization characteristics were compared across three levels of diabetes care (0 vs. 1, 2, or 3 diabetes tests received) using multinomial logistic regression odds ratios.

Among 19,443 individuals in Ontario with Diabetes and Schizophrenia, 2,998 (15.4%) had none, 5,666 (29.1%) had one, 6,155 (31.7%) had two and 4,624 (23.8%) had all three diabetes care tests. More outpatient psychiatrist visits were associated with better Diabetes care: 0 vs. 1 OR 1.02 (95% CI 1.01-1.03), 0 vs. 2 OR 1.03 (95% CI 1.02-1.04), 0 vs. 3 OR 1.04 (95% CI 1.03-1.05). The number of psychiatric hospitalizations was associated with worse Diabetes care: 0 vs. 1 OR 0.90 (95% CI 0.84-0.97), 0 vs. 2 OR 0.84 (95% CI 0.78-0.90), 0 vs. 3 OR 0.79 (95% CI 0.73-0.87).

These results suggest that good Diabetes quality of care is contingent upon good psychiatric care (psychiatric stability and frequent follow-up) for individuals with Schizophrenia and Diabetes.
Obstructive Sleep Apnea (OSA) has been recognised as an independent risk factor for the development and progression of cardiac arrhythmia. There is still debate whether Continuous Positive Airway Pressure (CPAP) treatment can decrease the recurrence and/or severity of cardiac arrhythmia. Our aim is to review the existing evidence of CPAP efficacy in patients with cardiac arrhythmia.

We have searched MEDLINE and PUBMED databases with combination of the following keywords: obstructive sleep apnea, continuous positive airway pressure, cardiac arrhythmia, atrial fibrillation, bradyarrhythmia, ventricular. We found studies investigating CPAP effects on: atrial structure/function (n=5), bradyarrhythmia recurrence (n=5), frequency of atrial fibrillation (AF) (n=4), AF recurrence post-interventions (n=8), and ventricular repolarization/arrhythmia (n=7).

Evidence-based studies showed that CPAP improves the left atrial function, reverses the electrical remodelling and provides more homogenous conduction between and within the atria. However, the ability of CPAP to reverse the structural changes in the atria and ventricle is still unproven. CPAP reportedly decreases the recurrence of bradyarrhythmia and AF, and improves the outcome of surgical ablation procedure in AF. Moreover, CPAP improves ventricular repolarization; therefore, it could potentially decrease the risk of ventricular arrhythmias.

To date, a small number of studies have assessed the impact of CPAP on cardiac arrhythmias, with only one randomized controlled trial. Furthermore, longitudinal studies are needed to detect CPAP’s ability in reversing structural remodelling of the heart. Therefore, carefully conducted research studies are still needed to determine effects of CPAP therapy in patients with cardiac arrhythmia and its clinical implications.
Obsessive Compulsive Disorder (OCD) is a severe neuropsychiatric disorder, which may in some cases be exacerbated or induced by stress. It was proposed that stress-related disorders might be influenced by mitochondrial efficiency to maintain high levels of energy, which is required in neuronal functioning.

Our objective was to examine the role of nuclear-encoded oxidative phosphorylation related genes in OCD risk and its phenotypes. We selected 28 genes involved in oxidative phosphorylation or involved in oxidative stress, mitochondrial biogenesis, inflammation and apoptosis. A total of 64 SNPs were analyzed in 484 OCD subjects. After quality control, 59 SNPs and 477 individuals were available for the statistical analysis.

Logistic regression was used for OCD risk analysis and linear regression was used to test association with the phenotypes of interest: age at onset and YBOCS dimensional factors. From case-control analysis, we observed nominal significant association for the SNPs rs4011457 in the NDUFS7 gene and OCD risk (N=856, \( P_{uncorrected} = 0.004 \)). Also, nominally significant evidence for association was observed for the SNP rs3820189 in the 5’ of the MFN2 gene and YBOCS total score (N=346; \( P_{uncorrected} = 0.002 \)) and for the SNP rs4246944 in the PPIF gene and Sex/Religion factor (N=371; \( P_{uncorrected} = 0.002 \)). A permutation-based test of all 59 SNPs jointly showed significant association with OCD (\( P_{perm} = 0.003 \)).

To the best of our knowledge, this is the first study to show evidence that nuclear-encoded mitochondrial genes may influence OCD.
To conduct a descriptive analysis of psychiatry e-consults referred from primary care.

A chart review of psychiatry e-consults completed between November 2014 and March 2016 on 2 pilot e-consultation platforms: Ontario Telemedicine Network and Consult Conduit. Descriptive analysis conducted to examine patient characteristics (demographics and diagnoses), types of referral questions, information included in the referral, time to consultant response and number of interactions required, and nature of the consultant response.

Data collection and analysis are underway. We have thus far completed chart review for 15 psychiatry e-consults. Two thirds of referrers attached a formal typed consult request to the e-consult. Lab results, cumulative patient profiles, and previous psychiatric treatment notes were attached on occasion. Mean patient age was 42.7 (range 16 to 87) and 11 patients (73.3%) were female. 11/15 cases included a diagnosis of depression or anxiety, 3/15 had bipolar or psychotic disorders, 2/15 had PTSD and 2/15 had ADHD. Most commonly, referral questions had to do with medication side effects and/or safety (11/15, 73%), or symptom management (7/15, 47%). The consultant responded within 1 day to 93% of consults. The e-consult was completed in 1 interaction in 87% of cases.

Primary care providers can use psychiatry e-consult for a wide range of patients. Most commonly e-consult referrals pertain to medication questions and/or management of symptoms. Consultant responses can be provided rapidly with an infrequent need for additional information. Additional study is required to determine if psychiatry e-consult is cost-effective and adoption strategies are needed.
While clinicians often caution patients against using non-prescription drugs and alcohol while recovering from traumatic brain injury (TBI), little is known about how these substances affect recovery. We examined whether attention and memory recovery from 2-5 months post-TBI were affected in those with a self-reported history of substance abuse.

Retrospective analysis of 200 patients from the Toronto Rehab TBI Recovery Study comprising moderate-severe TBI patients 18 years of age and older was undertaken. A High Alcohol/Substance Use group, comprising those with T-score of ≥60 on the Alcohol Problems and Drug Problems sub-scales of the Personality Assessment Inventory (n=36) was compared to matched TBI controls (n=36) on aggregates of Timed Attention (Trails A and B, Stroop sub-tests, symbol digit Oral and Written, and Verbal Fluency Phonemic), Untimed Attention (Visual Spatial and Digit Span Forward), Verbal Memory (Rey Auditory Verbal Memory and Logical Memory learning and recall sub-tests), and Visual memory (Rey Visual Design Learning Test learning and recall sub-tests).

The High Alcohol/Substance Use Group recovered improved significantly less for the Timed Attention Aggregate, $p<0.05$, cohen's $d$ effect size = 2.78. There were no other significant differences, but non-verbal memory showed a large effect size (1.33).

This self-report provides empirical evidence implicating substance abuse in poorer recovery of timed attention after TBI. Larger sample recovery studies examining the selective roles of alcohol vs. other substances, and the role of pre-morbid vs. post-injury use are needed.
While the elevated long-term prevalence of depression and anxiety after moderate-severe traumatic brain injury (TBI) have been well-established, little is known about the longitudinal course and profile of depression and anxiety from the sub-acute to the chronic stages of injury. We thus investigated prospectively the frequency of depression and anxiety from 2 to 24+ months post-TBI.

Participants. 161 individuals with moderate to severe TBI from the Toronto Rehabilitation Institute. Design and Procedures. Depression and anxiety symptoms measured with Beck Depression and Anxiety Inventories at 2, 5, 12, and 24+ months post-injury. Clinically significant depression and anxiety ("moderate-severe" symptoms) operationally defined with score of >18 or >15, respectively.

Repeated measured ANCOVA, controlling for antidepressants, revealed main effect of time (p < .05, within subjects) for depressive (but not anxiety) symptoms. Frequency of cases with moderate-severe symptoms increased from 7.1% to 20.7% (depression) and from 10.8% to 18.9% (anxiety) from 2-24 months post-injury.

Frequency of depression and anxiety nearly tripled and doubled, respectively, from the sub-acute to chronic stages of injury. As these disorders structurally affect the brain and have a deleterious impact on quality of life, a fuller understanding the predictors of long-term outcome, and screening for these predictors is needed. More than 1.1% of the population suffer enduring effects of TBI; given this scale, cost-effective, remote administration of evidence-based treatments such as cognitive behavioural therapy and mindfulness meditation are also needed.

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Intermittent theta-burst stimulation (Itbs) is an emerging repetitive transcranial magnetic stimulation (Rtms) protocol used in the treatment of major depressive disorder (MDD) and other medication-refractory psychiatric illnesses. Among patients undergoing Itbs, concurrent antipsychotic pharmacotherapy (AP) is common. However, recent evidence suggests that dopamine D2 receptor antagonism diminishes the effects of Itbs-induced neuroplasticity, as indexed by decreased motor evoked potentials following M1 stimulation. To date, the consequences of D2 blockade on Itbs of non-motor areas have not been clarified.

In this large, open-label case series, we examined the relationship between AP and clinical outcome in 105 MDD patients who underwent a full course of dorsomedial prefrontal cortex-Itbs (DMPFC-Itbs). Antipsychotic drug (APD) treatment regimens were recorded for all patients undergoing concomitant AP and DMPFC-Itbs, which were then converted to haloperidol and risperidone dose equivalents. Finally, haloperidol and risperidone dose equivalents were correlated with clinical outcome (Beck Depression Inventory-II percent improvement).

29 out of 105 patients underwent concurrent AP and DMPFC-Itbs. Among these patients, 14/29 (48%) achieved response and 12/29 (41%) achieved remission. For the remaining patients (non-AP), 26/76 (34%) and 18/76 (24%) achieved response and remission, respectively. We found no association between AP and clinical outcome, even after adjusting for covariates.

These results encouragingly suggest that AP does not affect clinical outcomes of DMPFC-Itbs in MDD; indicating that AP can be delivered throughout Rtms treatment without jeopardizing therapeutic efficacy. However, definitive evidence for the benign effects of AP on Itbs requires a more detailed and systematic analysis including data from large RCTs using protocols other than Itbs.
Onset and/or worsening of obsessive compulsive disorder (OCD) after streptococcal infection in children has contributed an autoimmune hypothesis for this disease although whether neuroinflammation occurs in OCD is unknown. Positron emission tomography (PET) imaging of translocator protein distribution volume (TSPO VT) is an index of the neuroinflammatory process of microglial activation. Our objective was to determine if TSPO VT is elevated in key regions implicated in OCD. To our knowledge this is the first investigation of inflammation in the brain of OCD.

[18F] FEPPA PET was applied to measure TSPO VT in the orbitofrontal cortex, ventral striatum, and insula in OCD subjects (n=13) and health (n=13). All subjects were drug and medication free, were non-smoking and had no additional psychiatric or medical illnesses. Cases and controls were matched for age and alleles of the rs6971 polymorphism which influences binding of [18F] FEPPA (and all second generation PET radiotracers) to TSPO.

TSPO VT was elevated in OCD subjects in the orbitofrontal cortex, ventral striatum, and insula by 21%, 20%, and 21% respectively (multivariate analysis of variance: effect of OCD versus health: F3,20 = 3.41, P < 0.038; effect of genotype: F3,20 = 12.7, P < 0.001).

Significantly greater TSPO binding occurs in OCD in the orbitofrontal cortex, ventral striatum, and insula. The most likely explanation is that this reflects the presence of activated microglia from neuroinflammation. The role of neuroinflammation in OCD extends beyond recent streptococcal infection and may represent a novel therapeutic target.
Mood and anxiety disorders are the leading causes of disability in established market economies such as in Canada. Current anxiolytic drugs have undesirable side effects. Thus better treatments are needed. Existing antidepressants with anxiolytic effects have been shown to reduce the level of G9a, a histone methyltransferase that methylates lysine 9 of histone H3 (H3K9). The methylation status of H3K9 plays an important role in mediating epigenetic responses to environmental stress. Thus, we reason that deliberately targeting G9a may be an effective strategy to discover new anti-anxiety medications.

We hypothesize that the G9a inhibitors UNC0642 and A-366 will have anxiolytic-like effects in established animal models of anxiety.

C57BL/6 mice were treated chronically (14 days) with 1mg/kg, 2mg/kg or 5mg/kg of UNC0642 or A-366. The anxiolytic-like effects of UNC0642 and A-366 on mouse behaviour were measured in the elevated zero maze (EZM), the marble burying test (MB) and on novelty suppressed feeding (NSF).

Chronic treatment of A-366 increased the amount of time mice spent in the open arm of the EZM, decreased the number of marbles buried and decreased latency to eat in the NSF test. Chronic treatment of UNC0642 increased the amount of time mice spent in the open arms of the EZM but did not affect MB or NSF behaviours.

UNC0642 and A-366 showed dose-dependent anxiolytic-like effects on mouse behaviour with chronic treatment. The anxiolytic-like effect was likely due to G9a inhibition, given the distinct chemical structures of the two G9a inhibitors.
Poster Presentation #19 (Brain and Therapeutics)

**Inhibitory Fronto-Polar rTMS for Treating Select Endophenotypes in Major Depressive Disorder: A Case Study**

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Repetitive transcranial magnetic stimulation (rTMS) is a safe and effective treatment option for medically refractory major depressive disorder (MDD), typically targeting the dorsolateral prefrontal cortex (DLPFC) or the dorsomedial prefrontal cortex (DMPFC). Blunted reward learning (anhedonia) has recently emerged as a key neural endophenotype of MDD, and the presence of anhedonia has been proposed to be a biomarker distinguishing responders and non-responders to classical rTMS treatments. Thus, targeting the reward circuitry non-invasively with inhibitory frontopolar (FP) rTMS could be potentially therapeutic for patients who present with highly anhedonic symptomatology. Here we present a case, with neuroimaging, of a woman with MDD who failed to respond to both DLPFC- and DMPFC-rTMS, but who showed full and sustained remission following FP-rTMS.

Resting state fMRI data was collected before and after 30 sessions of once-daily inhibitory (1Hz) FP-rTMS. Treatment remission was defined as a score of ≤ 7 on the clinician-administered Hamilton Rating Scale for Depression (HRSD). For pre- and post-treatment rs-fMRI, cortico-subcortical connectivity changes were examined with seed-based correlation analyses (using nucleus accumbens and subgenual cingulate cortex as a priori regions of interest) and fractional amplitude of low frequency fluctuations (fALFF).

HRSD score improved 66.7% following 30 once-daily sessions of FP-rTMS, reflecting a sustained remission from MDD symptomatology when measured at follow-up (HRSD=7). Cortico-subcortical connectivity changes following treatment showed modulations to the reward circuitry, which may represent a potential biomarker for successful treatment outcome.

The findings from this case-study warrant further investigation of FP-rTMS as a treatment option for those patients who present with the blunted reward learning depression endophenotype – a population previously thought to be resistant to rTMS therapy altogether. A larger, randomized sham-controlled trial would provide definitive evidence of the efficacy of FP-rTMS. Furthermore, our neuroimaging results provide a promising step towards the creation of biomarkers that may potentially be used to tailor and personalize rTMS treatments for those living with refractory depression.
**Pharmacological Effects of Psychotropic Medication on Long Term Potentiation in the Dorsolateral Prefrontal Cortex**

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Long-term potentiation (LTP) is a cellular mechanism mediating neural plasticity and associated with learning and memory. As learning and memory are largely governed by the dorsolateral prefrontal cortex (DLPFC), evaluating LTP in this region of the brain will undoubtedly shed light on the neural processes responsible for higher order cognition. Paired-associative stimulation (PAS) combined electroencephalograph (EEG) is a neurophysiological paradigm used to induce and measure LTP from the cortex. PAS consists of 180 repetitive simultaneous paring of transcranial magnetic stimulation (TMS) to the contralateral DLPFC, with electrical peripheral nerve stimulation (PNS) to the median nerve. This repeated pairing results in an LTP-like increase in cortical evoked activity captured through EEG, and proposed to be linked to Hebbian and Spike Timing Dependent plasticity mechanisms. Previous studies have shown that key neurotransmitters modulate LTP in the motor cortex. For example, levodopa (dopamine agonist) and rivastigmine (cholinesterase inhibitor) both enhance LTP. By contrast, dextromethorphan (glutamatergic antagonist), and baclofen, (GABA agonist) both inhibit LTP. However, the effects of these neurotransmitter systems have not been evaluated in the DLPFC.

To assess how PAS-induced LTP in the DLPFC is modified by cholinergic, dopaminergic, GABAergic and glutamatergic neurotransmission.

1. 50 mg baclofen and 150 mg of dextromethorphan will impair LTP in the DLPFC when compared to a placebo.
2. 100 mg of levodopa and 3 mg rivastigmine will enhance LTP in the DLPFC when compared to a placebo.

This study is a double-blinded, placebo-controlled within-subjects study. Twelve healthy participants were recruited to assess the effects of the levodopa, rivastigmine, dextromethorphan and baclofen on PAS-induced LTP in the DLPFC. Each participant was given the four experimental drugs in addition to a placebo agent over five separate sessions, each separated by at least one week. To evaluate LTP, 100 single TMS pulses were delivered to the contralateral DLPFC pre-and post-PAS. Using independent component analysis (ICA) EEG recordings were processed to remove artifacts and noise then averaged to identify change in cortical evoked activity from the electrode corresponding to the DLPFC, and left frontal.

12 subjects (3 females, and 9 males) participated in this study. All subjects tolertated the study well. Due to the nature of the study, being double blinded, the results are currently not available but will be available upon presentation.

To our knowledge this is the only in vivo study assessing LTP from the DLPFC. These findings, therefore, may ultimately lead to an improved understanding and enhanced treatments for disorders whose pathophysiology have been associated with impaired DLPFC LTP, such as Schizophrenia, and Alzheimer’s.
Impairment of Neuroplasticity in the Dorsolateral Prefrontal Cortex By Alcohol Intoxication

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Binge drinking has been demonstrated to impair neuroplasticity in the motor cortex. The dorsolateral prefrontal cortex (DLPFC) is a part of the brain reward circuitry and alcohol’s effects on neuroplasticity in the DLPFC may play a role in the pathophysiology of AUDs. The current study was aimed at evaluating the effect of a binge drinking episode on neuroplasticity in the DLPFC.

Paired associative stimulation (PAS) combined with electroencephalography (EEG) allows for induction of associative long-term potentiation (LTP)-like neuroplasticity in the DLPFC. In this within-subjects cross-over design study, 15 binge drinkers were administered PAS to the DLPFC following consumption of an alcohol or placebo beverage. Subjects were administered alcohol at a dose of 1.5g/l of body water. PAS induced neuroplasticity was measured at Post0, Post15, Post30 and Post60 minutes following PAS. The effect of alcohol on PAS-induced potentiation of theta-phase-gamma-amplitude coupling, which is believed to be related to working memory, was also explored.

Binge drinking of alcohol resulted in a significant impairment of mean potentiation and the maximum potentiation compared to the placebo beverage in the DLPFC. Additionally, PAS produced a significant increase in theta-phase-gamma-amplitude coupling following placebo beverage that was not observed following binge drinking of alcohol.

Findings suggest that binge drinking impairs neuroplasticity in the DLPFC. The impairment of PAS-induced neuroplasticity was associated with reduction of PAS-induced potentiation of theta-gamma-amplitude coupling. Impairment of neuroplasticity in the DLPFC is one possible mechanism underlying the transition from binge drinking to AUDs.
Paired associative stimulation (PAS) is a neurostimulation paradigm that assesses plasticity in the human cortex. When combined with electroencephalography, PAS indexes plasticity in the dorsolateral prefrontal cortex (DLPFC) by capturing the potentiation of neuronal oscillations, specifically gamma oscillations. PAS-induced plasticity in the sensorimotor and motor cortex has been associated with greater cortical thickness previously. To date, no studies have directly examined the relationship between DLPFC plasticity and thickness or surface area. We hypothesize higher levels of potentiation will be correlated with greater dorsolateral prefrontal cortical surface area and thickness on structural MRI in healthy subjects.

26 healthy right-handed subjects, age 18-85 were recruited. Localization and measurements of the DLPFC (middle frontal gyrus) were achieved through neuronavigation techniques using T1-weighted MRI scans. PAS was delivered to the DLPFC according to previously published methods. Correlation and regression analyses were performed between PAS-induced potentiation of gamma power and DLPFC thickness and surface area.

Gamma potentiation was significantly correlated with surface area (rho=0.523, p=0.006) thickness and (rho=0.432, p=0.027) in the caudal middle frontal gyrus. Multiple linear regression controlling for age revealed that surface area (β=0.486, p=0.008) and cortical thickness (β=0.484, p=0.013) predict PAS-induced gamma potentiation (R2=0.414).

Our findings confirm our hypotheses that greater cortical surface area and thickness are associated with plasticity of the same brain region as reflected by gamma potentiation. Our findings advance current knowledge on DLPFC plasticity. Further investigation into the nature of this relationship and DLPFC function is warranted.
GWAS for psychiatric disorders have revealed enrichment of disease associated markers (risk-alleles) within enhancer regions of the genome. The significance of risk-alleles in enhancers is unclear. Enhancers regulate transcription by looping-over to contact multiple target-gene promoters simultaneously. Hence, genetic variations in enhancers can impact cellular transcriptome profoundly. Risk-alleles were found particularly enriched on long stretches of enhancers, called super-enhancers, involved in regulation of cell identity. We are investigating the influence of risk-alleles in super-enhancers, on super-enhancer-promoter interactions, gene expression and disease-risk.

We explored the Schizophrenia GWAS database to identify super-enhancers enriched in risk-alleles. We used Capture-Hi-C data on human brain tissue and neural precursor cells (NPCs) to identify gene promoters that interact with these super-enhancers. A specific super-enhancer that interacts with several genes implicated in psychiatric disorders was selected for genetic manipulations. We deleted a specific portion of this super-enhancer using CRISPR/cas9 genome editing technique and are currently observing its effects on promoter interactions and gene expression in NPCs.

Our Capture-Hi-C results identified the interactions for the super-enhancer within the Schizophrenia loci in the RERE gene that interacts with multiple gene promoters, some of which (PARK7, PER3) are implicated in brain disorders. Our CRISPR/cas9 experiments deleted a portion of this super-enhancer in NPCs and in HEK293 cells, which we hypothesize is crucial for its interaction with the gene-targets.

Upon completion, this study will reveal the influence of risk-alleles on gene expression and disease-risk and enable the translation of GWAS findings into new treatments for psychiatric disorders.
Co-morbid cannabis dependence in Schizophrenia significantly exacerbates positive and negative symptoms; however the effects on cognition are unclear. Pervasive working memory deficits in Schizophrenia are associated with excessive gamma (30-50 Hz) oscillations in the dorsolateral prefrontal cortex (DLPFC). This study evaluated gamma oscillations during the N-Back working memory task prior to and following a 28-day abstinence period in cannabis dependent patients and non-psychiatric controls.

In 15 patients (mean age 30.93 ± 9.31 years) and 16 non-psychiatric controls (mean age 28.94 ± 6.39 years) male cannabis dependent participants performed the verbal N-back task administered at the 1- and 3-back working memory load. Gamma oscillatory power was measured from DLPFC for correct responses to targets using EEG. Abstinence was reinforced using low-cost contingency management.

No differences were observed in accuracy or reaction time at baseline. A repeated measures ANOVA found a significant working memory load x group interaction (F=4.60, df=1.27, p=0.041). Biochemically verified abstinence revealed greater gamma power among patients who relapsed (54.5%) compared abstinent (45.5%) (1-Back: t=-2.472, df=8, p=0.039; 3-Back: t=-2.441, df=9, p=0.037). No differences in gamma power were found among controls.

These preliminary findings suggest that gamma oscillations may provide a potential marker for treatment response for cannabis dependence in Schizophrenia. Moreover, these findings suggest that an adjunct treatment such as repetitive transcranial magnetic stimulation that has been shown to modulate gamma oscillations and improve working memory deficits may in turn improve abstinence rates in this disorder.
Increased oxidative stress in the brain may contribute to the pathophysiology of Schizophrenia. Existing evidence supports a decrease of prefrontal glutathione (GSH), an endogenous antioxidant in the brain, in Schizophrenia patients. The main objective is to investigate if there is a decrease of GSH in the medial prefrontal cortex (mPFC) in clinical high risk (CHR) and first episode of psychosis (FEP).

Nineteen CHR, 8 FEP and 33 healthy volunteers (HV) were scanned for GSH metabolite level in the mPFC using proton magnetic resonance spectroscopy (1H-MRS) with 3T MRI. The scanning protocols were adjusted specifically for GSH metabolite quantification. The MRS data was acquired using a modified J-editing difference method with water signal suppressed.

In mPFC, a one-way ANCOVA did not reveal significant group effects on GSH level (F=1.35, p=0.26), even when controlling for cannabis use. A lower trend in GSH level in FEP relative to HV was observed in exploratory pairwise comparisons (F=3.09, p=0.08, uncorrected). Exploratory correlational analyses found a negative trend of correlation between GSH level and PANSS negative symptoms in FEP (r=-0.74, p=0.06), a significant negative correlation between GSH level and visuospatial perception in CHR (r=-0.70, p=0.001) both controlled for cannabis use.

The preliminary data supports a decrease in prefrontal GSH levels in FEP but not in CHR. An increase in the sample is required to confirm results.
The Effect of Varenicline on Neurocognitive Performance in Non-Smoking Patients with Schizophrenia Compared to Non-Psychiatric Individuals

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Schizophrenia is associated with dysregulated central nicotinic acetylcholine receptors (nAChRs) that may relate to both the high smoking prevalence and pervasive cognitive deficits observed in this disorder. The nicotinic partial agonist varenicline, which is approved for smoking cessation, has been shown to enhance cognition in Schizophrenia, but its effects in non-smokers are unknown. This study assessed the effects of varenicline on cognitive function in non-smoking Schizophrenia patients compared to non-psychiatric controls.

In a randomized, placebo-controlled cross-over design, varenicline was administered at 3 doses (0, 1, 2 mg/day) over 3 days with a 1-week washout period in n=15 (mean age 40.13±11.1 years) Schizophrenia patients and n=15 (mean age 39.80±10.6 years) non-smoking non-psychiatric controls. A cognitive battery was administered following the final dose of varenicline.

A two-way ANOVA with diagnosis and dose as the between-subject factors was performed on all of the cognitive measures and revealed a significant effect of diagnosis on spatial working memory (F(1,84)=19.416, p<0.001), verbal memory (F(1,84)=22.068, p<0.001) and attention (F(1,81)=6.462, p<0.013).

Overall patients performed better on the 1mg/day dose across these tasks, while controls perform better on the 2mg/day dose. There was no change in symptom severity with varenicline indexed by the PANSS.

These preliminary findings suggest potential dose dependent effects in a non-linear fashion in the patient group compared to controls, and are consistent with deficits in nAChR function in this disorder. These findings have implication for the treatment of cognitive dysfunction in Schizophrenia.
Genome-Wide Association Studies (GWAS) have identified single nucleotide variants (SNVs) significantly associated with psychiatric disorders. Most of these associations cannot be explained by a non-synonymous coding region change, therefore it is predicted that risk variants underlying psychiatric disorders alter gene expression, including gene splicing. The specific SNVs that contribute to splicing changes in these disorders and their functional consequences on the RNA and protein are unknown. This study aims to identify splicing SNVs contributing to risk for disease.

Four datasets of SNVs were mined with predictions of altered splicing and were compared to SNVs associated with Schizophrenia. The relationship between SNVs and splicing was tested using DNA and RNA from brain tissue samples from 97 controls. These individuals were genotyped for the SNVs and cDNA expression levels were tested to determine altered splicing.

Twenty-three Schizophrenia-associated SNVs were identified that were predicted to alter splicing. Upon filtering, nine SNVs in five genes were prioritized and were genotyped and tested for their cDNA expression in the brain samples. In one gene, APOPT1, two splicing isoforms were identified: the full-length transcript and a transcript containing a skipped exon that causes a truncated protein. These isoforms are being quantified to determine the relationship between their expression and the brain sample genotypes for three SNVs that predict this splicing change.

This study will identify functional splicing variants that may be contributing risk to Schizophrenia. This approach of identifying splicing variants will be applied to other psychiatric disorders as associations are identified.
Reduced endocannabinoid metabolism in early psychosis and cannabis use: A pilot PET study using [11C]CURB for fatty acid amide hydrolase (FAAH)

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The endocannabinoid system (eCBS) is involved in brain responses related to cannabis and stress. In vivo imaging of the eCBS in psychosis has been limited to receptors and no study has examined the eCB-catabolizing enzyme Fatty Acid Amide Hydrolase (FAAH) in vivo in psychosis. We investigated FAAH in untreated first episode psychosis (FEP) and in clinical high risk (CHR) for psychosis while controlling for cannabis use, using PET imaging with [11C]CURB, a specific ligand for FAAH.

We included 9 FEP, 5 CHR and 11 healthy participants (HV). Participants underwent MRI and [11C]CURB PET scans. Regional [11C]CURB binding ($\lambda_k$) was calculated using an irreversible 2-tissue compartment model with a metabolite-corrected arterial plasma input function.

Analysis revealed a trend towards an effect of clinical group in striatum and a significant effect in DLPFC, with lowest binding in FEP. A main effect of cannabis was observed in striatum and a trend in DLPFC with lower binding observed in cannabis users.

Data from this small pilot sample provide the first in vivo evidence that FAAH is altered in psychosis and perhaps in those at clinical high risk for psychosis, and that FAAH is further reduced in individuals concurrently using cannabis.
Adolescents are especially vulnerable to metabolic dysregulation induced by atypical antipsychotic (AAP) medications and anthropometric measures routinely used to monitor metabolic side effects may underestimate cardiovascular and metabolic risk in this pediatric population. With the increase in prescribing of AAPs for adolescents, a better understanding of the extent of these side effects is necessary, given their association with the development of medical comorbidities, e.g. cardiovascular disease and type 2 diabetes mellitus.

Thoracic and abdominal MRI scans were performed prior to antipsychotic administration and after 12 weeks of treatment. These scans provide gold-standard measurements of pericardial, hepatic and visceral adipose tissue, and are compared to anthropometric measures and serum indices of insulin resistance.

Preliminary scans support the utility of this experimental design, with noted increases in visceral and hepatic adipose tissue. Established type 2 diabetes is associated with increased hepatic adiposity, while normal fasting glucose is not.

Though data collection is ongoing, preliminary results highlight the degree of metabolic burden in young patients treated with AAPs.
Monoamine Oxidase A in Bipolar Depression

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Bipolar disorder type I (BD) is a serious psychiatric illness with a prevalence of 1%. BD consists of manic and major depressive episodes (MDEs), with MDEs being more frequent. Many MDEs, especially in BD, are treatment resistant to monoamine reuptake inhibitors. Monoamine oxidase-A (MAO-A) is a pro-apoptotic, oxidative enzyme that metabolizes mood-regulating neurotransmitters like serotonin, norepinephrine, and dopamine. MAO-A levels are greater in the MDEs of major depressive disorder (MDD) but have never been investigated in BD.

We scanned 13 BD individuals and 13 MDD subjects experiencing MDEs. Participants matched on age, sex, and Hamilton Depression Rating Scale scores. Participants were non-smokers and free of illicit substance use. One subject was taking a serotonin-norepinephrine reuptake inhibitor. All other subjects were medication-free. MAO-A total distribution volume (MAO-A VT), an index of MAO-A brain density, was measured in prefrontal cortex (PFC), anterior cingulate cortex (ACC), anterior temporal cortex, caudate, putamen, thalamus, hippocampus, and midbrain.

MAO-A VT was lower in BD versus MDD in the PFC and ACC (F2,23 = 9.8, p = 0.001; lower by 27% in both the PFC and ACC). Similar findings were present in the other regions sampled.

This is the first study to measure MAO-A VT in the MDE of BD. These results suggest that the function of MAO-A and its regulation of monoamine metabolism is different in the MDEs of BD compared with MDD. Our findings may help explain the less robust response of MDEs in BD to monoamine inhibition and/or reuptake strategies.
The Effects of Repetitive Transcranial Magnetic Stimulation on Suicidality in Treatment Refractory Depression

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The goal of this project is to determine the role of Repetitive Transcranial Magnetic Stimulation (rTMS) as a treatment for suicidality in patients with Treatment Refractory Depression (TRD), and to use response to rTMS as a tool to characterize a neuroanatomical endophenotype of suicide.

This study is a secondary analysis of two large prospective randomized controlled trials on the effects of rTMS on TRD. Treatment groups compared are: unilateral rTMS, bilateral rTMS and sham rTMS, all targeting the Dorsolateral Prefrontal Cortex (DLPFC). The primary outcome of this study is remission from suicide, measured by the suicide sub-score of the Hamilton Rating Scale for Depression (HRSD). Comparisons of suicide remission to depression remission and of baseline depression to baseline suicide will also be completed.

Preliminary results show a dose-response relationship, in which bilateral is significantly greater than sham (z=2.26, p=0.02), and unilateral is non-significantly greater than sham (z=1.31, p=0.19) in inducing remission from suicide. There appears to be a significant relationship between baseline suicide and depression scores (z=3.28, p=0.001). Analysis of rates of remission from depression versus suicidality, by treatment type, is underway.

Bilateral rTMS appears to be superior to sham for treatment of suicidality in patients with TRD. Depression and suicidality are closely related. Further analysis will help characterize the nature of this relationship and its implications for the diagnosis and treatment of patients with TRD and comorbid suicidality. Dysfunction of the right DLPFC may be particularly prominent in depressed, suicidal patients.
In-Depth Analyses of An Evolutionarily Conserved Region Downstream of the Melanocortin 4 Receptor (MC4R) Gene, Implicated in Antipsychotic-Induced Weight Gain (AIWG)

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MC4R is primarily expressed in the hypothalamus and plays important roles in the regulation of appetite, energy expenditure and homeostasis. Genome-wide association studies have identified genetic variants downstream of MC4R such as marker rs489693 to be associated with risks of obesity, type 2 diabetes and substantial antipsychotic-induced weight gain. This study is designed to explore the mechanism of the MC4R gene regulation and the effects of the risk genetic variants on the gene expression, eventually resulting in the disease.

Bioinformatics analysis was performed to explore the MC4R gene locus. An evolutionarily conserved region was identified, which likely regulates MC4R gene brain specific expression. A luciferase reporter assay was used to measure the enhancer activity of this regulatory element. Transcription factors (TFs) were then investigated which might bind to it. Such potential TFs are currently being constructed into a lentiviral plasmid. Gain- and loss-of-function strategy will be used to explore the relationship among brain specific TFs, RNA transcribed from this element and MC4R brain specific gene expression.

The evolutionarily conserved region was located 248kbp downstream of MC4R gene. The region contains two functional elements. One element transcribes a RNA (non coding RNA). The second element is a RNA enhancer, which drives the RNA expression differentially and regulates the MC4R brain specific expression.

In conclusion, our data provides first insights into a remote MC4R brain specific regulatory region that may represent an important aspect of its function at the hypothalamus.
To investigate whether predictors of suicide risk are associated with brain weight in First Nations suicide completers.

A file review was conducted at the Ontario Office of the Chief Coroner on individuals of First Nations ancestry who completed suicide between 2013-2014 (n=37). Data was extracted on method and approximate time of suicide, and history of mental illness, psychiatric treatment, substance abuse/dependence, suicidal gestures, proximity to other suicides, stressful life events, and criminal involvement. Post-mortem brain weight (in grams) was analyzed across these factors using analysis of covariance (ANCOVA).

First Nations suicide completers consisted of 14 males (37.8%) and 23 females (62.2%) between 12-50 years (24.19±9.7 years) primarily living on-reserve (n=23, 62.2%). Thirty-three cases (89.2%) used hanging as their method of suicide compared to 2.7% of cases for each of carbon monoxide inhalation, drug overdose, firearms usage, and vehicular trauma. The most frequent time of death was overnight (n=25, 67.6%).

Post-mortem brain weight was significantly associated with gender, with higher brain weight among males (1481±98.8g vs.1374.43±124.7g, p=0.010). Age (p=0.733) and suicide method (p=0.110) were non-significant predictors. Gender was entered as a covariate. Using ANCOVA, history of psychiatric treatment was nominally associated with a lower post-mortem brain weight (1385.54±132.6g vs. 1430.58±121.5g, p=0.064). All other variables were non-significant.

Suicide risk factors may not directly affect post-mortem brain weight in First Nations suicide completers but use of psychiatric treatments may have limited influence. Future directions include increasing the sample size, and examining brain weight between suicide completers and age/gender-matched healthy controls.
Recent studies have demonstrated that mTORC1 activation may be related to the antidepressant action. However, the relation between mTORC1 signaling activation and currently prescribed antidepressants have not been well elucidated.

The aim of the present study was to find out whether alterations in mTORC1 signaling could be observed following treatment with tianeptine under toxic conditions induced by B27 deprivation. Additionally, we investigate whether this drug affect the synaptic proteins, neurite outgrowth and spine density via mTORC1 signaling.

Using Western blotting, we measured the phosphorylation levels of mTORC1, 4E-BP-1, p70S6K, Akt, and ERK in rat primary hippocampal neuron. Changes in BDNF, dendritic outgrowth, spine density, and synaptic proteins (PSD-95, synaptophysin, and GluR1) were measured.

Tianeptine significantly increased the phosphorylation of mTORC1, 4E-BP-1, p70S6K, Akt, and ERK. The increase in mTORC1 phosphorylation was blocked by the PI3K, MEK, and mTORC1 inhibitors. Tianeptine increased BDNF, dendritic outgrowth, spine density, and synaptic proteins, which were blocked by the mTORC1 inhibitor.

In this study, we demonstrated that tianeptine activates the mTORC1 signaling pathway and increases dendritic outgrowth, spine density, and synaptic proteins through mTORC1 signaling under toxic conditions.
Cannabis use is often higher among people with psychoses than the general population. Cannabinoids including cannabis, have been suggested to have neuroprotective and anti-inflammatory effects. This is particularly important as neuroinflammation has been implicated in the pathophysiology of several brain disorders including Schizophrenia. The aim of this study is to image neuroinflammation in-vivo in individuals at clinical high risk (CHR) for psychosis and healthy volunteers (HV) with concurrent cannabis use (CHR-CU and HV-CU, respectively) in comparison to HVs.

Eighteen HVs, 7 HV-CUs and 2 CHR-CUs underwent a baseline assessment, a MRI scan and a high resolution [18F]-FEPPA PET scan to quantify neuroinflammation in-vivo in brain. All participants completed a series of neuropsychological and clinical assessments. Images were analyzed using the validated two-tissue compartment model to obtain total distribution volumes (VT) in the hippocampus and dorsolateral prefrontal cortex.

No significant differences in [18F]-FEPPA binding were observed between groups. Similarly, no significant correlations were observed between [18F]-FEPPA VT and measures of psychopathology or cognition. However, in HV-CUs, there was a positive trend toward significance between the marijuana craving questionnaire and [18F]-FEPPA binding, which did not survive correction for multiple comparisons.

This is the first in-vivo study to investigate the role of cannabinoids on neuroinflammation, and its relevance for psychosis. Results, although preliminary, suggest no difference in the level of neuroinflammation between CHR-CUs and HV-CUs compared to matched HVs. Increased sample size is required to confirm the results.
The objective of this study was to evaluate the feasibility of using paired-associative stimulation (PAS) to study excitatory and inhibitory plasticity in adolescents while examining variables that may moderate plasticity (e.g., sex, environment).

We recruited 34 healthy adolescents (aged 13-19, 13 males, 21 females). To evaluate excitatory plasticity we compared mean motor evoked potentials (MEPs) elicited by single-pulse TMS before and after PAS at 0, 15, and 30 min. To evaluate inhibitory plasticity, we concomitantly evaluated the cortical silent period (CSP) elicited by single-pulse TMS in the pre-activated hand before and after PAS at 0, 15, and 30 min.

All participants who began PAS completed the study. No adverse events occurred. PAS was well tolerated. PAS induced significant increases in the ratio of post-PAS MEP to pre-PAS MEP amplitudes (p
Depression is highly prevalent and associated with worse prognoses in patients with coronary artery disease (CAD). Oxidative stress, and particularly lipid peroxidation, represents an emerging mechanism implicated in both depressive and cardiovascular etiopathologies, but its role in depression has yet to be examined in CAD. The objective of the present study was to elucidate the relationship between lipid peroxidation and depressive symptoms in CAD patients.

Depressive symptoms were assessed with the self-administered Center for Epidemiological Studies Depression Scale (CES-D). Lipid hydroperoxides (LPH), early-stage products of oxidative damage to lipids, as well as the late-stage lipid peroxidation markers 4-hydroxynonenal (4-HNE) and 8-isoprostane (8-ISO) were measured using spectrophotometric assays from serum samples provided by study patients. Ratios ((4-HNE+8ISO)/LPH) were calculated to reflect lipid peroxidation progression.

In patients with CAD (n=84, mean age=61.3±8.5, 76.2% male, mean BMI=28.4±4.0), a general linear regression model found that a higher lipid peroxidation ratio was associated with higher CES-D scores (adjusted R2=0.139, B=0.272, p=0.009) after controlling for age, gender, BMI, and antidepressant use.

Oxidative stress, and ensuing conversion of early- to late-stage lipid peroxidation, may be an important correlate of depression in a CAD population. Further investigating markers of lipid peroxidation may help to better characterize the pathways underlying depression in CAD and reveal potential biomarkers of etiologic and prognostic value to this patient population.
The brain-derived neurotrophic factor (BDNF) plays an important role in the development of the central nervous system and is known to regulate food intake. Recently, the dopaminergic pathway was linked to spontaneous food intake in pre-school children. Since BDNF plays an important role in the development and maintenance of dopaminergic neurons, BDNF Val66Met (rs6265), a functional polymorphism, may also be linked to an impulsive eating trait. We sought to determine whether BDNF Val66Met predicted performance on two neurocognitive measures of response inhibition relevant to eating behaviour in pre-school children.

We investigated the association between BDNF Val66Met and two measures of response inhibition in a developmental cohort: The Snack Delay Task (at age 3) and The Stop Signal Task (at age 4). Gender was used as a covariate and then as an interaction term.

Results indicate a genotype by gender interaction on Snack Delay Task performance ($F = 6.322, df = 1, p = 0.013$). Upon stratification by gender, the Met allele in males ($F = 7.859, df = 1, p = 0.006$) was associated with a lower score on the Snack Delay task, which is indicative of an impulsive phenotype.

These results suggest that male carriers of the BDNF Met allele may have a more impulsive trait detectable only in the context of a food stimulus. Since the Snack Delay has been reported to be associated with BMI, performance on this task could be a mediator between the effects of BDNF Val66Met and an overeating phenotype.
Ischemic stroke impacts cognitive functions such as memory. Increased brain volume after drug treatment has been associated with improved verbal memory. Lithium has been shown to increase grey matter volume in bipolar patients. Therefore, we hypothesized that treatment with the neurotropic agent lithium would be associated with improvement in verbal memory in post-stroke patients.

Patients who met the WHO-NINDS criteria for a recent (< 1 year) ischemic cortical stroke (confirmed by MRI) were given lithium carbonate, open-label, for 60 days (0.4-0.8mmol/L target). Verbal memory (delayed recall in Hopkins Verbal Learning Test-Revised [HVLT-R], primary), stroke severity [NIHSS] and cognition (Montreal Cognitive Assessment [MoCA], Standardized Mini-Mental State Evaluation [sMMSE]) were assessed at baseline and termination, and compared using repeated-measures ANOVA, with cumulative lithium dose as a covariate.

To date, 11 patients (45% male, mean [SD] age = 70.3 [12.1], sMMSE = 26.8 [3.4], MoCA = 20.9 [5.0], HVLT-R delayed recall z-score = -1.3 [1.0]) have been recruited, on average, 87 (±68) days after mild stroke (NIHSS score ≤ 2). Cumulative lithium dose received ranged from 0 (screen drop) to 26850mg. Lithium was discontinued in 3 patients for tolerability reasons but there were no serious adverse events. Cumulative lithium dose was significantly associated with improvement in delayed recall over time (F = 5.41, p = 0.045). There was no association between lithium and changes in other measures.

These initial results suggest that lithium treatment may be associated with improved verbal memory after stroke, with a preliminary signal suggesting a dose-response relationship. These findings are consistent with lithium’s suggested neuroprotective and neurotrophic effects.
Our thoughts, behavior and emotions are influenced by our personality. Observable personality is characterized primarily by neuroticism, extraversion, openness, agreeability and conscientiousness, and are thought to be represented by specific brain networks. Neuroticism, characterized by emotional fluxes, displays tonic activity in the frontal hemispheres. In this study, we aim to compare personality traits against neural oscillatory activity in the frontal cortex. Specifically, this study will use electroencephalograph (EEG) activity as a proxy for spectral differences across neuroticism.

EEG recordings were obtained from 23 healthy participants while they completed the computerized 2-back memory task (15 minute duration). Participants also completed the NEO-Five Factor Inventory measuring the 5 domains of personality. Finally, DNA was collected from blood or saliva samples. A Fourier analysis (FFT) was used to quantify neural oscillations from the EEG sessions.

The NEO-FFI data indicate that neuroticism ranged from 20 to 59 with a median score of 25.5. Average delta FFT power ranged from 31.1 percent to 88.9 percent with a median power of 54.0 percent. An inverse correlation can be seen between neuroticism and average delta FFT; individuals with lower neuroticism displayed higher average delta FFT in channels across the prefrontal cortex.

Baseline EEG’s could be used as a substitute for objective assessment of personality if neural oscillatory activity could be quantified to illustrate personality domains. Specifically, oscillatory activity in areas we know to be representative of traits such as neuroticism, could function as an alternative diagnostic measure for identifying psychopathological states.
There is evidence in the literature for an association between atopic disorders (asthma, atopic dermatitis, allergic rhinitis/conjunctivitis, environmental allergies) and ADHD in childhood, most recently summarized in a systematic review concluding in 2010. The goal of this systematic review is to determine the current level of evidence for this association, as well as any potential mechanisms.

A systematic literature search was conducted in February-March 2016 for studies published from 2010 to 2015. Electronic searches through Medline and PsycINFO was supplemented by manual search.

This review included thirteen studies (eight case control, three prospective cohort, two cross-sectional). All studies reported a statistically significant elevation in risk ratio (HR, OR, RR) for ADHD in children with at least one atopic disorder, relative to controls. Asthma was the most frequently studied atopic disorder. One study reported a statistically significant dose-dependent relationship between the number of atopic comorbidities and risk of developing ADHD. All three prospective cohort studies demonstrated that early atopic disorders predisposed children towards ADHD in later years. Three studies showed that both ADHD and atopic disorders were positively correlated with higher urbanization. Two twin studies for shared genetic risk failed to achieve statistical significance. There was significant variability in study design, including assessment instruments and populations.

The studies included in this systematic review all report findings in support of an association between atopic disorders and ADHD. However, there is significant variability in study design. Additionally, there is a shortage of good quality evidence regarding possible mechanisms.
Neurocognitive deficits are evident in youth and adults with bipolar disorder (BD). In psychiatrically healthy populations, retinal vascular caliber, which is a proxy for cerebral microvasculature, has been shown to be associated with cognitive deficits. This study examines the association between neurocognition and retinal vascular caliber among adolescents with BD.

Subjects were 14 adolescents with BD and 15 psychiatrically healthy control (HC) adolescents (13 - 20 years old). Neurocognition was measured using the Cambridge Neuropsychological Tests Automated Battery. Retinal vascular structure was measured with Analyze 12.0 software, using digital retinal photographs to measure central retinal artery equivalent (CRAE) and central retinal vein equivalent (CRVE).

In the whole group (BD + HC) poorer performance on the Rapid Visual Information Processing task, a task of sustained attention, was associated with narrower CRAE ($\rho = 0.377$, $p = 0.044$). Furthermore, within the BD group, CRVE was correlated with performance on frontal-executive tasks, including the Stockings of Cambridge (SOC) task and the Intra-Extra Dimensional set-shifting task (IED). Wider CRVE was negatively associated with SOC performance in the BD group, but not in the HC group ($r = -0.577$, $p = 0.031$ and $r = -0.209$, $p = 0.455$, respectively). Wider CRVE was also negatively associated with IED performance in the BD group, but not in the HC group ($\rho = -0.538$, $p = 0.047$ and $\rho = 0.349$, $p = 0.203$, respectively).

Preliminary evidence indicates that retinal vascular caliber is associated with frontal-executive dysfunction among adolescents with BD but not among HC. Direct visualization of retinal vasculature may offer insights regarding the vascular-cognition link in adolescent BD.
Bipolar disorder (BD) confers risk of increased and premature cardiovascular disease (CVD) compared to the general population. Non-invasive retinal imaging methods can potentially offer insights regarding underlying biology linking BD and CVD. We examined whether cardiovascular risk factors (CVRFs) and inflammation were associated with retinal vascular caliber in adolescents with BD and healthy controls (HC).

Subjects were 30 adolescents (16 BD, 13 HC), 13 - 20 years old. Semi-structured interviews (KSADS-PL) determined diagnoses. Retinal photographs were analyzed with ANALYZE 12.0. to determine central retinal arteriolar equivalent (CRAE) and venular equivalent (CRVE). Narrower CRAE and wider CRVE have been associated with CVRFs. Inflammation was determined based on blood levels of high-sensitivity C-reactive protein (hsCRP).

In HC narrower CRAE is associated with higher systolic blood pressure ($\rho = - .591, p = .033$), and higher BMI ($\rho = - .659, p = .014$). In BD, wider CRAE is associated with higher hsCRP ($\rho = .503, p = .047$), and lower diastolic blood pressure ($\rho = - .587, p = .017$). There were meaningful nonsignificant differences in CRAE and CRVE between symptomatic and asymptomatic BD adolescents ($d = 0.41$-$0.55$). There were no significant differences between HC and BD groups for CRAE or CRVE.

This study found that retinal vascular structure is associated with CVRFs among both BD and HC adolescents, in a manner consistent with prior studies. Inflammation has been previously associated with wider CRVE; the unexpected association between hsCRP and wider CRAE warrants confirmation in a larger sample. Retinal vascular imaging may offer insights regarding the relationship of peripheral inflammation and CVRFs with cerebrovasculature.
Differences in substance use and treatment seeking motivation have been studied across various subgroups. Youth have recently become more represented in this research (Goodman et al., 2015). The aim of the present study is to examine the influence of age and gender on the way that youth view the pros and cons of their substance use, and how these factors influence their readiness to change and motivation to seek treatment.

Data were collected from 164 youth (60.4% male) aged 15-24 (M=19.49) presenting to an outpatient treatment program for substance abuse and concurrent disorders in Toronto, Canada. Youth completed the following measures: the Substance Use Decisional Balance Scale to assess pros/cons of their substance use, the Treatment Entry Questionnaire to assess motivation, and the Contemplation Ladder to assess readiness to change.

Results showed that female youth endorsed significantly more pros of their substance use than males. Moreover, endorsing more pros of substance use was positively correlated with external motivation and a low score on the Contemplation Ladder. In contrast, endorsing more cons of substance use was associated with internal motivation and a high score on the Contemplation Ladder. Lastly, age was positively correlated with readiness to change, internal motivation, and the endorsement of more cons of substance use.

This study expands upon previous research and demonstrates that, in youth seeking substance use treatment, there are both age and gender differences in reasons for substance use. Implications for gender-informed and developmentally-informed treatment will be discussed.
There are anatomical, physiological and hormonal differences in the brain of males and females. Recently, there has been increased research suggesting that occurrences and recovery from traumatic brain injury (TBI) may be affected by these differences. To our knowledge there are limited studies analyzing the difference in clinical outcome between the sexes following a TBI event. The purpose of this study is to determine whether there is significant difference in how the sexes overcome brain injury and how clinicians can utilize this difference to make personalized treatments.

We will review 100 head injury patients seen by Dr. Shree Bhalerao (50 males and 50 females) and analyze key markers of brain injury. The data collection will be from Dr. Bhalerao’s consult notes, questions 1-12 on the Concussion Care Strategy Ontario Clinician Report Measures, and the Concussion Care Strategy Baseline Patient Questionnaire. Furthermore, we will be conducting a t-test and chi square test to analyze statistical significance.

Our REB application is pending thus the data has not been collected yet, however, the results and implications will be complete in the next few weeks. We predict females will have less occurrences and more successful recovery when faced with TBI.

Once our data is collected, we expect to find a statistically significant difference between male and female outcome following TBI. Specifically, we expect to find that females have faster rates of recovery. Our findings can result in doctors reinventing their strategies and procedures for patients suffering from TBI.
Patients with neurosurgical issues are at a high-risk of psychiatric issues post-operatively. Neurological disease, in combination with surgical manipulation and medication use increases the likelihood for delirium, mood symptoms, and psychosis. However, empirical literature is lacking in this area. This project aims to examine this gap for future areas of research.

We conducted a scoping review of the current existing literature on this subject, by searching three online databases MEDLINE, EMBASE, and PsychINFO. Articles were screened for relevance through a step-wise process reviewing titles, abstracts, and full articles. Reference lists of included articles will also be hand searched. In addition, a retrospective cohort review of consecutive referrals from the neurology, neurosurgical, and neurological ICU services to a Consultation-Liaison Psychiatry Service over a four year period was conducted.

The initial literature search identified 12,456 articles. A preliminary review indicated that the majority of articles on this topic are theoretical overviews, with few exploring it empirically. Over a four year period, 181 referrals to CL psychiatry were received. Among 181 referrals, 71 were from neurosurgery, with mood assessments (n=30, 42.3%) and confusion (n=13, 18.3%).

Based on our preliminary review of the literature, there is a lack of empirical data on the relationship between neurosurgical interventions and psychiatric presentations. Empirical work in this area could improve the care of patients with these complex disorders.
Acute intermittent porphyria is a rare entity that classically presents with acute episodes of abdominal pain, behavioral abnormalities and in rare occasion neurological symptoms like tetraplegia. Given the rarity of this disease, and its high morbidity, it is important to research and understand management options, especially for psychiatric symptoms.

Here we will present a case of a 24 year old female with AIP and concomitant anxiety that hampered her medical recovery, and discuss the therapeutic challenges faced when managing anxiety in an AIP patient, and how tailoring a visualization psychotherapeutic approach could be a viable and sufficient option for similar patients.

Tailoring visualization tools that focused on non-bodily functions (colors, distraction techniques, visualization of safe places) deemed extremely helpful in a patient with AIP suffering from anxiety and tetraplegia, and who otherwise has maximized on their pharmacotherapeutic options. The patient demonstrated a considerable improvement in anxiety symptoms, was successfully titrated off her vent and was able to participate effectively in the remainder of her treatment plan.

This is an important case study of an otherwise poorly understood highly morbid illness. Given the few cases published, and the unclear management approach this case study highlights the importance and value of visualization tools in patients with severe AIP, especially those presenting with tetraplegia, patients admitted to the ICU or patients that are intubated.
Whether or not antidepressants can be safely prescribed to patients with carcinoid/neuroendocrine tumor (NET) is a controversial topic. Some have argued that antidepressant use precipitates carcinoid syndrome and should be avoided in patients with carcinoid/NET. Others have reported long-term antidepressant use with no adverse outcomes. To our knowledge, no systematic reviews of antidepressant use in carcinoid/NET exist. We aim to address this gap.

We searched five databases: CENTRAL (Wiley Cochrane Library), CINAHL (EBSCO), EMBASE, PsycINFO (OVID), and PubMed. The strategy consisted of synonyms for “antidepressive agents” OR synonyms for “depression”, then limited to the concept “carcinoid”. Identified articles were independently reviewed. The project was developed according to PRISMA guidelines. Outcome measures included demographics, antidepressant name, dose, duration, and frequency, as well as frequency of adverse outcomes related to the antidepressants.

The initial search identified 679 articles for possible inclusion. After screening by independent reviewers, 17 articles met inclusion criteria. Three cases report on adverse outcomes while nine cases report no adverse outcomes. At least 25 additional cases were reported to be taking antidepressants though details were not provided.

There is an overall lack of robust evidence to suggest avoiding antidepressants in patients with carcinoid/NET. We hope that our findings will also help guide future research in this understudied area.
Informal caregivers make significant contributions to the overall care of cancer patients, and trends toward longer survival and more ambulatory and home care of advanced cancer patients increase the length of time their caregivers are burdened. As a first step in developing an intervention for the caregiver population, we obtained focus group feedback on caregiver-identified intervention needs, perceived barriers to intervention access and completion, and strategies to address these obstacles.

We completed 2 focus groups, one with current informal caregivers, and one with past (bereaved) caregivers. Focus groups were 90-min long, and were audiotaped and transcribed verbatim.

Content analysis assisted in identifying important needs of informal caregivers, including information needs regarding palliative care and advance care planning, as well as the need for time and space to attend to their own emotions and their own losses and adjustment. Our analysis also identified important factors that facilitate informal caregivers' resilience as well as barriers that challenge informal caregivers’ ability to access support.

This study is the first step in developing an intervention for the caregiver population, and has important implications for theoretical understanding, clinical intervention, and social policy regarding the wellness of informal caregivers of advanced cancer patients.
We have long been of the view that if one asked the average physician to write a three page essay on the function of the heart, lungs or kidneys they would have little difficulty. However if the task was to write on the function of sleep they would be hard pressed to write more than a page.

In the meantime Donald Weaver, a renowned neurologist, researcher, the director of the Krembil Research Institute, promoting his the most recent discovery about maple syrup may prevent Alzheimer’s sparks via the massive engagement of mass media and social networks, emphasizes the importance of educating the society.

We have created a number of easy to read booklets which are highly illustrated and visually appealing.

They are on a range of topics - some sleep related (e.g. SLAM jet-lag; Working the Shift) and others on topics in which sleep is a pertinent component of the problem (e.g. Don’t Tic me off (on Tourettes).

The book was distributed via the link Toronto Sleep Clinics, Ontario Sleep Clinics - For a Better & Healthier Sleep to healthcare professionals and families; and the response rate was high.

These booklets have had a significant impact on the community education about sleep importance in children and adults as well as its link to physical and psychological wellbeing. The issue of educating children about sleep needs to be a higher priority and we urge sleep specialists to consider doing this in a more concerted way.
An Intersectional Approach to a Scoping Review of the Empirical Literature on Immigrant and Refugee Youth Mental Health in Canada

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This study summarizes the findings of an intersectionality informed scoping review (using Arksey, & O'Malley’s five-stage framework, 2005) that addresses the question “what does the literature on immigrant and refugee youth in Canada inform us about the intersection of gender, race/ethnicity, culture, age, and socio-economic class on immigrant and refugee youth mental health at personal, family and societal level?”

PubMed, Sociological Abstracts, Social Sciences Abstracts, CINAHL, and PsycINFO databases were searched for published, peer reviewed primary studies between the year 1995-2015 focusing on the mental health of non-precarious status immigrant and refugee youth (ages 13-24) in Canada. Using a combination of search terms, fourteen selected studies met inclusion and exclusion criteria.

Three broad themes were identified 1) Determinants of mental health 2) Coping and adaptation, and 3) Racism and discrimination. Determinants of mental health included school adjustment, parent-child relationships problems, and intra-personal conflict. Ethnic identity and perceived discrimination affected sense of belonging and mental health. Family, school and cultural connectedness reduced settlement stress, developed resilience, and improved mental health. Gender was a powerful influence on perceptions of mental health and coping/adaptation strategies.

An equity perspective in research, practice and policy is essential. Through a “whole community approach” to promoting resilience, and integration of inter-sectoral and anti-discriminatory approaches in schools, resettlement services, and health and social systems immediate challenges (such as language competencies, family economic barriers) and long-term integration outcomes (such as school success, cultural inclusion) immigrant and refugee youth’s positive mental health can be supported.
The Online Psychiatric Education Network (OPEN) Neurobiology of Trauma module takes an innovative approach to educating family physicians to build capacity for assessment and management of trauma and PTSD. This continuing professional development (CPD) eLearning initiative was jointly developed by psychiatrists and biomedical communication specialists from Women’s College Hospital and the University of Toronto.

A novel series of medical animations were created to convey clinical information in an unfolding case scenario. Medical visualizations were designed to provide explanations of the neurobiology of trauma. Animations are encapsulated within an educational framework to support knowledge building and translation to practice. A design research case study was conducted with a sample population of family physicians and psychiatrists.

Pre/post test results and eLearning Survey outcomes from Likert-scale questions and open-ended qualitative responses will be reviewed. Feedback on eLearning design, usability, interactivity, and content clarity will be incorporated in the iterative design process. Medical animation samples and design research results will be presented.

The final Trauma module will be offered a CPD course through the Faculty of Medicine, University of Toronto. A second study will be conducted at the time of implementation to assess physician knowledge translation outcomes, i.e., changes in practice and patient care.
Poster Presentation #53 (Geriatric Psychiatry)

Evaluating the Association Between Neural Oscillations and Working Memory in Individuals with Remitted Late-Life Depression

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Reza Zomorrodia, Centre for Addiction and Mental Health;
Zaid Ghazalaa, Centre for Addiction and Mental Health, University of Toronto;
Daniel M. Blumberger, Centre for Addiction and Mental Health, University of Toronto;
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Working memory impairments among persons with late-life depression (LLD) are prevalent; yet little is known about the mechanisms underlying these impairments. Neural oscillations, specifically theta, gamma, and the modulation of gamma by theta (i.e. theta gamma coupling), are essential to memory functioning. This study aims to evaluate the association between neural oscillations and working memory in LLD.

Sixteen participants with remitted LLD (Mean age = 71.8, SD = 5.0) and seventeen older controls (Mean age = 75.2, SD = 5.4) performed the N-back memory task, at three memory loads (1-, 2- and 3-back). Oscillatory activity was assessed using electroencephalography (EEG) during N-back performance.

There were no significant accuracy differences between the LLD and control groups. However, a repeated measures ANOVA for reaction time revealed a group*memory load interaction (p = 0.03), with a slower reaction time in the LLD group on the 3-back [t(31) = -2.414 p = 0.022]. While there were no significant group differences on gamma (p = 0.52) or theta gamma coupling (p = 0.17), a repeated measures ANOVA for theta revealed a main effect of group (p = .027), with significantly higher theta in the LLD group at the 1- and 2-back. [t(20.6) = -2.2, p = 0.036 and t(26) = -2.35, p = 0.027].

Our results suggest that compared to older healthy individuals, those with remitted LLD may be able to maintain a similar level of working memory accuracy, yet at a slower pace and with increased theta activity. Confirmation of these findings in a larger sample is needed.
This project will assess the impact and feasibility of implementing a collaborative care evidence-based Integrated Care Pathway (ICP) in addressing three risk factors for developing Alzheimer’s Dementia: anxiety, depression, or mild cognitive impairment (MCI). This is a combined multi-site quantitative and qualitative study.

The quantitative component is a longitudinal prospective cohort study examining the impact of the ICP on diagnosis rates, time-to-treatment initiation, and impact of the ICP on patient outcomes among participants with anxiety, depression or MCI. The qualitative component will utilize a qualitative descriptive design (i.e. surveys and focus groups) to examine the process of implementation of the ICP in primary care settings.

We will recruit 75 clinic patients born in 1951 or 1955, who will go through the diagnostic and treatment stages of the ICP. We will compare them to 75 clinic patients born in 1952 and 1956 receiving treatment as usual.
A recent Health Canada warning limited the maximum recommended dose of citalopram and escitalopram because of potential for QTc prolongation, based on limited scientific evidence. We conducted a retrospective study to assess the association between citalopram/escitalopram and QTc interval, torsades de pointes, or sudden cardiac death in a sample of older adults.

Electronic health records from Baycrest were searched from April 2008 to July 2015 to identify patients on citalopram/escitalopram who had an EKG within 90 days following the initiation or dosage change of these medications. When available, baseline EKGs were included for analysis to determine absolute change in QTc interval following changes in medication dosage. Charts were reviewed for reports of torsades de pointes or sudden cardiac death. We also recorded medical conditions and medications that can prolong the QTc interval.

Sixty-four patients on citalopram (25 males, mean age: 83 years) and 27 patients on escitalopram (10 males, mean age: 80 years) were identified. We will use linear regression to examine the impact of drug dosage on QTc as a continuous measure. Covariates (e.g., age, gender, medication conditions, other medications) will be assessed for their association with QTc. Those significant at $p < .10$ will be included in the multivariable model.

These findings will allow clinicians to better understand the impact of citalopram/escitalopram on the QTc interval and, therefore, be able to weigh the risk and benefits of higher dosages in an older adult population.
Major Depressive Disorder (MDD) is a major risk factor for suicide. Familial, adoption, and twin studies suggest that the risk for suicide is both genetic and heritable. However, to date, there are no robust genetic predictors of suicide or suicide attempt in major depression. Several serotonin genes have been studied as candidate genes in suicidal behaviour such as HTR1A, HTR2A, HTR1B, HTR2C, TPH1, TPH2, 5HTT, and MAOA. The findings drawn from candidate gene studies in suicidal behavior are inconsistent.

We genotyped 18 functional variants of eight selected serotonin genes in a well characterized sample of older patients with MDD (n=466). The genetic variants of each gene were compared between suicide attempters and non-attempters using Pearson chi-square.

We found rs25531, HTTLPR, and 5HTT-VNTR in intron 2 in 5HTT significantly associated with suicide attempt.

We found that the G allele in the HTTLPR region is associated with suicide attempt, suggesting that this rare variant should be analyzed independently from the nearby long/short polymorphism. All previous studies on suicide attempt have neglected or combined this rare variant with the long/short polymorphism. Future studies need to confirm that the G allele in the HTTLPR region should be considered as a single marker in studies of genetic predictors of suicidality.
Standardized care is growing in popularity but has limited presence in psychiatry.

At CAMH, a Late-Life Schizophrenia (LLS) Care Pathway was implemented with 105 patients currently enrolled. Indicators assessing pathway compliance include monitoring side effect burden of antipsychotic agents and cognition. Overall compliance was 84% and only 5 patients were on medications that deviated from the Integrated Care Pathway (ICP) algorithm and 8% of patients were on two antipsychotic agents.

In the literature however, only six studies assessed efficacy of ICPs in Schizophrenia. Five were trials involving some form of control group without randomization and one had no comparator. Only two studies demonstrated positive results in favor of ICPs in clinical outcomes such as reduced use of restraints. These studies had variable designs and methodological limitations that make interpreting effectiveness difficult and none focused on late-life Schizophrenia.

This study will
1. Review evidence for standardizing care in LLS
2. Discuss development and implementation of LLS Care Pathway
3. Discuss evaluation of LLS Care Pathway

This presentation will examine the process of developing, implementing and evaluating the efficacy of a standardized pathway for a late-life Schizophrenia clinic.

To date we have consented and screened 16 subjects, 11 were randomized to LLS-ICP or TAU. 7 subjects completed the acute phase and 1 was lost to follow up. 4 clients experienced serious adverse events.

The LLS-ICP can promote more evidence based care that is patient focused, avoids pitfalls such as polypharmacy and failure to monitor side effect burden. These can directly impact cognitive and functional outcomes. The LLS-ICP reduces unnecessary variations in care which results in more complete, accessible data collection for audit. There is a need for more robust data to support these outcomes.
Cognitive impairment is considered a core feature of bipolar disorder, major depressive disorder, and Schizophrenia and it is linked to associated functional disability and poor quality of life. The nature and course of cognition and related function remain unclear across the lifespan of patients with these disorders. The objective of this systematic review is to clarify the relationships among aging, cognition, and function in these populations and identify potential predictors, moderators, or mediators of change across the adult lifespan. To our knowledge, this is the first review to systematically compare the longitudinal trajectory of cognition and function across these three diagnoses.

PUBMED, PsychINFO, and Embase databases were searched for each diagnosis using variants of "cognition" AND "function" AND "longitudinal" OR "follow-up." Our search was completed on September 1st, 2015 and identified a total of 538 unique articles that were independently reviewed by two authors for study inclusion. A total of 463 articles were excluded.

Overall, 75 studies met inclusion criteria and were included in the analysis. Preliminary results suggest cognition is a predictor of function across all diagnoses. However, the strength of this association and cognitive domain type varies among diagnostic groups.

Our preliminary analysis suggests that the longitudinal trajectory of cognition and function differs with respect to diagnostic group. However, available studies are limited by follow-up period and the lack of using objective performance-based functional assessments.
Deficits in frontal lobe functions including deficits in working memory are common across all stages of Alzheimer’s disease (AD). Working memory has been found to correlate with frontal cortical oscillations in theta and gamma bands and in particular the modulation of gamma amplitude by theta phase (theta-gamma coupling) in healthy individuals. These neurophysiological mechanisms depend upon robust synaptic neuroplasticity. Paired associative stimulation (PAS) involves repetitive pairing of electrical stimulation of the median nerve with transcranial magnetic stimulation (TMS) pulse to contralateral DLPFC. PAS simulates the induction of long-term potentiation, a prototype of synaptic neuroplasticity. Relevance of these measures of neuroplasticity in AD has not been investigated so far.

Participants with early AD and healthy controls (Mini Mental Status Exam score ≥16) are enrolled in this study. Baseline measurement of neuroplasticity are done using electroencephalography (EEG) during PAS and N-Back working memory test (PAS-EEG and N-Back-EEG). Participants are then randomized to receive a 2-week course of active PAS (PAS-25) or control condition (PAS-100).

Preliminary findings from baseline data suggest that as compared with healthy individuals, participants with AD have, (1) impaired DLPFC neuroplasticity as measured by PAS induced cortical evoked activity, (2) impaired performance on the N-back task, (3) impaired theta-gamma coupling in association with impaired N-back performance (data will be presented at the meeting).

TMS-EEG can index neuroplasticity deficits in early AD. Theta gamma coupling can serve as a surrogate marker of neuroplasticity and impaired working memory in early AD.
Antipsychotics have been associated with cognitive deficits in persons with Schizophrenia, which in turn are strong predictors of function in this population. However, little is known on antipsychotics impact on function. This is highly relevant to older persons with Schizophrenia as function declines with age.

Sixty clinically stable participants with Schizophrenia, age 50 or above, were assessed using UPSA Communication and Comprehension/Planning domains and divided into three groups: low antipsychotic burden (LOW) (equivalent of = 6 mg of risperidone). Two multiple linear regressions were used to assess the association between antipsychotic burden groups and Communication or Comprehension/Planning, co-varying for age, gender, education, and PANSS.

Sixteen participants (Mean Dose = 1.2 mg, SD = 0.7) were classified in LOW, 23 participants (Mean Dose = 4.1 mg, SD = 1.2) in MED, and 21 participants (Mean Dose = 9.7, SD = 4.6) in HIGH. Antipsychotic burden group was associated with only Comprehension/Planning (p = 0.007). Post-hoc analyses showed that LOW group performed significantly better than MED (Cohen’s d = 0.91) and HIGH (Cohen’s d = 0.97) groups, and no difference in performance between MED and HIGH groups.

Medium and high antipsychotics burden had a large negative impact on comprehension and planning capacity of older persons with Schizophrenia. This raises the question of whether high antipsychotics burden contribute to cognitive and functional decline in this population.
Impaired insight into illness in Schizophrenia is associated with illness severity and deficits in premorbid intellectual function, executive function, and memory. In a previous study of patients aged 60 years or above, we found that illness severity and premorbid intellectual function accounted for variance in insight impairment.

Using one large sample of participants (n=171) with Schizophrenia aged 18 to 79 years, we aimed to test whether similar relationships are observed in earlier life. We assessed insight into illness using the Positive and Negative Syndrome Scale (PANSS) item G12 and explored its relationship to illness severity (PANSS Total Modified), premorbid intellectual function (Wechsler Test of Adult Reading, WTAR) and cognition.

Insight impairment was more severe in later life (≥60 years) than in earlier years (t=3.75, p<0.001). Across the whole sample, the variance of impaired insight was explained by PANSS Total Modified (Exp(B)=1.070, p<0.001) and WTAR scores (Exp(B)=0.970, p=0.028). Although age and cognition were correlated with impaired insight, they did not independently contribute to its variance. Age, however, strengthened the relationships between impaired insight and illness severity, and cognition, particularly working memory.

These results suggest there may be opportunity for intervention with cognitive enhancing neurostimulation or medications to improve insight into illness in Schizophrenia across the lifespan.
Cognitive deficits are among the strongest predictors of function in individuals with Schizophrenia. No pharmacological interventions reliably improve these impairments. As patients grow older, additional age-related declines are observed. Cognitive Remediation (CR) improves cognition in individuals with Schizophrenia. Cognitive Behavioural Social Skills Training (CBSST) improves social and instrumental function by incorporating cognitive techniques and social skills training. This talk will discuss the implementation of CR together with CBSST into the clinical setting as part of a Psychosocial Interventions Clinic.

We adapted a CR protocol involving restorative and strategy-based methods for older outpatients with Schizophrenia. CR is provided in twelve, biweekly, two-hour didactic sessions with online clinic-based practice exercises. Computerized drill and practice exercises are used with bridging to activities of daily life. We modified computer lab ergonomics to accommodate mobility needs. CBSST is provided in 18-weekly, two-hour sessions covering cognitive, social skills and problem solving modules. Participants for both programs are assessed at baseline and end-of-study using clinical and cognitive assessments.

CBSST has been provided to two groups of participants; one group has received CR. All participants are over the age of 60 and have a diagnosis of Schizophrenia. Qualitative feedback from participants and infrastructure accommodation suggest that the clinics are tolerable and feasible.

These modalities are well tolerated by most older outpatients with Schizophrenia and is a feasible addition to an integrated care plan. Further analysis is underway to assess for empirical improvements in cognition and social functioning with the current frequency and number of sessions.
Current pharmacological recommendations for the management of agitation in AD call for the judicious use of antipsychotics despite their modest benefits and high risk-profiles. Nabilone, a synthetic cannabinoid, has a distinct pharmacological profile which may provide a safer and more effective alternative to treat agitation, while having benefits for pain and weight. We describe a clinical trial to investigate the safety and efficacy of nabilone in the treatment of agitation, pain and weight, in patients with moderate-to-severe AD.

This will be a double-blind, cross-over randomized placebo controlled trial (RCT) comparing 6 weeks of nabilone to 6 weeks of placebo, with a 1-week washout preceding each treatment phase. Eligible patients with moderate-to-severe AD and clinically significant agitation will be randomized to receive nabilone (.5-2 mg) or placebo (1:1 ratio) for 6 weeks each. The primary outcome will be agitation. Secondary outcomes include behaviour, cognition and global impression. Exploratory outcomes include pain, nutritional status, safety and biomarkers of oxidative/nitrosative stress, inflammation and cholesterol metabolism.

This RCT will establish the therapeutic relevance of nabilone in the treatment of AD by examining its efficacy in the treatment of agitation, pain and weight, while collecting double-blind information on safety.

If positive, the findings of this study will provide rationale for the feasibility of a larger, multicentre trial. Additionally, a safe and efficacious pharmacological intervention for agitation, pain and weight loss in patients with moderate-to-severe AD could increase quality-of-life, reduce caregiver-burden and avoid unnecessary institutionalization and related increases in health care costs.
Apathy has been associated with executive dysfunction and increased risk of conversion to vascular cognitive impairment (VCI). To better understand underlying mechanisms, the present study aimed to assess apathy as a predictor of changes in executive function in a group at risk of VCI, comparing those with and without endothelial dysfunction.

Patients with coronary artery disease (CAD) were recruited. A standardized battery of cognitive tests was used to assess executive function at baseline and 6 months. Z-scores for Trail Making Test B and Controlled Oral Word Association Test were summed to reflect performance in the executive function domain. Apathy was assessed using the Apathy Evaluation Scale (AES). Endothelial function was measured by reactive hyperemia index (RHI) via peripheral arterial tonometry at baseline. Repeated measures analyses were used to assess AES score as a predictor of cognitive performance over 6 months in those with normal endothelial function (RHI≥1.67) compared to those with endothelial dysfunction (RHI<1.67) while controlling for age and gender.

In 34 participants (mean±SD age=66±7 years, 83% male), higher AES scores were associated with less improvement in executive function over CR (F1,30=4.55, p=0.04). This finding was significant in those with endothelial dysfunction (F1,11=16.09, p=0.002, n=15) but not in those with normal endothelial function (F1,15=0.61, p=0.45, n=19).

Apathy may be an important predictor of early cognitive changes in a population at-risk for VCI. Since endothelial function can be reversed by lifestyle modifications, exercise may be an effective strategy to preserve cognitive function in these patients.
The Association Between Pain and Agitated Behaviours in Patients with Moderate-to-Severe Alzheimer’s Disease

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Pain becomes challenging to detect and undertreated with advancing Alzheimer’s Disease (AD) due to difficulties in verbalising. As a result, pain often manifests as agitation, but may also be associated with additional neuropsychiatric symptoms (NPS). This study examines the association of pain with NPS in patients with moderate-to-severe AD.

Patients with moderate-to-severe AD (Standardized Mini-Mental Status Exam (sMMSE) ≤ 20) and clinically significant agitation (Neuropsychiatric Inventory (NPI)-Agitation subscale ≥ 3) were assessed. Pain (Pain Assessment in Advanced Dementia scale: PAINAD), agitation (Cohen-Mansfield Agitation Inventory: CMAI), and NPS (NPI) were also measured.

To date, 8 patients have been enrolled in the study (mean ± SD age = 87±9, BMI = 22.0±4.2, NPI = 32.5±17.5, CMAI = 67.8±18.5, sMMSE = 6.0±3.7, 75% male). At baseline, all patients had some degree of pain, with 5 patients having mild levels (PAINAD 1-3, mean score ± SD = 2.2±.08) and 3 patients having moderate levels (PAINAD 4-6, mean score ± SD = 4.3±0.6). Compared to the mild pain group, patients with moderate pain had higher scores on the NPI-Total (t(6) = -3.2, p = .02), NPI-Anxiety (t(6) = -2.8, p = .03) and NPI-Aberrant Motor Behaviours (t(6) = -2.8, p = .03).

All agitated AD patients experienced some degree of pain. Individuals with higher levels of pain demonstrated more anxiety, aberrant motor behaviours, and overall NPS. Given the negative impact of these NPS on quality of life, pain management should be re-evaluated in those with these NPS.
The objective of this study was to explore whether attentional bias towards dysphoric stimuli can be used to assess depressive symptoms in geriatric patients.

Patients included those with Alzheimer’s disease (AD, NINCDS-ADRDA criteria), mild cognitively impaired (MCI, NIH criteria) and cognitively-intact elderly mood disorder patients. Attentional bias towards dysphoric images was assessed with an eye-tracking technology. Participants viewed 16 slides, each containing 2 neutral, 1 social and 1 dysphoric image. We measured relative time spent on each image (relative fixation time, RFT). Participants were assessed for cognition (Standardized Mini-Mental State Examination, sMMSE), neuropsychiatric symptoms (Neuropsychiatric Inventory, NPI), depression (Cornell Scale for Depression in Dementia, CSDD), apathy (Apathy Evaluation Scale, AES) and attention (Conners’ Continuous Performance Test, CPT).

This study included 46 mild-to-moderate AD, 8 MCI and 25 elderly mood disorder patients. A linear regression revealed greater RFT towards dysphoric images (t = 2.46, p = 0.017), adjusting for cognition, neuropsychiatric symptoms, apathy and attention, was associated with more severe depression. Better cognition (t = 3.36, p = 0.001) and more neuropsychiatric symptoms (t = 5.55, p < 0.001) were also significant predictors. The total model accounted for 51% of the variance (R2 = 0.51, Adjusted R2 = 0.47, F5,71 = 14.48, p < 0.001).

These results suggest that attentional bias towards dysphoric images can be used to predict depressive symptoms in geriatric patients, regardless of cognitive impairment. Measurements of visual scanning behaviour may provide a non-verbal and objective tool to monitor depression in this population.
Transcatheter Aortic Valve Implantation (TAVI) is a minimally invasive method of treating severe aortic stenosis in an elderly, multi-morbid patient population. Cognitive impairment and neuropsychiatric symptoms such as depression and apathy are risk factors for poorer outcomes in the elderly, but have not been studied extensively in TAVI. This study determined the prevalence of these risk factors before and after TAVI.

Patients referred to the Sunnybrook TAVI clinic were enrolled. Cognitive impairment (Montreal-Cognitive Assessment; MoCA15), apathy (Apathy Evaluation Scale; AES>42) and health status (EQ-5D-5L) were assessed. Paired t-tests were used to compare scores before and 6 months post-TAVI.

Of 13 patients to date (age: 83±6, 46.2% female, years of education: 13.5 ± 4.3), 9 (75%) showed cognitive impairment, 5 (38%) depressive symptoms and 3 (25%) apathy. At baseline, higher depressive symptoms (r=-0.74, p=0.004) and apathy (r=-0.71, p=0.010) were associated with poorer health status. No significant changes were observed in cognition (t (7) =0.32, p=0.76), depressive symptoms (t (8) =1.85, p=0.10) or health status (t (9) =1.58, p=0.15) post-TAVI, although apathy scores improved (t (9) = 1.85, p=0.04).

These results suggest that TAVI may be associated with improved apathy, with cognition, depression and health status remaining unchanged. Given the high prevalence and potential impact of these risk factors, our findings support the need to screen for these symptoms in TAVI patients. They might also be taken into consideration for future management and treatment strategies in these patients.
Patients with emotional dysregulation and Borderline Personality Disorder are high utilizers of acute healthcare services and are often challenging for front-line mental health staff. DBT is an evidence-based treatment for this population. This capacity-building project trained front-line providers in DBT Skills in order to improve the access to and the quality of mental health care.

Following a learning needs assessment (N = 130) in which DBT was highly ranked, a capacity-building project was developed, starting with a 2-day workshop (N = 70), and progressing to bi-monthly small group supervision (N = 30), and subsequent supervision for 10 participants who were starting DBT Skills Groups. Longitudinal supervision involved case-based skills teaching, reflection, therapist behaviour checklists and simulations. Participants completed the Counselling Self-Estimate Inventory measure (Larson) before and after the training, and participated in focus groups.

Participants reported increased DBT technique use over time, and significant improvements in counselling self-efficacy, particularly in “managing difficult client behaviors” (p = 0.02). Focus groups revealed participants were able to incorporate DBT into their clinical work, and felt more competent and confident as a result for the level of guidance and feedback received. Several new DBT skills groups were formed in acute care and community-based settings.

This multi-phased capacity-building model for implementing evidence-supported psychotherapy improved the access to and the quality of mental healthcare, marrying academic expertise and education scholarship with social responsibility to an underserved and high needs clinical population. Further study of evidence-supported psychotherapy implementation through capacity-building is needed, with patient and health utilization outcomes.
Psychiatry residency training includes clinically supervised Psychodynamic Psychotherapy and Cognitive Behavioral Therapy (CBT). Evaluation based on observation provides opportunity to evaluate adherence and competence. This exploratory pilot study examines the frequency of PGYII psychiatry residents’ use of CBT and Psychodynamic techniques over time with training.

Five PGYII psychiatry residents recorded their clinically supervised sessions with CBT (5) and Psychodynamic (5) patients. Trained external raters used the Psychotherapy Process Q Set to analyze randomly selected CBT (72) and Psychodynamic (85) sessions (inter-rater reliability r=0.609, p < 0.001). We conducted separate growth models using Hierarchical Linear Modeling predicting ratings as a function of session number, nested within patients and therapists.

Residents adhered to processes of Psychodynamic ideals (19%), t(3)= 8.346, p=0.004, and CBT ideals (39%), t(3)= 15.493, p<0.001, respectively at the outset of treatment. In Psychodynamic Psychotherapy, adherence was maintained, and did not change significantly over time, t(3)= 0.78, p=0.492, whereas in CBT, adherence significantly increased over time, t(3)= 3.669, p=0.035.

Improved CBT adherence over time likely reflects this model’s ‘teachability’ of technical elements. Psychodynamic Psychotherapy with its more complex processes and techniques, likely takes more than one year of training to demonstrate increased adherence. Given our small sample size, the results should be regarded as preliminary; however, adherence rating as a component of competency with review of audiotaped sessions is feasible. Further psychotherapy education research with larger samples, patient outcomes and measures of process elements and therapist behaviours is needed to improve psychotherapy training and competency-based evaluation.
Through Competence By Design, the Royal College is promoting a transition from time-based medical education to Competency-Based Medical Education (CBME), a framework that emphasizes the achievement of specific competencies as the basis of resident evaluation and promotion. These competencies, or Entrustable Professional Activities (EPAs), provide a basis upon which educational experiences are structured, deemphasizing the importance of time-on rotation and ensuring attainment of specific skill sets. The Department of Psychiatry at the University of Toronto is developing a CBME pilot project to be implemented in July of 2016. We are seeking to define foundational, early residency EPAs for emergency psychiatry.

A group of experts in the field of emergency psychiatry developed a number of EPAs through an iterative consensus process. Resident input was sought and final results were approved by a CBME steering committee.

Five EPAs were developed, including 1) Performing psychiatric assessments in the emergency setting, 2) Evaluating the medical stability of psychiatric patients in the emergency setting, 3) Conducting a risk assessment in the emergency setting, 4) Assessing and managing agitated patients in the emergency setting, and 5) Using the Mental Health Act in the emergency setting. Each EPA was further delineated into milestones and sub-milestones.

The foundational skills and activities of emergency psychiatry were broadly categorized into five EPAs. These EPAs will inform educational goals and objectives for the CBME pilot project and psychiatric residency training.
This study presents and compares knowledge and attitudes about electroconvulsive therapy (ECT) by type of healthcare professional and mental health experience. This study also identifies any potential gaps in knowledge or attitudes that might influence patients’ experience with ECT.

Ninety-eight healthcare professionals, who worked in inpatient/outpatient mental health in a Canadian Public Hospital, were asked to complete an anonymous survey (paper or electronic formats) over 3-week period. Demographic information, ECT knowledge/attitudes using QuAKE developed by Orrell, and open-ended were completed by 44% (n=43). Participants included nurses and other health care professionals (Occupational Therapists, Recreation Therapists, Crisis Workers, Social Workers).

Overall, participants were knowledgeable and had positive views about ECT. A significant correlation was found between attitudes and knowledge exhibited by healthcare professionals (\( r = .55, p < .01 \)). Additionally, there was significant variation in levels of knowledge (\( F(2,36) = 7.028, p = .003 \)) and attitudes (\( F(2,38) = 4.420, p = .019 \)) exhibited by different types of mental health professionals. However, those who did not disclose profession had less favourable views of ECT. Analysis of specific items provides additional information; e.g., those with less experience were of the view that psychiatrists’ use ECT due to lack of treatment options.

Although most participants had sound knowledge and positive outlook, some may benefit by learning more about ECT to provide better support for patients. Thus, providing materials to help newly trained mental health professionals can help promote better understanding and attitude in current and future clinicians.
To identify those factors that contribute to patients not completing their prescribed series of electroconvulsive therapy (ECT). While some researchers have speculated on reasons and factors that contribute to dropout from mental health treatment, no research has focused specifically on treatment adherence to ECT. The dropout phenomenon may be unique to patients receiving this treatment given their concern about side effects such as memory loss, stigma, misconceptions of the treatment and the reason why ECT is being prescribed. Results of this study provide support for potential strategies to foster completion of ECT as prescribed.

The health records of 162 patients (93 female, 69 male) of a Canadian Public Hospital were reviewed to identify factors that contributed to dropout. Drop out is defined as failing to continue either acute or maintenance treatment. Analysis was carried out using quantitative statistical measures (e.g. ANOVA, chi-square).

Overall, 29% of inpatients who received ECT dropped out, whereas dropout rate for outpatients was 34%. Patients who received a greater number of treatments were less likely to drop out. Interestingly, patients who had been diagnosed as having a personality disorder were more likely to drop out of the treatment ($\chi^2 = 11.322$, $p = .001$). Other factors are also explored.

Initial education and support might be beneficial for patients when starting ECT treatment; this might include expectations, side effects, need for series of treatments for ECT to manage depression. Patients with diagnosis of personality disorder may benefit from additional support.
The primary objective of this project is to create an educational documentary to share knowledge about psychiatric illness as it relates to ice hockey concussion. The high incidence of concussion in ice hockey, together with the subsequent post-concussive psychiatric sequelae, forms a complex and dangerous health issue that requires further investigation and educational initiatives.

Phase 1- Conduct a qualitative analysis of interviews with key ice hockey stakeholders to highlight major themes and knowledge gaps on issues surrounding the psychiatric effects of ice hockey concussion. Phase 2- Create and distribute “A Dark Room”, a evidence based educational documentary on the psychiatric effects of concussion in ice hockey Phase 3- The film will be distributed to over two hundred schools across Canada in an event called The Virtual Classroom. Pre and post film standardized questionnaires will be conducted to measure the film’s efficacy in educating individuals about psychiatric issues associated with ice hockey concussion will impact students’ knowledge and attitudes surrounding the mental health effects from concussion.

Furthermore, the film will provide an educational platform to help with concussion prevention, and help those who do suffer a concussion to seek the appropriate help.

The film helps to educate the public on the psychiatric effects of concussions and the breakthroughs in concussion diagnosis and treatment. It advocates that mental health needs to be discussed more openly in the hockey community to help prevent, recognize and treat the consequences of concussions in the future.
### Afternoon Oral Presentation Session A Schedule: 1:00 to 2:15 PM

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**Sina Hafizi;** Huai-Hsuan Tseng; Miran Kenk; Pablo M. Rusjan; Alan A. Wilson; Sylvain Houle; Romina Mizrahi<br>
*Microglial Activation in First Episode Schizophrenia: A PET Study with [18F]-FEPPA*

**Arash Nazeri;** Arash Nazeri; Benoit Mulsant; Tarek Rajji; Melissa L. Levesque; Nicholas H. Neufeld; Jon Pipitone; Tina Roostaei; Laura Stefanik; Anne L. Wheeler; David J. Rotenberg; Aristotle Voineskos<br>
*Gray Matter Neuritic Microstructure In The Major Psychoses*

**Huai-Hsuan Tseng;** Miran Kenk; Gary Remington; Pablo Rusjan; Alan Wilson; Sylvain Houle; Romina Mizrahi<br>
*Stress-induced Alterations in Prefrontal Dopamine Levels in the Prodromal and antipsychotic-naive Early Psychosis*

**Saba Shahab;** Joseph D. Viviano; Jon Pipitone; Francisco Canas; George Foussias; Aristotle N. Voineskos<br>
*Neuroimaging and Machine Learning Algorithms to Identify Biological Subtypes of Schizophrenia*

**Ishraq Siddiqui;** Sarah Saperia; Gagan Fervaha; Jon Pipitone; Joseph D Viviano; Eliyas Jeffay; Konstantine K Zakzanis; Ofer Agid; Aristotle N Voineskos; Gary Remington; George Foussias<br>
*White Matter Connectivity Correlates of Goal Planning and Execution in Schizophrenia in a Virtual Environment*

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**Malgorzata Maciukiewicz;** Joseph Geraci; James L. Kennedy; Susan Rotzinger; Jane A. Foster; Sidney H. Kennedy; Daniel J. Müller<br>
*GWAS-based machine learning approach to predict duloxetine response in major depressive disorder*

**Amanda Lisoway;** Clement C. Zai; Gwyneth Zai; Akhil Nair; Sasha Ebrahimi; Arun K. Tiwari; Arturas Petronis; Viviane Labrie; Zachary A. Kaminsky; James L. Kennedy*; Margaret A. Richter*<br>
* co-senior authorship<br>
* Genetic and Epigenetic Variation in SKA2 and Disease Severity in Obsessive-Compulsive Disorder*

**Chelsea Lowther;** Marsha Speevak; Christian R. Marshall; Stephen W. Scherer; Dimitri J. Stavropoulos; Elizabeth McCready; Anne S. Bassett<br>
*Molecular characterization of NRXN1 deletions from 19,263 clinical microarray cases identifies exons important for neuropsychiatric disease expression*

**Victoria Marshe;** Maciukiewicz M; Rej S; Tiwari AK; Sibille E; Blumberger D; Karp J; Kennedy JL; Lenze EJ; Mulsant BH; Mueller DJ<br>
*Association of noradrenergic and serotonergic system gene variants across multiple antidepressant remission phenotypes in depressed geriatric patients*

**Vincenzo Deluca;** Ali Bani Fatemi<br>
*Deletion Screening of Chromosome 22 in suicide attempters with Schizophrenia*
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<td><strong>Pushpal Desarkar; Tarek Rajji; Stephanie Ameis; Daniel Blumberger; Zafiris J. Daskalakis</strong>&lt;br&gt;Assessing and Stabilizing aberrant neuroplasticity in Autism Spectrum Disorder using Transcranial Magnetic Stimulation: Preliminary findings from a proof-of-principle study</td>
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<td><strong>Chantel Kowalchuk; Margaret Hahn; Chantel Kowalchuk; Gary Remington; Adria Giacca; Virginia Wilson</strong>&lt;br&gt;Olanzapine induces hypothalamic insulin resistance</td>
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<td><strong>Ofer Agid; Gary Remington; Gagan Fervaha</strong>&lt;br&gt;Antipsychotic treatment algorithm for first episode Schizophrenia – a guide for clinicians</td>
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<td><strong>Nuwan Hettige; Ariel Graff; Clement Zai; Jiali Song; Vincenzo De Luca</strong>&lt;br&gt;The Effect of Ethnicity and Migration in Treatment Resistant Schizophrenia</td>
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<td><strong>Paul Kurdyak; Simone Vigod; Binu Jacob; Thérèse Stukel</strong>&lt;br&gt;Impact of Schizophrenia on diabetes quality of care and outcomes</td>
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<td><strong>Suze Berkhout; Juveria Zaheer; Gary Remington</strong>&lt;br&gt;Purity and Progress: Historical and Philosophical Foundations of First Episode Psychosis</td>
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<td><em>Impact of a Mental Health Education Program on Student Functioning and Access to Care in Nicaragua</em></td>
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<td><em>Lessons learned from implementing a mental health integration program based on scaling up of a psychosocial therapy to Primary care in Ethiopia: The Biaber Project</em></td>
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<td><strong>Amy Gajaria</strong>; Magda Esther Castrillo; Andrés Herrera Rodríguez; Arun V. Ravindran</td>
<td><em>A qualitative inquiry into educators’ perspectives of the mental health needs of young people in León, Nicaragua</em></td>
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<td><strong>Martin Rotenberg</strong>; Andrew Tuck; Rachel Ptashny; Kwame McKenzie</td>
<td><em>The Role of Ethnicity in Pathways to Emergency Psychiatric Services for Clients with Psychosis</em></td>
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<td><em>Short postpartum psychiatric hospital admissions: A population-based study</em></td>
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<td><strong>Paul Benassi</strong>; Saima Awan; Paul Kurdyak; Peter Voore</td>
<td><em>Reducing Agitation in Psychiatric Emergency Department through Improved Tobacco Withdrawal Management: A Quality Improvement Project</em></td>
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<td><strong>Deborah Kahan</strong>; Daniel Poremski; Daniel Pauly; Debbie Wise-Harris; Vicky Stergiopoulos</td>
<td><em>Frequent ED users in mental health: perceived service needs and preferences in a large urban centre</em></td>
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**Arron Metcalfe; Bradley J. MacIntosh; Monica Emode; Daphne Korczak; Benjamin I. Goldstein**

A single bout of aerobic exercise enhances resting state networks in adolescent bipolar disorder

**Fiona Zeeb; Zhaoxia Li; Daniel C. Fisher; Martin H. Zack; Paul J. Fletcher**

Repeated exposure to uncertain rewards sensitizes the dopamine system and increases risky decision-making: implications for modelling gambling disorder in rats

**Colin Hawco; Jennifer K. Steeves; Erin W.E. Dickie; Aristotle N. Voineskos; Zafiris J. Daskalakis**

Direct Neuronal Effects of TMS are Highly Reliable but not Correlated with Resting State Connectivity: A concurrent TMS-fMRI study

**Nicholas Neufeld; Joseph Viviano; Tarek Rajji; George Foussias; Benoit Mulsant; Aristotle Voineskos**

Corticostriatal resting state functional connectivity differs amongst stable patients with bipolar disorder, Schizophrenia, and psychotic depression

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<td><strong>Yoshihiro Noda; Mera S. Barr; Reza Zomorrodi; Robin F.H. Cash; Tarek K. Rajji; Robert Chen; Zafiris J. Daskalakis; Daniel M. Blumberger</strong> Short-latency afferent inhibition from the dorsolateral prefrontal cortex in patients with Schizophrenia: a TMS-EEG study</td>
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**Sarah Peters; Katharine Dunlop; Jonathan Downar**

The Salience network as a Predictor of Response to rTMS and iTBS in Major Depression

**Yinming Sun; Daphne Voineskos; Faranak Farzan; Natasha Radhu; Tarek K. Rajji; Daniel M. Blumberger; Willy Wong; Zafiris J. Daskalakis**

TMS-EEG Measures of Cortical Inhibition for Understanding Treatment Resistant Depression

**Jae-Hon Lee; Sung Keun Park; Jae-Hong Ryoo; Chang-Mo Oh; Rodrigo B. Mansur; Jeffrey E. Alfonsi; Yena Lee; Roger S. McIntyre; Ju Young Jung**

The impact of sleep duration and quality on functional and structural change of left ventricle in general Korean population

**Anastasios Daskalakis; Reza Zomorrodi; Lisa Tran; Angela Ziluk; Daniel M. Blumberger; Tarek K. Rajji**

Electrophysiological Evidence for Impairment of Somatosensory Evoked Response in Schizophrenia
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<tr>
<td>Abstract:</td>
<td>Baseline Neurocognitive Performance on a neurocognitive battery in a cohort of patients with Major Depressive Disorder (MDD) relative to healthy controls</td>
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<td>Abstract:</td>
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| speaker:| Sarah Dermody; Jennifer W. Tidey; Rachel L. Denlinger; Lauren R. Pacek; Mustafa al’Absi; David J. Drobes; Dorothy K. Hatsukami; Ryan Vandrey; Eric C. Donny |
| Abstract:| The Impact of Smoking Very Low Nicotine Content Cigarettes on Alcohol Use |

| speaker:| Anthony Levitt; Roula Markoulakis (Co-Presenter); Keera Fishman; Theresa Kim; Jacob Levitt |
| Abstract:| The Climate Change Anxiety Scale: Examining climate change knowledge and climate change related anxiety |

| speaker:| June Lam; Paul S. Links; Samuel Law; Wes Shera; A. K. Tat Tsang; W. L. Alan Fung; Annette Zhang; Rahel Eynan; Pozi Liu; Juveria Zaheer |
| Abstract:| The Role of Filial Piety in Mediating Risk and Recovery in Chinese Women With a History of Suicidal Behaviour: A Cross-Cultural Qualitative Study |

<p>| speaker:| Joshua Rosenblat; Ron Kakar; Michael Berk; Lars V. Kessing; Maj Vinberg; Bernhard T. Baune; Rodrigo B. Mansur; Elisa Brietzke; Roger S. McIntyre |
| Abstract:| Anti-Inflammatory Agents in the Treatment of Bipolar Depression: A Meta Analysis |</p>
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<td><strong>Tara Burra;</strong> Jose Silveira</td>
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<td><em>Reducing Rapid Readmissions Through Collaborative Care</em></td>
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<td><em>A Bahaus Design Framework for the Mental Health Care System: Ensuring Form Follows Function within an Integrated System of Care</em></td>
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<td><em>Can We Fix What We’ve Broken? Randomized Controlled Trial of a Group Therapy to Address Body Image Disturbance and Sexuality Following Treatment with Breast Cancer</em></td>
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<td><strong>Sarah Smith;</strong> Blake Woodside</td>
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<td><em>Correlates of Response to Inpatient Eating Disorder Treatment</em></td>
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<td><em>A Pilot Study of Diffusion Tensor Imaging in Anorexia Nervosa: Comparison across Underweight and Weight-Recovered Subjects, their Unaffected Siblings, and Unrelated Controls</em></td>
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<td><em>The Impact of Project ECHO on Primary Care Outcomes: A Systematic Review</em></td>
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Oral Presentation Abstracts
A growing body of literature suggesting a prominent role of neuro-inflammation in Schizophrenia. Positron emission tomography (PET) targeting mitochondrial translocator protein 18 kDa (TSPO) is a unique way to study microglia activation as an in-vivo marker of neuro-inflammation. Previous PET studies were limited by low affinity of radiotracer used, resolution of scanners used, and the confounding effect of antipsychotics. No previous report assessed neuro-inflammation in drug-naïve patients with first episode Schizophrenia (FEP).

Using a novel second-generation PET radiotracer for TSPO [(18)F]-FEPPA, we evaluated neuro-inflammation in dorsolateral prefrontal cortex (DLPFC), and hippocampus of FEP. Twenty-three drug-naïve FEP and 20 healthy volunteers underwent [(18)F]-FEPPA PET, using a high-resolution research tomograph, and a structural MRI. PET data were analyzed using the validated 2-tissue compartment model (2TCM) with an arterial plasma input function to determine the total volume of distribution (VT). All subjects were categorized as high-, medium- or low-affinity binders based on their rs6971 genotype, and results were adjusted based on these information. The association between severity of symptoms and neuro-inflammation were also assessed in the patients.

No significant group effects were found for [(18)F]-FEPPA binding across different ROIs after controlling the results for rs6971 genotype. No significant correlations were observed between [(18)F]-FEPPA VTs and severity of symptoms and cognitive performance for any regions of interest, after controlling for multiple comparisons (p>0.05).

Result of this study, while preliminary, does not suggest increased [(18)F]-FEPPA binding in the brain of drug-naïve patients with FEP as compared to matched healthy volunteers.
Post-mortem studies have shown lower dendritic neuritic marker density, dendritic tree arborization, and spine density in persons with Schizophrenia and bipolar disorder (BD-I). Drawing a direct link between the gray matter (GM) macrostructural deficits (e.g. lower cortical thickness) in these disorders and the underlying pathology has proven difficult. Modeling GM microstructural properties, which is now possible with a recently proposed diffusion-weighted MRI modeling technique (Neurite Orientation Dispersion and Density Imaging [NODDI]), may bridge the gap between in vivo neuroimaging approaches and histopathological features of these disorders.

Schizophrenia patients (n=38), BD-I (n=23), and healthy controls (HC; n=37) group-matched by gender and age were recruited (age range: 19-57). Multi-shell diffusion-weighted (1000, 3000, 4500s/mm²; 30 directions each) and high-resolution structural images were acquired using a 3T MR750-GE scanner. GM-based spatial statistics (GBSS) was used to investigate NODDI-driven GM microstructural measures (orientation-dispersion index [ODI] and neurite density index [NDI]) in a voxel-wise manner. We investigated whether combination of GM microstructure and cortical thickness results in more accurate prediction of disease status.

In comparison to HC, Schizophrenia patients demonstrated significantly lower GM-NDI in right (family-wise-error-[FWE]-corrected-p=0.021) and left (FWE-corrected-p=0.037) temporal pole and anterior parahippocampal gyrus, while no significant difference was observed between BD-I and HC or Schizophrenia patients. NDI and cortical thickness enhanced each other’s diagnostic accuracy to distinguish between Schizophrenia from HC (AUC-NDI: 0.90; AUC-cortical thickness: 0.85; AUC-combined: 0.95). Across all groups, higher performance in spatial-span (non-verbal working memory) was significantly associated with higher gray matter NDI throughout the cerebral GM (FWE-corrected-p<0.05).

NODDI-driven microstructural indices may serve as robust biomarkers for major psychotic illnesses and cognitive performance.
Recent evidence suggests decreased prefrontal cortex (PFC) dopamine release during amphetamine challenge in Schizophrenia (SCZ). However, PFC response to a stress challenge in SCZ and in those at clinical high risk (CHR) for psychosis is unknown. This is important as environmental stress remains a key trigger for psychosis. The current study aims to examine PFC dopamine level alterations in response to validated psychosocial stress task in drug-naïve SCZ-related disorders and CHR as compared to healthy volunteers (HV).

We used a very high-affinity dopamine D2/3 PET radiotracer: [11C]FLB457 to image cortical D2/3 receptors. The percent change in binding potential in PFC between control and stress conditions was calculated ($\Delta$BPND = BPND[stress] - BPND[control])/BPND[control]) to reflect alterations in synaptic dopamine levels. $\Delta$BPND differences were tested with analysis of covariance (ANCOVA), controlling for the BPND[control], cannabis use, age and injected mass.

14 HV, 21 CHR (7 cannabis users) and 21 SCZ (10 cannabis users) were included. We found a significantly lower control BPND[control] in SCZ (F=4.28, df=2, 50, p=0.019). Stress elicited an increase in PFC BPND in HV (8.62%±2.94), but did not in CHR (-1.07%±2.42) or SCZ (-0.52%±2.62). A trend of positive associations was observed between PFC $\Delta$BPND and severity of overall (r=.39, p=0.078) and negative psychotic symptoms (r=.37, p=0.097) in SCZ patients.

The decreased SCZ PFC BPND in the control condition may suggest an increased endogenous PFC dopamine during the control cognitive task. The stress-induced reduction of PFC BPND we observed in HV was absent in CHR and SCZ, indicating altered dopamine stress reactivity in prodromal and early psychosis.
Research has shown that conventional treatments are less effective at treating Schizophrenia patients who suffer from persistent negative symptoms (PNS). We have previously shown that patients with the deficit Schizophrenia subtype (DS), who suffer from chronic PNS, have altered diffusion-based measures of certain white matter tracts compared to non-deficit patients (NDS). In this study, multivariate classification methods were used on neuroimaging scans to identify features that predict differences between the DS and NDS groups.

T1 and DTI scans were collected for 18 DS and 18 NDS patients. Cortical thickness (gray-matter) and diffusion-based measures (white-matter) of white matter tracts were compared between the two groups. A random forest classifier was used to run three separate models: gray-matter only, white-matter only, both combined. Area under the ROC curve (AUC) was used to compare the three models. Finally, a ridge regression model was run.

Comparison of the three models showed that the white-matter only model (AUC=77%, Accuracy=77%, Positive Predictive Power (PPV)=75%) was superior to both the gray-matter only (AUC=44%) and the combined (AUC=70%) models. The ridge regression model provided an additional level of optimization than random forest alone: AUC=84%, Accuracy=77%, Sensitivity=72%, Specificity=83%, and PPV=81%.

Diffusion-based measures of white matter provide good accuracy in classifying Schizophrenia patients. Classification may provide a way for clinicians to provide group-specific interventions prior to full expression of PNS. Our work also helps confirm the neural circuitry of DS, which can accelerate therapeutic innovation. We are currently working on a replication cohort that could provide further evidence for these findings.
To evaluate planning and executing goals in Schizophrenia we administered an ecologically valid task, the Multitasking in the City Test (MCT), and assessed associations between task performance and structural brain connectivity using diffusion tensor imaging (DTI).

Participants fulfill errands in a virtual city, while the number of errands completed, completion time, errors committed, and distance travelled are monitored. Overall, 49 Schizophrenia patients (SZ) and 55 healthy controls (HC) completed the task and underwent comprehensive clinical characterization. A subsample of 20 SZ and 19 HC underwent neuroimaging. Fractional anisotropy (FA) values for fibre tracts associated with the motivation system were computed based on the (Enhancing NeuroImaging Genetics through Meta Analysis) ENIGMA DTI protocol.

SZ performed worse than HC in all aspects of the task (p < 0.007). Motivation correlated with MCT performance in SZ (|\(\rho\| = 0.430 – 0.451, p < 0.003) and overall (|\(\rho\| = 0.245 – 0.310, p < 0.013). Several MCT metrics were significantly correlated with FA values of the right external capsule and bilaterally the anterior internal capsule (|\(\rho\| = 0.332 – 0.463, p < 0.043). Errors correlated with the left external capsule and right sagittal stratum, and distance travelled correlated with the left superior longitudinal fasciculus (|\(\rho\| = 0.354 – 0.385, p < 0.030).

Motivational impairments in SZ manifest as incapacity to fulfill goals, and as reduced efficiency in applying motivation towards this end. The imaging results support the notion that these overlapping aspects of motivation are somewhat distinct, potentially at a neurobiological level.
Schizophrenia (SCZ) may be a syndrome of accelerated aging. Direct comparisons of healthy aging populations with SCZ patients on measures of brain structure and cognitive performance, along with inclusion of other disease groups may help inform this theory. This study assessed the effects of age and diagnosis on cortical thickness (CT) and white matter (WM) microstructure (represented by fractional anisotropy [FA]), in younger and older healthy controls (HC), SCZ patients, and bipolar (BD) patients. We are currently also analyzing whether markers of oxidative stress may underlie these neural alterations.

Eighty-one HC, 59 clinically stable SCZ patients and 55 euthymic BD patients underwent magnetic resonance imaging on a research-dedicated 3T Discovery MR750 system and cognitive testing (using the MATRICS). T1-weighted images were processed using CIVET and DTI images using FSL. We analyzed the effects of age, diagnosis and cognitive function on both CT and FA using general linear models.

Both CT and FA decreased with age across diagnoses. SCZ patients had lower CT and FA compared to both HC and BD patients. This decrease was more evident in younger participants, with almost no differences found across diagnostic groups in older participants. Finally, CT and FA were associated with working memory, attention, verbal learning and processing speed.

Our results provide evidence for a non-progressive early ‘hit’ in SCZ. Euthymic BD patients were more similar to HC than to SCZ patients in brain structure. Relationships between brain structure and cognitive performance appear to be independent of diagnosis.
A Single Bout of Aerobic Exercise Enhances Resting State Networks in Adolescent Bipolar Disorder

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Differences in resting state functional connectivity (rs-FC) in adult bipolar disorder (BD) are well known, whereas data in adolescent BD is sparse. This study examined the concept of dysbalance between default mode network (DMN) rs-FC and salience and executive networks. Exercise is known to impart benefits on mood and cognition and increase rs-FC in healthy samples (HC). We therefore examined rs-FC at baseline and in response to a single bout of aerobic exercise among BD adolescents and HCs.

Adolescents (13-19 years; n=32 BD, n=32 HC) matched for age, IQ, and sex completed 20 minutes of recumbent cycling maintaining 60-80% of age-estimated maximum heart rate. Seed-to-voxel resting state connectivity of the anterior DMN was tested (ventral medial prefrontal cortex, MNI coordinates: -1, 47, -4). Results were evaluated for significance at p<.01, cluster corrected for family-wise error at p<.05.

Pre-exercise, there was greater inter-network anterior DMN connectivity to salience (anterior insula) and executive (prefrontal and parietal) networks in BD and less connectivity to medial parietal intra-network DMN nodes. Post-exercise in BD, intra-network synchronization with posterior DMN increased and inter-network connectivity decreased. These changes were supported by significant Group by Session interaction. For BDs, DMN connectivity negatively correlated with depression score before exercise (r=-.36, p=.045), but not after (r=-.27, p=.132).

Conclusions/Implications:
Adolescents with BD showed anomalous rs-FC in large-scale brain-networks at baseline. After exercise, rs-FC dysbalance was not found. There was evidence this change related to depression symptoms. Acute exercise constitutes a meaningful diagnostic of BD neural response with therapeutic potential.
Gambling Disorder (GD) is a public health concern and an animal model would advance our understanding of GD and aid in the development of effective treatments. Pathological gamblers demonstrate neural correlates of dopamine (DA) sensitization. Additionally, risky decision-making may be a hallmark feature of GD and pathological gamblers choose disadvantageously on the Iowa Gambling Task (IGT). We hypothesize that repeated exposure to gambling scenarios (uncertainty) induces sensitization and increases risky decision-making.

Male rats responded on a predictable fixed ratio (FR) or unpredictable variable ratio (VR) schedule of reinforcement for 56 sessions. Rats yoked to the FR/VR groups were also included (Y). To determine if sensitization occurred, locomotor activity following an injection of saline or amphetamine was assessed. Risky decision-making was then evaluated using the rat gambling task (rGT), a rodent analogue of the IGT. The optimal strategy on the rGT (and IGT) is to favour options that yield smaller immediate reward but less loss and avoid risky options associated with greater rewards, but greater long-term loss.

Compared to the FR group, rats in the VR and Y groups demonstrated increased sensitivity of the DA system. At the end of rGT training, animals in the FR and Y groups significantly preferred the advantageous options. However, rats in the VR group did not show a significant preference for the advantageous options over the disadvantageous options.

Actively responding for uncertain reward sensitizes the DA system and impairs the ability to make optimal decisions, possibly similar to patients with GD.
Transcranial magnetic stimulation (TMS) is a neuromodulatory approach used to treat a variety of psychiatric disorders. One proposal to optimize treatment efficacy is to use Resting State fMRI (rs-fMRI) connectivity to optimize individual specific targets. To date there has been no direct examinations of the relationship between the propagation of neural activity following TMS and resting state connectivity. This study used concurrent TMS-fMRI to address this issue.

Twenty-two participants completed a 10 minute rs-fMRI and four 10 minute TMS scans in which a single TMS pulse was administered 50 times. Scans alternated supra-threshold TMS pulses and a low-intensity, sub-threshold TMS control. Direct neuronal effects of TMS pulses were examined by contrasting high intensity trials to low intensity controls. Resting state connectivity was examined via whole-brain seed connectivity with the TMS target site as the seed region.

Several cortical regions shows changes following a TMS pulse, including medial prefrontal, lateral temporal-parietal, and cingulate cortex. A Jackknife reliability analysis (a variant on the bootstrap) demonstrated the observed clusters were highly reliable. Eight ROIs were selected based on the activation map. No ROIs showed a significant correlation (all p > 0.1) between intrinsic resting connectivity and TMS effects.

This is amongst the first studies to directly examine the relationships between propagation of neuronal activity following TMS and intrinsic functional connectivity. In healthy individuals, we did not observe a relationship between TMS propagation and intrinsic resting connectivity. This has implications for the basic mechanisms of TMS and treatment approaches.
Corticostriatal Resting State Functional Connectivity Differs Amongst Stable Patients with Bipolar Disorder, Schizophrenia, and Psychotic Depression

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Aberrant patterns of corticostriatal resting state functional magnetic resonance imaging (RfMRI) connectivity have been observed amongst patients in the state of psychosis or depression. We hypothesized that stable patients who have had such episodes would continue to have aberrant corticostriatal connectivity when compared with healthy controls.

Healthy controls (HC, n = 33) and patients with bipolar disorder (BD, n = 27), Schizophrenia (SZ, n = 27), and psychotic depression (PD, n = 17) underwent T1-weighted and RfMRI scans. Preprocessing included regression of signals arising from head motion, white matter, and cerebrospinal fluid, lowpass filtering, and registration to MNI space. Subject specific striatal connectivity maps were defined as the correlation between the mean bilateral striatum timeseries with every voxel in the brain. Four-level ANOVA and pairwise t-tests were performed to elucidate group connectivity differences. All results were cluster corrected at p < 0.05.

Relative to HC, there were no statistically significant corticostriatal connectivity differences in patients with BD. SZ had hyperconnectivity between the striatum and bilateral occipital cortex. PD had hyperconnectivity between the striatum and bilateral sensorimotor and middle cingulate cortices.

SZ and PD had specific patterns of corticostriatal hyperconnectivity while no aberrant corticostriatal connectivity was observed in BD. These results may aid in diagnosis or targeted treatments.
Major depressive disorder (MDD) is one of the most prevalent psychiatric disorders, affecting up to 350 million people worldwide. MDD is typically treated with antidepressants, including duloxetine, which often results in large inter-individual variability in response. Machine learning (ML) can offer predictive models to help clinicians provide personalized medicine.

We utilized a sample of MDD patients treated with duloxetine (N=186, available through H. Lundbeck A/S), which we iteratively subdivided into ten random train and test sets (70% and 30%, respectively). Standard quality control and imputation for genome-wide data preceded our analyses. We defined response as >50% decrease in MADRS score and ran GWAS on the training sets in PLINK to capture potentially associated variants (p<0.05). We selected features with LASSO regression to subsequently create classification-regression trees (CRT) and support vector machines (SVM) candidate models with using ten-fold, repeated cross-validation in R.

The LASSO regression selected 20 gene variants. CRT models were characterized by 71.8\% accuracy. SVM models had an accuracy of 63.5\% and reasonable sensitivity (78.1\%). In the pre-imputation dataset, accuracy equaled 71.9\% for CRT and 76.9\% for SVM. Including treatment length and age as non-genetic features, accuracy increased to 78.2\% for SVM and CRT (71.9\%). Although the sensitivity reached 87.6\% for SVM, the specificity remained on the random level (55.5\%).

Discussion:
Our models managed to capture a fraction of responders, but failed to filter out non-responders. Although ~80\% of accuracy and sensitivity seemed promising, further refinement of our model is necessary.
**Oral Presentation: A2. Advances in Psychiatric Genetics**

**Genetic and Epigenetic Variation in SKA2 and Disease Severity in Obsessive-Compulsive Disorder**

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OCD has a strong genetic component, is highly comorbid with MDD, and is often triggered by stress. Genetic and epigenetic variation in SKA2 has been implicated in mediating stress response, and has recently been associated with suicidal behavior in MDD (Kaminsky, 2014). The SKA2 polymorphism rs7208505 exhibits allele-specific methylation. We hypothesized that genetic and epigenetic variation at SKA2 may play a role in OCD disease risk and severity.

A sample of n=64 OCD patients, divided equally by presence/absence of comorbid MDD, and age and gender matched, were selected. Y-BOCS score was used to measure disease severity. Genotypes for rs7208505 were compared to Caucasian controls (n=379, 1000 Genomes Project) using Fisher’s Exact test. The relationship among the rs7208505 variant, OCD disease severity, and MDD status was analyzed using ANCOVA. DNA methylation levels were quantified using bisulfite pyrosequencing. Pearson’s r was used to investigate the correlation between percentage methylation and OCD symptom severity.

The SKA2 rs7208505 genotypes significantly differed between OCD patients and controls ($\chi^2=10.21$, $p=0.006$). The CC genotype was significantly associated with lower symptom severity than the CT/TT genotypes ($F(3,52)=4.709$, $p=0.006$). Percent methylation was negatively correlated with OCD severity ($r=-0.438$, $n=56$, $p=0.001$), prior to controlling for genotype. Neither genetic nor epigenetic variation of rs7208505 was associated with comorbid MDD status.

These results provide some evidence that SKA2 genetic and epigenetic variation may be a predictor of OCD risk and severity, regardless of MDD comorbidity; however, replication in larger samples is required. Further work will include interrogating additional genetic and epigenetic variations in SKA2.
Oral Presentation: A2. Advances in Psychiatric Genetics

**Molecular Characterization of NRXN1 Deletions From 19,263 Clinical Microarray Cases Identifies Exons Important for Neuropsychiatric Disease Expression**

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Deletions overlapping NRXN1 exons have been identified in individuals with neurodevelopmental and neuropsychiatric conditions. These deletions are non-recurrent and are found across the entire length of this large 1.1 Mb gene. The purpose of the current study was to assess the relative penetrance of NRXN1 deletions.

We used a large (n=19,263) clinically ascertained cohort from southern Ontario, Canada and 15,264 population-based controls to investigate the penetrance of NRXN1 deletions. CNV data from high resolution genome-wide microarrays allowed systematic evaluation of the burden of secondary CNVs that we used as a proxy to estimate the relative penetrance of exonic and intronic NRXN1 deletions.

We identified 41 (0.21%) previously unreported exonic NRXN1 deletions ascertained for developmental delay/intellectual disability, significantly greater than in controls [OR=8.14 (95% CI 2.91–22.72), p<0.0001]). Ten (22.7%) of these had a second clinically relevant CNV. Subjects with a deletion near the 3’ end of NRXN1 were significantly more likely to have a second rare CNV than subjects with a 5’ NRXN1 deletion [OR=7.47 (95% CI 2.36-23.61), p=0.0006]. The prevalence of intronic NRXN1 deletions was not statistically different between cases and controls (p=0.618). The majority (63.2%) of intronic NRXN1 deletion cases had a second rare CNV, a two-fold greater prevalence than for exonic NRXN1 deletion cases (p=0.0035).

The results support the importance of exons near the 5’ end of NRXN1 in the expression of neurodevelopmental disorders. Intronic NRXN1 deletions do not appear to substantially increase the risk for clinical phenotypes.
Oral Presentation: A2. Advances in Psychiatric Genetics

Association of Noradrenergic and Serotonergic System Gene Variants Across Multiple Antidepressant Remission Phenotypes in Depressed Geriatric Patients

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Finding predictive biomarkers for antidepressant treatment response is imperative in the geriatric population to optimize response and minimize side effects. We investigated the putatively functional variant rs2242446/T-182C of the norepinephrine transporter (SLC6A2, NET) and 5-HTTLPR of the serotonin transporter (SLC6A4, SERT) in association with remission to the dual serotonin-norepinephrine reuptake inhibitor, venlafaxine. As an exploratory analysis, we also investigated 20 variants of other serotonergic system genes (HTR1A, HTR2A, HTR1B, TPH1 and TPH2).

Our sample comprised of 350 participants (≥60 years) assessing efficacy of venlafaxine treatment using a randomised, double-blind, placebo-controlled design. Participants diagnosed with major depression (MADRS≥15) were prospectively assessed for approximately 12 weeks. Associations with remission status (MADRS≤10) were conducted using multivariate binary logistic regression. We conducted mixed-models analysis for response trajectories as well as investigated time-to remission using Kaplan-Meier survival and log rank (Mantel-Cox) analyses.

The NET variant rs2242446, but not the SERT 5-HTTLPR, was significantly associated with remission after adjusting for covariates and correcting for number of tests (OR=1.68, 95% C.I. [1.15, 2.45], p=0.007). Individuals with the C/C genotype (73.1% remitters) were more likely to remit than those with either the C/T (51.5%) or T/T genotypes (48.3%). Mixed-models analysis also revealed a significant difference in response trajectories across eight time-points (χ²=10.47, p=0.005). Individuals with the C/C genotype reached remission faster (M=8.13±4.63 weeks) than those with the C/T (M=9.98±3.90 weeks) or T/T (M=10.25±4.34 weeks) genotypes (Mantel Cox, χ²=7.88, p=0.019).

Our findings suggest that NET rs2242446/T-182C mediates response to venlafaxine in late-life depression.
Suicide and suicide attempts are complex behaviors that result from the interaction of different factors, including genetics that increase the susceptibility to suicidal behaviors. Copy number variations (CNVs) are deletions or duplications of a DNA sequence usually larger than one kilobase. These structural genetic changes, although quite rare, have been associated with genetic liability to mental disorders, such as autism and Schizophrenia.

Based on single-nucleotide polymorphism Illumina array data, we followed the SVS standards to detect CNVs in 122 Schizophrenia subjects.

The initial algorithms did not find any deletion on chromosome 22 in suicide attempters and non-attempters, run of homozygosity combined with imputation confirmed this finding.

Although our findings suggest that chromosome 22 deletion does not play an important role in the etiology of suicidal behaviors, the application of the run of homozygosity strategy is a potentially useful tool to screen for chromosome 22 deletion in large GWAS sample.
Short-Latency Afferent Inhibition From the Dorsolateral Prefrontal Cortex in Patients With Schizophrenia: A TMS-EEG Study

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Transcranial magnetic stimulation (TMS) techniques provide a non-invasive indication of various inhibitory and excitatory processes in the human brain. One such a paradigm involves short-latency afferent inhibition (SAI) that captures a central cholinergic activity traditionally from the motor cortex (M1). Recently, we have established a method to index SAI in the dorsolateral prefrontal cortex (DLPFC), an area implicated in the pathophysiology of Schizophrenia (SCZ). Here, we aimed to investigate SAI in both M1 and the DLPFC in patients with SCZ compared to healthy controls (HC).

Eleven SCZ (8 male, mean age 42±9 yrs) and 12 HC (6 male, mean age 39±12 yrs) were examined with combined TMS-electroencephalography (EEG). Individual N20 latency was determined from somatosensory-evoked potentials prior to the SAI procedure. SAI from the left motor cortex (M1-SAI) and the DLPFC (DLPFC-SAI) was indexed by conditioning a single suprathreshold TMS pulse with right median nerve stimulation at interstimulus intervals of N20+2 (M1-SAI) and N20+4 ms (DLPFC-SAI), respectively.

In patients with SCZ, there were no significant TMS-evoked potential (TEP) changes with M1-SAI, however, we observed a significant TEP N100 attenuation in the left frontal area with DLPFC-SAI (t10=-8.746, p<0.0001). Further, the TEP N100 modulation was significantly different between SCZ and HC (t21=4.579, p<0.0001; SCZ<HC).

The N100 modulation with DLPFC-SAI paradigm could be a potential biomarker to detect the cholinergic dysfunction from the prefrontal cortex in patients with SCZ. These preliminary findings warrant further study which may help to understand high smoking rates among Schizophrenia.
Repetitive transcranial magnetic stimulation (rTMS) of the dorsolateral prefrontal cortex (dLPFC) is a safe, effective treatment for major depressive disorder (MDD), but requires extensive sessions that may be difficult to endure. Intermittent theta burst stimulation (iTBS) provides similar antidepressant effects, but can be delivered in as little as three minutes per session. Investigators have previously classified response to both treatments by (a) scores on the Hamilton Rating Scale for Depression (HRSD), and (b) network-based resting state functional connectivity (rsFC). Here, we investigated whether baseline functional connectivity within the salience network predicted response to traditional dLPFC-rTMS or dLPFC-iTBS.

We collected rs-fMRI data from 147 patients with MDD who received daily sessions of either standardized 10 Hz rTMS or iTBS. Seed-based correlation analyses, independent component analyses, and dual regressions were performed on pre- and post-treatment rs-fMRI in both groups using regions of interest in core nodes of the salience network.

Comparing the two treatment protocols, improvement on the HRSD was differentially predicted by baseline functional connectivity between the left dLPFC and left anterior insula. Additional core nodes of the salience network, including the dorsal anterior cingulate cortex, demonstrated similar patterns of predictive and correlative value with regards to symptom improvement.

Preliminary results suggest that baseline salience network function is predictive of and correlates with treatment outcome following either traditional 10 Hz rTMS or iTBS of the left dLPFC. Salience network rsFC or associated cognitive function could serve as important indicators for successful response to dLPFC stimulation.
Major depressive disorder (MDD) is a debilitating psychiatric condition that affects 16% of the population. Previous studies have found abnormalities in GABAergic mediated inhibitory neurotransmission for patients with MDD. Combined transcranial magnetic stimulation and electroencephalography (TMS-EEG) can non-invasively probe the inhibitory circuits of specific cortical regions, including the dorsolateral prefrontal cortex (DLPFC). The purpose of the current study is to use TMS-EEG measures of cortical inhibition to understand the pathophysiology of MDD, especially those who are considered treatment resistant.

Nineteen patients with treatment resistant MDD and 19 matched healthy subjects were recruited and analyzed. All subjects received single and paired pulse stimulation (100 ms interstimulus interval) delivered to the DLPFC and motor cortex. Measures of interest include the N100 peak of the single pulse TMS evoked potential (TEP) and the suppression of the paired pulse TEP relative to the single pulse TEP (i.e. long interval cortical inhibition [LICI]).

Comparison of LICI values indicates significantly higher cortical inhibition for MDD patients than healthy controls. The difference was localized to the site of stimulation for the DLPFC condition and also extended to the contralateral cortex when stimulation was directed at the motor cortex. Comparison of N100 values shows that MDD patients had a trending higher cortical inhibition for the motor cortex condition.

These results support the hypothesis of abnormal GABAergic inhibition in patients with MDD. The sample is being expanded to verify the results.
Inadequate sleep is associated with increased risk of clinical cardiovascular events; however, the associations between sleep duration or quality and cardiac function or structure are not well elucidated. Herein, we aimed to evaluate the effects of sleep duration and quality on functional and structural left ventricular (LV) deterioration in a large sample cross sectional study from the Kangbuk Samsung Health Study in South Korea.

We enrolled a total of 31,598 healthy adult Koreans. All subjects were assessed using echocardiography and the Pittsburg Sleep Quality Index. The study population was stratified into five groups according to self-reported sleep duration as well as into two groups according to subjective sleep quality. The odd ratios (ORs) for abnormal LV relaxation, remodeling and hypertrophy were compared between groups using multivariable logistic regression analyses.

After adjustment for multiple relevant confounding factors (e.g. age, smoking, body mass index, hypertension, diabetes, physical activity), there was a statistically significant association between short sleep duration (i.e. less than 5 hours) and LV hypertrophy (adjusted OR = 2.10, 95% CI 1.26 – 3.41). There were no statistically significant differences between poor (or good) sleep quality and unfavorable LV change.

Our study demonstrates that short sleep duration (i.e. less than 5 hours) is associated with LV hypertrophy in the general population. The foregoing observation suggests that sleep duration may moderate the development of cardiovascular events and presents a promising target for preventive strategies.
Electrophysiological Evidence for Impairment of Somatosensory Evoked Response in Schizophrenia

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Many patients with Schizophrenia exhibit a variety of symptoms relating to alterations in the somatosensory system. Little is known, however, about the neural substrates underlying somatosensory impairments in Schizophrenia.

The median nerve was stimulated using a peripheral nerve stimulator in 30 healthy subjects (mean age = 38.8, SD = 18.7) and 18 patients with Schizophrenia (mean age = 38.9, SD = 13.9). The peripheral nerve stimulus intensity was adjusted to three times sensory threshold and delivered at 0.1 Hz. Somatosensory evoked potentials (SSEPs) were acquired through EEG. We averaged 100 trials; and the recording electrodes of interest were the C3/CP3 electrodes representing the motor cortex and the F7/F5 electrodes representing the DLPFC. A time window of -50 to 250 ms was used for the analysis. ICA was used for reducing signal artifact.

In patients with Schizophrenia there were alterations in SSEPs in DLPFC compared with healthy subjects. That is, the N30 amplitude was significantly lower in SCZ (-1.16 ± 1.1) compare to HC (-2.4±2.2) (P=0.03). Also, the N30 component was detected earlier in patients with Schizophrenia (N30 latency = 32.16 ± 4.13 ms) compares to healthy subjects (N30 latency = 33.97 ± 2.06) (P=0.04).

Our findings suggest that patients with Schizophrenia demonstrate abnormalities in the processing of somatosensory information. These results may help to develop a model of somatosensory dysfunction in Schizophrenia that can be used to direct treatments for somatosensory related cognitive deficits. These treatments may ultimately lead to improved symptoms in this disorder.
Oral Presentation: A3. Advances in Neurodevelopmental Disorders


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To gather evidence to support aberrant hyperplasticity in the brain in adults with Autism Spectrum Disorder (ASD), and to study if hyperplasticity can be reversed with a 'mechanism-driven' inhibitory repetitive Transcranial Magnetic Stimulation (rTMS).

Using a randomized cross-over design, we so far assessed neuroplasticity in the motor cortex in 7 right-handed ASD subjects and compared them to 5 sex and age matched controls. We further randomized the ASD subjects (1:1) to receive a single session of active or sham rTMS (6000 pulses at 20Hz, inter-train interval of 30s) and then reassessed neuroplasticity on the next day following rTMS. To calculate neuroplasticity, Theta burst stimulation (TBS), which comprises of 2 paradigms- intermittent TBS or iTBS and continuous TBS or cTBS, was applied. cTBS results in long lasting suppression of cortical activity that is analogous to Long Term Depression (LTD) and iTBS results in long lasting enhancement that is analogous to Long Term Potentiation (LTP). The LTD- and LTP-like activities were calculated by measuring the duration of suppression (to cTBS) and enhancement (to iTBS) of TBS-induced cortico-spinal excitability (primary outcome measure).

iTBS-induced LTP-like neuroplasticity is already significantly excessive in the ASD group (mean + SD: 99.28+26.9 min), compared to controls (mean + SD: 47+19.8min) (p=0.004). Active rTMS attenuated both LTP (n=1; duration reduced by 80min) and LTD-like (n=1; duration reduced by 50min) neuroplasticity in ASD subjects (n=2), but the same wasn't observed in the sham group (n=5).

To our knowledge, this is the first study attempting to stabilize aberrant hyperplasticity in ASD using rTMS. Since aberrant neuroplasticity has been linked with autistic behaviours, if successful this information will pave the way for treatments based on etio-pathogenetic mechanism. Given that successful treatment of ASD is still elusive, a novel and effective treatment for ASD will be transformative for the field.
Women with intellectual and developmental disabilities (IDD) have high rates of adverse perinatal outcomes. However, the perinatal health of women with co-occurring IDD and mental illness (dual diagnosis) is largely unknown. Our objectives were to describe a cohort of women with dual diagnosis in terms of their social and health characteristics and compare their risks for adverse maternal and neonatal outcomes to those of women with IDD only.

We conducted a population-based cohort study using linked Ontario (Canada) health and social services administrative data to identify singleton obstetrical deliveries to women with dual diagnosis (N = 2,081) and women with IDD only (N = 1,851) (2002-2012). Primary maternal outcomes were gestational diabetes, gestational hypertension, preeclampsia/eclampsia and venous thromboembolism. Primary neonatal outcomes were preterm birth, small for gestational age, and large for gestational age. We also examined several secondary outcomes.

Women with dual diagnosis were more likely than women with IDD only to live in poor neighbourhoods and to have pre-pregnancy health conditions but had more frequent prenatal care. Infants born to women with dual diagnosis had increased risks for preterm birth ($aRR \ 1.31, 95\% \ CI \ 1.08-1.59$) and neonatal morbidity ($aRR \ 1.35, 95\% \ CI \ 1.03-1.76$) compared to infants born to women with IDD only. All other primary and secondary outcomes were non-significant.

Comorbid mental illness contributes little additional risk for adverse perinatal outcomes among women with IDD. Women with IDD require increased surveillance for maternal and neonatal complications, whether or not they also have a mental illness.
Oral Presentation: A3. Advances in Neurodevelopmental Disorders

Patient Similarity Networks as a Framework for Genetic Case-Control Prediction in Autism Spectrum Disorders

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Autism spectrum disorders (ASD) are heritable, childhood-onset disorders that affect 1-2% people worldwide. Screening identifies genetic causes in 10-30% of cases; DNA copy-number variants (CNV) are present in >10% of cases and contribute to disease risk. We have developed a predictor for ASD case-control status based on the genomic location of rare CNV deletions (Autism Genome Project; 1,485 cases; 1,806 controls).

Our method uses patient similarity networks based on shared CNV overlap and uses the GeneMANIA machine learning algorithm for network integration and prediction. Our algorithm uses extensive cross validation strategies to improve predictor generalizability. We also use nonparametric statistics to exclude pathways that are not enriched in cases, which substantially improves predictor performance.

Using similarities in individual genes resulted in chance performance, consistent with nonoverlapping disrupted genes in ASD. In contrast, using similarities in pathways improved performance to AUC=0.71, beyond those of other pathway-based predictors. At recommended stringency levels, our predictor accounts for 8-15% of all cases with rare CNV deletions. Feature selected pathways recapitulate mechanisms previously identified in ASD genetics, including cell proliferation, neuronal development and function, and signal transduction.

Future challenges include extending the predictor to non-coding genomic regulatory data – one-third of patients have intergenic CNVs --, single nucleotide variants, clinical data and medical history. Patient similarity networks permit integration of heterogeneous data sources and can handle missing or sparse data. This method also naturally provides network-based visualization of patient similarities and predictive pathways, making an intuitive tool for clinical and basic research.
To examine the association between cortical thickness in social brain regions and overall social processing abilities in children with neurodevelopmental disorders.

Social processing abilities of children with autism spectrum disorder (ASD, n=126), attention deficit hyperactivity disorder (ADHD, n=54), obsessive-compulsive disorder (OCD, n=40), or control subjects (n=10), were assessed using the Reading the Mind in the Eyes Test (RMET) and the Social Communication Questionnaire (SCQ). Data from structural MRI scans were processed using CIVET and MAGet brain into 10 social brain regions. Regression models were used to examine the association between cortical thickness, and social processing abilities, while controlling for age, sex, +/- IQ and diagnosis.

Preliminary analyses on a subset of neuroimaging data indicate that increased cortical thickness in several brain regions (e.g. right temporal parietal junction, right superior temporal gyrus, and bilateral temporal poles) is associated with higher accuracy on the RMET, surviving correction for multiple comparisons at a significance level of 0.05. When diagnosis and subsequently IQ were controlled for as factors in the model, significant differences persisted in several regions.

Results suggest that greater cortical thickness in specific social brain regions is associated with better social processing abilities in children and youth with neurodevelopmental disorders. Full neuroimaging data, as well as single nucleotide polymorphism genotype for several neuropeptide receptor genes [oxytocin (OXTR) and vasopressin (AVPR1a)] are anticipated shortly and will also be presented. Results will help clarify the complex relationship between genotype, brain structure, social abilities, and diagnosis.
Cognitive impairments are acknowledged in the DSM-5 criteria for a Major Depressive Episode (MDE); “diminished ability to think or concentrate, or indecisiveness” and almost 90% of the MDD patients examined in the STAR*D (Sequenced Treatment Alternatives to Relieve Depression) trial reported cognitive difficulties at baseline assessment.

In the Canadian Biomarker Integration Network in Depression (CANBIND) study neurocognitive measures were obtained using the CNS (Computerized Neurocognitive Assessment Software) at baseline on 86 MDD patients and 46 healthy controls. Cognitive performance was measured by the domains of Memory, Psychomotor speed, Reaction Time, Cognitive Flexibility, Complex Attention and Executive Function. Low domain scores were defined as more than one standard deviation (SD) below mean and depression severity was assessed using MADRS scale.

The patient and control groups were compared using t-tests (parametric data) and/or Wilcoxon (non-parametric data) tests. We applied qqplots and Shapiro-Wilk tests to determine variable distribution. We computed correlations coefficients to explore potential association between MADRS severity and cognitive performance scores.

We noticed significant (p<0.05) difference in CNS performance between treatment and control groups for all, except for reaction time and complex attention domains. 19.7% of our treatment group showed impairment defined as 1 SD or more below mean, the same situation appeared in 6.5% of controls. We observed weak, negative (r between -0.3 and -0.2, p<0.05) correlations between depression severity and cognitive performance.

This study emphasizes that cognition impairment is prevalent in MDD and should be targeted for treatment in addition to other depressive symptoms.
Elevated blood homocysteine level is proposed to be a modifiable risk factor for late-onset Alzheimer’s disease (AD). However, unlike observational studies, clinical trials have reported inconsistent results for the effect of altering homocysteine on AD-related outcomes. Using a mendelian randomization approach we determined whether blood homocysteine is merely a byproduct of or is a causal contributing factor to AD pathophysiology.

Thirteen genome-wide significant SNPs influencing plasma homocysteine level (van Meurs et al., 2013) were used to perform mendelian randomization study (using IGAP SNP-AD associations’ summary statistics, AD=17,008, nondemented-controls=37,154) and polygenic score studies (using ADNI, ADGC, GenADA, and ROS/MAP data, age>=65, European descent). Polygenic score studies were performed using linear mixed models while accounting for fixed effects of age, sex, and number of APOE-ε4 alleles, and random effects of study groups/genotyping platforms.

Mendelian randomization analysis (using an inverse-variance weighted approach) did not support causal association between genetically-predicted plasma homocysteine level and risk for AD (O.R. for a one-SD predicted increase in plasma homocysteine[95%CI]=1.01[0.89-1.15]). Mega-analysis of association between plasma homocysteine polygenic score and risk for AD (AD=3,866, nondemented-controls=2,691) was also non-significant (O.R.[95%CI]=1.02[0.96-1.08]). Additional analyses among AD patients showed no evidence for association between plasma homocysteine polygenic score and baseline MMSE score (n=1,179, P=0.81) or longitudinal change in MMSE score (775 observations on 239 ADNI participants, mean follow-up=17months, P=0.18).

Our analyses demonstrate that genetically-determined plasma homocysteine levels do not influence risk for, and severity and progression of AD. This suggests that plasma homocysteine is a biomarker of AD rather than a causal factor.
Prior to the 1960s, acute lymphoblastic leukemia (ALL) was uniformly lethal. Fortunately, 5-year survival rates now approach 95%. While chemotherapy effectively cures ALL, there is growing concern that it may also cause damage to brain and lead to deficiencies in functional abilities in survivors. The overarching goal of the study was to elucidate brain structure in relation to cognitive abilities in childhood ALL survivors who were treated with chemotherapy protocols.

ALL survivors (n=24) and age- and sex-matched controls (n=21) between 8 – 18 years old underwent 3T structural MRI. T1-weighted anatomical scans were processed using the CIVET pipeline. Motor response inhibition and working memory were assessed with the Stop Signal Task (SST) and the N-Back Task respectively.

Frontal and parietal white matter volume were significantly reduced in ALL survivors compared with controls (FDR-corrected p-value, q < 0.1). Additionally, cortical surface volume deficits in ALL survivors were evident in the temporal lobes and the occipital lobes (q < 0.1). Relative to controls, ALL survivors had more difficulties with response inhibition and working memory. Significant correlations were observed between frontal white matter volume and response inhibition (average r = -0.31, p < 0.05), and between orbitofrontal and temporal cortical volume and working memory performance (r = 0.37 and r = 0.36, both p < 0.01).

Exposure to chemotherapy, especially at a young age, may change brain development and lead to functional impairments in ALL survivors. Identification of the pathophysiology of chemotherapy-induced brain damage will facilitate the search for remedies and prevention.
Amnestic mild cognitive impairment (aMCI) is often characterized as a prodromal stage of Alzheimer’s disease. With the use of positron emission tomography (PET) we sought to investigate whether neuroinflammation is present in this transitional stage, and its relationship with amyloid burden.

A total of 21 participants: 10 aMCI patients and 11 healthy controls underwent one or both PET scans ([18F]-FEPPA PET scan and [11C]-PIB PET scan) to quantify neuroinflammation and amyloid burden respectively, and a MRI scan. All participants completed a battery of neuropsychological tests. Given the known inter-individual variability of [18F]-FEPPA binding to TSPO in the brain, only high-affinity binders (HABs) were included. [18F]-FEPPA PET was analyzed using the validated 2-tissue compartment model with full arterial input function. [11C]-PIB PET was analyzed using Logan analysis with cerebellum as a reference region.

No significant differences in [18F]-FEPPA binding were observed between aMCI patients and healthy controls in our pilot study. aMCI patients had significantly more amyloid in the cortical regions as reflected by increased [11C]-PIB binding. The largest difference, nearly two-fold, was found in the prefrontal cortex (t(6.220)=4.033, p=0.06). No spatial relationship was found between neuroinflammation and amyloid burden. In aMCI patients, [18F]-FEPPA binding in the temporal cortex (R=-0.809, p=0.028) and hippocampus (R=-0.813, p=0.026) was inversely correlated with performance on an immediate memory task.

So far, we did not find an increase in neuroinflammation in individuals with amnestic mild cognitive impairment compared to healthy controls. Amyloid pathology, however, is evident in this transitional stage.
This study aims to assess the association of Montreal Cognitive Assessment (MoCA) and Mini-Mental State Exam (MMSE) scores with Cognitive Dementia Rating (CDR) cognitive and functional domains in participants with MCI.

Seventy-four participants with MCI (mean age (SD): 72.96(7.46); mean education(SD): 15.63(2.82) years; male: 39(53%)) were classified as impaired (CDR=0.5) or intact (CDR=0.0) across six domains (Memory, Orientation, Judgment/Problem Solving, Community Affairs, Home and Hobbies, Personal Care). Correlations between i) MoCA and ii) MMSE and each CDR domain guided variable selection for 12 logistic regression models.

MoCA and MMSE were significantly correlated (r=0.52, p<.05). Only two CDR domains were significantly correlated with MoCA and MMSE using Spearman’s rho. CDR Memory was negatively correlated with MoCA (rho=-0.35, p<.05), but not MMSE (rho=-0.09, p>.05). CDR Community Affairs was negatively correlated with MMSE (rho=-0.41, p<.05), but not MoCA (rho=-0.14, p>.05). Adjusting for education, our models demonstrated an association between CDR Community Affairs impairment and low MMSE (adjusted OR(aOR)=0.44, 95% Confidence Interval (CI)=[0.24-0.82], p<0.01) but not MoCA (aOR=1.14, 95% CI=[0.84-1.56], p>.05). Age, sex, and race did not significantly modify this relationship.

Preliminary data suggests that, compared to the MoCA, the MMSE is more robustly associated with a functional CDR domain, Community Affairs. Future analyses with a larger sample will explore this relationship.
Atypical antipsychotics (AAPs) such as olanzapine (OLA) are widely prescribed but associated with high rates of type 2 diabetes (T2D). Historically the risk of T2D was attributed to their weight gain propensity, which varies among AAPs. However, existing work shows that: a) independently of weight gain AAPs have an immediate effect, and b) they act at least in part via the brain, to perturb glucose homeostasis. Intriguingly, links between central insulin pathways and AAP therapeutic efficacy have been proposed. Thus understanding brain-mediated glucose dysregulation may be critical not only to treating these side-effects, but to maximizing AAP efficacy.

Employing our established rodent model of AAP-induced glucose dysregulation we examined if OLA causes insulin resistance via an impairment of hypothalamic insulin sensing. Gold-standard euglycemic pancreatic clamps were used to measure glucose kinetics (hepatic glucose production (HGP) and peripheral glucose disposal). This procedure allows maintenance of basal peripheral insulin levels and separate manipulations of central insulin levels. Rats were treated with an acute subcutaneous dose of OLA (dose based on therapeutic D2 brain occupancy) or vehicle during the clamp procedure according to our established model of OLA-induced insulin resistance. A central infusion of insulin (established to suppress HGP) or vehicle was administered into the 3rd ventricle during the clamp.

OLA fully abolished the ability of the central insulin infusion to suppress hepatic glucose production.

For the first time, in an in vivo system we demonstrate that OLA induces hypothalamic insulin resistance. This work is critical to furthering our understanding of a very serious adverse effect (glucose dysregulation), which through the brain may overlap with treatment dimensions of Schizophrenia.
Clinicians treating first-episode Schizophrenia are faced with numerous choices in terms of antipsychotic, dose, formulation, etc. In addition, assessing response can be difficult due to lack of clarity regarding definition of response, remission, and the appropriate time to achieve each.

We developed a treatment algorithm for first-episode Schizophrenia using standardized clinical rating scales to evaluate response. The algorithm assumes that early and effective disease management may favorably influence outcome. Further assumptions include: early onset of action of antipsychotics; treatment resistant Schizophrenia (TRS) can be identified during the earliest stages; and, relapse prevention efforts should be implemented as soon as possible.

The algorithm progresses according to response, moving patients through two non-clozapine second generation antipsychotic (SGA) trials followed by clozapine. Patients achieving response are advised to switch to SGA-long acting injectable (LAI) formulations.

457 patients were offered treatment according to the algorithm, of these, 338 (74%) commenced treatment and completed at least one antipsychotic trial. At 6-month antipsychotic treatment was: oral SGA 154 (45.6%); LAI 100 (29.5%); clozapine 79 (23.3%); FGA/Polypharmacy 5 (1.5%).

We provide findings from an established algorithm that is evidence based and addresses practical issues often not captured by randomized clinical trials (RCTs). Our own experience indicates that approximately 50% will be treated with an oral SGA, 30% with a LAI SGA, and 20% with clozapine. This distribution might serve as an index for good clinical practice in first-episode Schizophrenia clinics.
The Effect of Ethnicity and Migration in Treatment Resistant Schizophrenia

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Treatment resistance is a common phenomenon among Schizophrenia patients treated with antipsychotics. According to the American Psychiatric Association (APA) guidelines, treatment resistant status is little or no symptom reduction to at least two antipsychotics. The aim of the current study is to determine whether ethnicity and migration are associated with the development of treatment resistance.

We included 278 participants with Schizophrenia. The genetic analysis was performed using Structure including the sample of this study and three HapMap samples with known origins: European, African, and Asian, thus, three populations were assumed.

Based on our analysis of 292 SNPs, the overall proportion of ancestry of the sample was 0.578 European, 0.165 African and 0.257 Asian. The binary logistic regression model revealed no significant association between ethnicity and treatment resistance Schizophrenia regardless of whether European ethnicity was determined by self-report or genetic analysis. However, self-report white Caucasians who were born in Canada had higher likelihood of being treatment resistant than non-white Canadian born patients and migrants.

Due to the public healthcare system in Ontario, Canadians and residents of Canada of all ethnicities have equal access to treatment for their Schizophrenia, which may explain why neither ethnicity nor migrant status was significantly associated with treatment resistance. However, Canadian-born white patients may be more likely to express negative experiences of their antipsychotics to doctors, which may result in more frequent changes in the prescription such as dosage changes and switching to another antipsychotic.
The objective of this study was to determine the quality of diabetes care and diabetes-related outcomes among individuals with and without Schizophrenia.

We identified all individuals with diabetes in Ontario alive as of April 1, 2011. We identified individuals who had a diagnosis of Schizophrenia prior to April 1, 2011. We measured quality of diabetes care and diabetes-related Emergency Department visits and hospitalizations between April 1, 2011 and March 31, 2013. We estimated the quality of care and diabetes outcomes with Schizophrenia as our primary exposure adjusting for demographic, illness severity, and health service utilization variables.

We identified 1,131,181 individuals with diabetes, among whom 19,433 had Schizophrenia. Individuals with Schizophrenia were younger, more likely to be female and to live in low income neighbourhoods. Individuals with Schizophrenia had more primary care physician visits than individuals without Schizophrenia (mean (SD): 9.2 (10.3) vs. 6.6 (6.7). Individuals with Schizophrenia were 40% less likely to receive optimal diabetes care (all 3 of HbA1c, lipid testing, and eye exams) than individuals without Schizophrenia (OR (95% CI): 0.60 (0.57-0.63)) but 32% more likely to have a diabetes-related hospitalization (OR (95% CI): 1.32 (1.24-1.41)).

Individuals with diabetes and Schizophrenia have poorer diabetes quality of care and worse diabetes-related outcomes than individuals without Schizophrenia. The poor quality of care exists despite higher frequency contact with primary care. Delivering high quality health care and achieving good health care outcomes for individuals with Schizophrenia and diabetes likely requires highly integrated and intensive health service delivery.
Since the 1990s, first episode psychosis (FEP) has garnered significant attention and resources. While there has been an expansion of clinical services for FEP, there is a lack of scholarly work that critically engages with concepts embedded in the early intervention paradigm. Here, we investigate the emergence of FEP as an entity in psychiatric research and practice in order to offer a more nuanced understanding of the domains of psychotic illness and functional recovery in early psychosis.

Utilizing close reading and discourse analysis, we examine institutional documents, scholarly literature, and popular media to construct the emergence of FEP. Situating the text materials in a social and historical context, thematic coding was undertaken; an analysis of text structure and semantics (rhetorical devices, metaphorical language) was additionally carried out.

Although scattered references to “prodrome” exist in the historic psychiatric literature, FEP emerged as a distinct chronological stage of psychotic illness in the late 1980’s in response to a desire for a homogeneous, medication-naïve population within psychiatric research. Preliminary thematic findings demonstrate a concern with “purity” as well as notions of “progress,” informed by enlightenment ideologies.

Within FEP it is hoped that earlier interventions will translate into shorter durations of untreated illness, improved utilization of services, and better prognoses for recovery. While these are laudable goals, they are steeped in assumptions about biomedical progress and idealizations of clinical populations. A robust approach to recovery in FEP entails a critical engagement with such assumptions.
Randomized clinical trials have established the efficacy of naltrexone for reducing quantity of alcohol consumption and incidence of relapse to heavy drinking in treatment-seeking patients with alcohol dependence. To evaluate potential treatment mechanisms, human laboratory studies have examined naltrexone’s effects on alcohol responses and self-administration during short-term medication protocols. Results from these studies are somewhat inconsistent and have yet to be examined in aggregate.

This meta-analysis aimed to quantify naltrexone’s effects on alcohol self-administration and craving in the context of placebo-controlled human laboratory trials. Potential moderators of medication effects were also examined, including study population (dependent vs. non-dependent drinkers), number of dosage days, and characteristics of laboratory paradigms. Meta-analyses of alcohol self-administration (k = 9, N = 490) and craving (k = 15, N = 673) outcomes demonstrated that, under controlled experimental conditions, naltrexone reduces the quantity of consumption (Hedges’ g = -.277, SE = .074, 95% CI = -.421, -.133, p < .001) and magnitude of self-reported craving (g = -.287, SE = .070, 95% CI = -.424, -.149, p < .001) relative to placebo. Subgroup and moderation analyses found no evidence that effect sizes differed based on population, laboratory paradigm, or duration of medication exposure.

Results also supported that naltrexone significantly reduces craving both prior to and following exposure to acute alcohol or alcohol cues. These results substantiate prior evidence for reductions in event-level craving and consumption as potential treatment mediators and establish effect sizes to inform future human laboratory trials. From a clinical perspective, these results also provide further support for naltrexone’s efficacy for reducing consumption in non-dependent drinkers and in acute or sub-acute dosing contexts—approaches that have received empirical support but are likely uncommon in practice.
Reducing the nicotine content in cigarettes could improve public health by reducing smoking and toxicant exposure, but may also have unintended consequences on alcohol use. The primary objective of this study was to examine the effect of reducing the nicotine content in cigarettes on alcohol outcomes. The secondary aim was to examine whether the effects of these cigarettes on alcohol outcomes were mediated by changes in nicotine exposure, smoking behavior, or withdrawal.

Between June 2013 and July 2014, we conducted a 7-arm, double-blind, randomized clinical trial at 10 U.S.-based sites. Daily smokers not currently interested in quitting (n = 839) were assigned to equally sized groups to smoke for 6 weeks cigarettes containing either normal nicotine content (NNC; 15.8 mg/g, 9 mg tar), moderate nicotine content (5.2 mg/g nicotine, 9 mg tar), or very low nicotine content (VLNC; 0.4 to 2.4 mg/g, 9 to 13 mg tar). This investigation focused on a subsample of current drinkers (n = 403). Each reduced nicotine content cigarette condition was compared to the NNC control condition with respect to trajectories over the 6-week period of average daily alcohol use and occurrence of binge drinking. Moderating variables were considered. Mediation analyses tested potential explanatory processes including changes in nicotine exposure, cigarettes per day, and withdrawal.

Over time, reduced nicotine exposure and smoking rate mediated effects of VLNC cigarette use on reduced alcohol use. There was no evidence of compensatory drinking in response to nicotine reduction or nicotine withdrawal, even among subgroups expected to be at greater risk (e.g., relatively heavier drinkers, highly nicotine-dependent individuals).

The findings suggest that compensatory drinking is unlikely to occur in response to switching to VLNC cigarettes. In contrast, reducing the nicotine content of cigarettes may reduce alcohol use.
Global climate change increasingly disrupts biodiversity, weather patterns, and general health. With greater public awareness of the effects of climate change, the potential for mental health issues, particularly anxiety, increases. This study examined the prevalence and predictors of climate-related anxiety.

An online survey was administered to 2,035 participants across Canada and the United States. The newly constructed Climate Change Anxiety Scale (CCAS) explores anxiety and depression associated with climate change as well as climate change knowledge, beliefs, experiences, and general well-being.

A total of 355 (17.5%) respondents (163 males, 184 females, 8 undisclosed/unknown) reported high levels of climate-related anxiety. The following demographic factors significantly predicted anxiety: living in Canada ($\beta=0.62$, 95%CI[0.01,1.35]), a community of 25,000 to 100,000 people ($\beta=0.44$ [0.04,0.85]), a West Central geographic location ($\beta=-0.41$ [-0.79,-0.03]), being female ($\beta=0.48$ [0.21,0.74]), and age 18-29 years ($\beta=0.68$ [0.01,1.35]). These variables accounted for 3.16% of variance in climate change anxiety. When controlling for demographics, knowledge, attitudes, experience and information, personal actions, general actions, and personal importance of climate change were significant predictors of climate change anxiety. This model accounted for 73.68% of the variance in anxiety. The prevalence of high climate change anxiety along with help-seeking and high levels of dysfunction (climate change anxiety “disorder”) was 3.5% (34 males, 37 females).

Climate change anxiety may represent an important emerging public health issue warranting further research. These findings may have implications for public policy and education that can help reduce climate change anxiety in North America.
Oral Presentation: B4. Advances in Clinical Research II

The Role of Filial Piety in Mediating Risk and Recovery in Chinese Women With a History of Suicidal Behaviour: A Cross-Cultural Qualitative Study

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Filial piety involves the Confucius view that one's life is the continuation of one's parents' lives. Family harmony is prioritized over personal goals. Filial piety has been described as both a risk and a protective factor in depression and suicide. The dual filial piety model describes differences between authoritarian and reciprocal filial piety. The former involves submitting to rigid familial hierarchy while the latter involves internalizing this virtue based on mutual two-way affection. The role of filial piety in the suicidal behaviour of Chinese women is not well studied, and findings in this area can clarify culturally-appropriate strategies for prevention and treatment of suicidal behaviour.

Collaborating with Tsinghua University, qualitative interviews were conducted with Chinese-born Canadian (n=10) and Chinese women (n=30) with a history of suicidal behaviour. Filial piety data were extracted and analyzed using constructivist grounded theory.

Every woman in the Chinese Canadian sample described duty to parents and lack of agency in their family as distressing, sacrificing personal interests for their parents'. Several Chinese women, largely from families experiencing reciprocal filial piety, described filial piety as protective, as suicide would dishonour their parents.

Filial piety has a nuanced role in the risk and recovery of Chinese women with a history of suicidal behaviour. While filial piety was a source of distress for the Chinese Canadian women, several Chinese women described filial piety as protective for suicide. This difference may be partially understood through the dual filial piety model.
Inflammation has been implicated in the risk, pathophysiology and progression of mood disorders and as such has become a target of interest in the treatment of bipolar disorder (BD). Therefore, the objective of the current meta analysis is to determine the overall antidepressant effect of adjunctive anti-inflammatory agents in the treatment of BD depression.

Completed and ongoing clinical trials of anti-inflammatory agents for BD published prior to May 15, 2015 were identified through searching the PubMed, Embase, PsychINFO, and Clinicaltrials.gov databases. Data from randomized controlled trials (RCTs) assessing the antidepressant effect of adjunctive mechanistically diverse anti-inflammatory agents were pooled to determine standard mean differences (SMD) compared to standard therapy alone.

Ten RCTs were identified for qualitative review. Eight RCTs (n=312) assessing adjunctive nonsteroidal anti-inflammatory drugs (n=53), omega3 polyunsaturated fatty acids (n=140), N-acetylcysteine (n=76) and pioglitazone (n=44) in the treatment of BD met inclusion criteria for quantitative analysis. The overall effect size of adjunctive anti-inflammatories on depressive symptoms was 0.40 [95% confidence interval 0.14 to 0.65 (P=0.002)], indicative of a moderate and statistically significant antidepressant effect. Heterogeneity of the pooled sample was low [I²=14%; P=0.32]. No manic/hypomanic induction or significant treatment emergent adverse events were reported.

Overall, a moderate antidepressant effect was observed for adjunctive anti-inflammatory agents compared to conventional therapy alone in the treatment of BD depression. The small number of studies, diversity of agents and small sample sizes limited interpretation of the current analysis.
Nicaragua has high rates of mental illness, addictions and suicide, particularly among youth, but mental health resources and awareness are limited. Schools could be used as sources of mental health knowledge and support. This project evaluated the efficacy of a school-based mental health program in enhancing well-being and access to care among youth in Leon, Nicaragua.

Students (15-19 years) at the 4 high schools and the local university in Leon participated. Some schools and university departments received a 12-week mental health curriculum (intervention group), and the rest were the control group. Intervention group teachers were trained to deliver the curriculum and identify and support/refer distressed students, as needed. Students completed self-report measures of mental health knowledge and personal functioning at baseline, 12 weeks and 6 months.

A total of 913 students (567 intervention, 346 control) participated. The groups had similar demographics and baseline scores on the self-report measures. After 12 weeks, intervention students had better mental health knowledge and health behaviours and lower stigma and perceived stress than controls (p≤0.05), and increased help-seeking compared to baseline (p≤0.05). Referrals of students for additional care increased significantly among intervention teachers, but not among control teachers (p≤0.05). These findings were sustained at 6 months.

A school-based mental health program was effective in improving functioning, mental health knowledge and help-seeking among Nicaraguan
Power imbalances complicate partnerships between low- and middle-income country (LMIC) researchers and collaborators from higher income countries. To quantify this issue, we conducted a bibliometric analysis of recent health research in LMICs, emphasizing Africa and investigating the relationship between country affiliations and author positions, where first and last author are most prestigious.

We searched PubMed for articles on LMIC-related health research using search terms containing “low or middle income countries” or “low income countries” or “Africa” and “health” and “resource-limited” in the title, abstract, and/or MeSH headings, from January 1, 2014 to February 28, 2016. We exported the XML file of results and used SAS to compute descriptive statistics of author affiliations.

Our search yielded 3609 articles; 3426 had affiliation information. The top three country affiliations were the US, UK, and South Africa. Authors affiliated with those three countries were first and last author more frequently than middle author. In contrast, the next top African countries—Uganda, Kenya and Nigeria—generally had more representation amongst middle authors.

Authors from high-income countries dominate recent LMIC-related health research; however, in Africa, South Africa is an exception. Apart from South Africa, our data suggest that those credited for LMIC-based health research are rarely from LMICs, and LMIC researchers who publish occupy less prestigious middle author positions more frequently than first or last. This lopsided literature suggests that innovative approaches are required to reform collaborative health research and ensure credit is given where credit is due.
Oral Presentation: A5. Advances in Global Health

Lessons Learned From Implementing a Mental Health Integration Program Based on Scaling Up of a Psychosocial Therapy to Primary Care in Ethiopia: The Biaber Project

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The purpose of this project was to scale up screening and treatment of Common Mental Disorders using culturally adapted interpersonal psychotherapy-based therapy (IPT-E) in 19 health centers across Ethiopia, decreasing MH stigma and integrating mental health care within a general health system.

We employed a ‘train-the-trainers method’ to train psychiatrists, mental health professionals, and primary care workers, in screening and treating, using IPT-E, common mental health problems in primary care across 19 health centers in five regions of Ethiopia. Amharic language training and mentorship materials were developed and used.

A total of 497 health care professionals were trained (11 Psychiatrists, 47 mental health professionals, 426 primary care nurses and 13 Family Medicine residents). A harmonized network of health professionals working towards mental health integration in primary care implemented the scale up in 19 health centers. 20,274 patients were screened and with a 6% prevalence of CMDs, 1365 were treated with IPT-E for up to four sessions. Primary care workers’ knowledge and satisfaction improved.

Integration of mental health care into primary care is feasible, Primary care workers are willing and able to do mental health work provided that there is adequate and regular mentorship. Primary care workers are able to modify and adapt in the context of changes to their work environment as a result of integration efforts. Mental health professionals have potential to play a non-clinical role as mentors to facilitate integration, within a supportive policy environment that is central to success.
A Qualitative Inquiry Into Educators’ Perspectives of the Mental Health Needs of Young People in León, Nicaragua

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There has been limited research into explanatory models of mental illness among young people in Nicaragua, particularly in relation to mental health programme development. We aimed to understand teacher’s perspectives of mental illness in adolescents in the context of evaluating the implementation of a mental health literacy curriculum.

Ethics approval for this qualitative study was obtained from the Ministry of Education. Focus groups were completed in Spanish in León, Nicaragua. Public high school and university educators were recruited via convenience sampling. Translated and transcribed recordings were coded and analyzed through an iterative coding process for common themes using grounded theory.

43 teachers participated. Teachers described a model of mental illness in which isolation from family and community was a marker and result of mental illness. They describe the development of mental illness primarily as socio-political rather than biological, focusing on failures of family, social, and religious structures. Their description of interventions focused on the need to help adolescents reintegrate into society and return to functioning within their community.

Preliminary results from this study suggest that educators in Nicaragua view mental illness in adolescents as a result of failed social structures. Such a perspective is in keeping with a cultural focus on the primacy of the family and the importance of community. Future mental health initiatives in Nicaragua are more likely to be successful if they acknowledge this explanatory model and address how mental health interventions might promote effective community function and decrease isolation and family conflict.
To examine the role of ethnicity, socio-demographic, clinical and neighbourhood factors in pathways to emergency mental healthcare for clients with psychosis in Toronto. There are differences in pathways to care for immigrant groups. However, a recent Ontario study demonstrates that pathways may be different in two cities; raising the question whether ethnic differences may be explained by neighbourhood effects.

A chart review of East-Asian, South-Asian, Black-African, Black-Caribbean, White-European, and White-North American clients presenting with psychosis to an emergency department. Regression models examined the relationship between presentation by police, crisis team or ambulance, individual level factors and neighbourhood level poverty, ethnic density and residential instability.

765 clients were included in this study. East-Asian (2.12 OR, 95% CI 1.21-3.71) and Black-African (2.00 OR, 95% CI 1.10-3.64) groups had increased odds of presenting by emergency services in unadjusted models compared to the White-North American group. After adjusting for involuntary detention, there were no significant differences between groups. When adjusting for neighbourhood variables the odds were 2.1 times greater for the East-Asian group (95% CI 1.01-4.36). None of the other groups had significant differences compared to White-North Americans. Neighbourhood level residential instability increased the odds, and GP involvement decreased the odds. Poverty and ethnic density did not have a significant impact.

East-Asian clients with psychosis had increased odds of a negative mode of arrival. Clients living in areas with greater residential instability are more likely to encounter negative pathways, which may argue for increased deployment of services in such areas.
A Qualitative Study of Young Adult Bariatric Surgery Patients: 
Psychosocial Challenges and Developmental Difficulties

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Obesity rates are increasing to epidemic proportions; young adults are no exception (Ogden et al., 2014). Bariatric surgery is an evidence-based treatment for severe obesity (Rianthavorn & Ettenger, 2005); however, the unique developmental and psychosocial needs of young adults can complicate care. Objectives: (1) to identify themes regarding the experiences of obese young adults (18-25) seeking bariatric surgery; (2) to identify psychosocial difficulties of young adults seeking bariatric surgery; and (3) to understand how developmental needs within this population impact experiences of the bariatric surgery process.

In-depth, semi-structured individual interviews were conducted on 10 young adult bariatric patients who were seeking or had undergone bariatric surgery within the last 5 years. Data collection is still underway as saturation of themes has not yet been reached. Analysis of interviews used a constant comparative analysis consistent with a grounded theory approach.

Our data analysis generated the following themes: (1) improved quality of life for patient and family members, (2) parents as both “supporters” and “controllers”; (3) pre- and post-operative psychosocial concerns; (4) desired characteristics of health care providers; and (5) unique developmental difficulties.

Results suggest a potential multifactorial framework regarding young adult bariatric surgery patients’ experiences within an adult health care system. These experiences appear to encompass familial relationships, psychosocial and developmental concerns as well as needs sought from healthcare providers. By understanding the complex experiences of young adults with medical and psychiatric comorbidities, healthcare providers might be able to provide better care for these patients.
Conventional treatments for eating disorders are associated with poor response rates and frequent relapse. Novel treatments are needed, in combination with markers to characterize and predict treatment response. Here, resting-state functional magnetic resonance imaging (rs-fMRI) was used to identify predictors and correlates of response to repetitive transcranial magnetic stimulation (rTMS) of the dorsomedial prefrontal cortex (dmPFC) at 10 Hz for eating disorders with refractory binge/purge symptomatology.

28 subjects with anorexia nervosa, binge-purge subtype or bulimia nervosa underwent 20-30 sessions of 10 Hz dmPFC rTMS. rs-fMRI data were collected before and after rTMS. Subjects were stratified into responder and nonresponder groups using a criterion of ≥50% reduction in weekly binge/purge frequency. Neural predictors and correlates of response were identified using seed-based functional connectivity (FC), using the dmPFC and adjacent dorsal anterior cingulate cortex (dACC) as regions of interest.

16 of 28 subjects met response criteria. Treatment responders had lower baseline FC from dmPFC to lateral orbitofrontal cortex and right posterior insula, and from dACC to right posterior insula and hippocampus. Responders had low baseline FC from the dACC to the ventral striatum and anterior insula; this connectivity increased over treatment. However, in nonresponders, frontostriatal FC was high at baseline, and dmPFC-rTMS suppressed FC in association with symptomatic worsening.

Enhanced frontostriatal connectivity was associated with responders to dmPFC-rTMS for binge/purge behavior. rTMS caused paradoxical suppression of frontostriatal connectivity in nonresponders. Rs-fMRI could prove critical for optimizing stimulation parameters in a future sham-controlled trial of rTMS in disordered eating.
A Pilot Study of Diffusion Tensor Imaging in Anorexia Nervosa: Comparison across Underweight and Weight-Recovered Subjects, Their Unaffected Siblings, and Unrelated Controls

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Anorexia Nervosa (AN) is a highly heritable and frequently chronic psychiatric disorder, the neural correlates of which are poorly understood. In order to identify structural differences that may confer vulnerability to AN, this study aims to compare measures of white matter (WM) microarchitecture across four groups: underweight women with a current diagnosis of AN (uAN), weight-recovered women with a past diagnosis of AN (recAN), unaffected sisters of the aforementioned women (sibHC), and unrelated female controls (nonsibHC).

A 3T GE scanner is being used to acquire diffusion-weighted images via application of a single-shot spin-echo EPI pulse sequence and 60 gradient directions. Within FSL TBSS, general linear models including age as a covariate are being used to identify regions of significant between-groups difference in fractional anisotropy (FA) and mean diffusivity (MD), and multiple regression is being used to assess the functional correlates thereof.

To date, 66 women (18 uAN, 18 recAN, 6 sibHC, 24 nonsibHC) have been imaged, revealing significant between-groups differences (pFWE < 0.05) in FA and/or MD along four major WM tracts: internal capsule, corona radiata, corpus callosum, and superior longitudinal fasciculus. For uAN and recAN women, peak values along these tracts show strong associations with state (i.e. BMI) and trait (i.e. anxiety) variables, respectively.

Alterations in FA and MD, measures thought to reflect various physiological processes including inflammation, edema, and myelination, may contribute to premorbid disease vulnerability and/or malnutrition-induced symptom exacerbation. Continued recruitment of unaffected sisters will further illuminate these findings.
Breast cancer (BC) and its treatments have significant impact on body image and sexual functioning, reducing quality of life. 20-45% of BC survivors report significant body image disturbance or decreased sexual functioning up to several years post-diagnosis.

A prospective randomized controlled study was conducted testing an 8-week group intervention for BC survivors. The intervention incorporated guided imagery to promote emotional expression and insights related to difficulties in body image, provided coping strategies, psychoeducation and incorporated women-centred therapy strategies to increase insight on relevant sociocultural factors at play. With a 2:1 randomization, 128 women received the group intervention and 65 were in control group receiving usual clinical care and reading materials. Standardized measures of body image, quality of life and sexual functioning were completed at baseline, post intervention, 6 months and 1 yr.

Participants were on average 49 yrs of age (26-75), 63% were married, 64% had a mastectomy. At baseline, there was a high prevalence of body image disturbance, lower adjustment levels, decreased sexual functioning and poorer quality of life compared to reports of similar or other medical populations. There was a statistically significant improvement for the group on body image, particularly body stigma compared to controls. Improvements in sexual functioning and overall quality of life occurred but did not reach significance at six months. There was a statistically significant difference on quality of life at one year. Results suggest that the guided imagery/group support program was effective in addressing body image disturbance.
Anorexia nervosa (AN) is a serious and often chronic medical illness with high rates of morbidity, mortality and treatment resistance. However, little is known about what factors predict response to treatment. The purpose of this study was to explore how patients who require multiple inpatient admissions differ from those who stabilize after only one admission.

Participants were 288 patients with Anorexia Nervosa admitted to the inpatient eating disorder program at Toronto General Hospital between 2000 and 2005. All participants completed a series of psychological measures including inventories of demographic variables, eating disorder symptoms (EDE-Q), depressive symptoms (BDI) and suicidal ideation (BSI). Their weight gain and eventual treatments outcomes were also recorded. Participants were then categorized by their number of prior admissions.

Patients who required multiple admissions were more likely to have the Binge-Purge subtype of Anorexia Nervosa, had lower admissions BMIs, longer lengths of illness, more severe eating disorder psychopathology and more depressive symptoms. These patients were also more likely to not complete the treatment program. Additional analyses identified purging in the absence of binging as predictive of group membership.

Our research identified several factors that are associated with response to inpatient eating disorder treatment. Further exploration of these prognostic factors may allow for individualized treatment planning and potentially lead to the identification of novel targets in the treatment of Anorexia Nervosa.
Little is known about postpartum psychiatric admissions where women are hospitalized and discharged after only a brief period of stabilization. We aimed to describe women with these short-stay psychiatric admissions in the 1st year postpartum, with comparison to women with longer admissions.

From all women in Ontario, Canada with a psychiatric admission within 1 year postpartum (2007-2012) ($n=1,702$) we compared women with short admissions (< 72 hours) to women with longer admissions on sociodemographic, clinical characteristics and mental health service use at 7, 30 and 365 days post-discharge, including outpatient physician visits, emergency department (ED) revisits (without readmission) and readmissions.

About 37% of admissions were < 72 hours ($n=631$). More women with short vs. long admissions were adolescents (11.7% vs. 7.3%), fewer were employed (16.6% vs. 25.9%) and fewer had prior psychiatric admissions (16.7% vs. 59.0%). Index diagnoses of alcohol or substance use (12.5% vs. 7.8%) and adjustment disorders (15.8% vs. 6.3%) were more common in the short vs. longer stay group; admissions for psychotic (5.8% vs. 19.5%) and bipolar disorders (2.1% vs. 14.2%) were less common. Women with short admissions were more likely to use outpatient services by each follow-up point. They were at similar risk for readmission at 7 days and 30 days post-discharge, but at lower risk at 1 year post discharge (19.5% vs. 28.8%, aOR 0.63, 95% CI 0.46-0.85)

Women with short-stay postpartum admissions have fewer readmissions at 1 year post-discharge but are a clinically distinct group that would benefit from targeted management.
Readmission to hospital following discharge occurs for ~10% of psychiatric patients. While readmission rates in men and women are similar, some risk factors for readmission differ by sex. We aimed to develop sex-specific models to predict readmission.

We conducted a population-based cohort study to derive and validate separate predictive models of 30-day readmission risk for men and women. Using sociodemographic and health administrative data, we identified and described all men and women admitted to acute psychiatric units in Ontario (2008-2011). We randomly divided each sex cohort in half (derivation and validation samples). Using the derivation sample, we created successive predictive models of readmission. We then validated each model, generating odds ratios for individual predictors and c-statistics (discrimination) for the derivation and validation samples.

We identified 33,353 women and 32,436 men, of whom 3,030 (9.1%) and 3,014 (9.3%) were readmitted within 30 days, respectively. Many predictors for readmission were consistent across sex. For women only, temporary residence, personality disorder diagnosis, positive symptom rating, depression rating, and stressful life events were significant predictors. For men only, number of mental health visits, criminal activity, and inability to care for self (admission and discharge) were significant predictors. Both models had moderate discrimination (women: derivation c-statistic 0.644, validation c-statistic 0.652; men: derivation c-statistic 0.659, validation c-statistic 0.653).

The sex-specific models of readmission we derived and validated in this study could assist in guiding clinical and policy interventions for men and women to reduce the rates of psychiatric readmission to hospital.
Despite the high rates of tobacco use among individuals with mental disorders and the known effects of nicotine deprivation increasing agitation, management of tobacco withdrawal remains inconsistent and delayed. Through the Tobacco Withdrawal Management (TWM) quality improvement project, we aim to reduce the time between arrival to CAMH Emergency Department (ED) and administration of Nicotine Replacement Therapy (NRT).

We established a multi-disciplinary work team and utilized the Model of Improvement and LEAN methodology framework for our project design. We performed a comprehensive diagnostic evaluation of current processes, involving qualitative focus groups with frontline staff, review of incident reports, and process observations. We established a dashboard of measures including time between ED arrival and NRT administration, number of individuals receiving tobacco screening at triage, number of completed NRT medical directives, number of positively screened smokers who received NRT, and number of NRT supplies dispensed per week.

TWM project is still in progress. Interventions are going through Plan-Study-Do-Act (PDSA) cycles to test efficacy and feasibility. Interventions include new tobacco screening question on electronic triage form, changes to accessibility of NRT supplies, and staff training around nicotine withdrawal and NRT dosing. We will compare pre- and post-interventions measure outcomes to assess effectiveness.

The TWM Project aims to improve how the needs of tobacco users are addressed within CAMH’s ED by engaging front-line staff in quality improvement and generating local change ideas.
Frequent ED Users in Mental Health: Perceived Service Needs and Preferences in a Large Urban Centre

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Daniel Pauly, St. Michael’s Hospital;
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Vicky Stergiopoulos, St. Michael’s Hospital.

Frequent emergency department (ED) use has been associated with a significant burden of illness and social disadvantage. This study aimed to explore the profiles, perceived service needs and preferences of mental health and addictions frequent ED users participating in a brief intensive case management intervention.

Semi-structured interviews were conducted with 20 frequent ED users with mental health and addictions concerns and 13 service providers who were participating in a four to six month intensive case management intervention implemented in Toronto, Ontario. Thematic analysis was used to explore service user characteristics and service needs and preferences.

Service users and providers described complex health and social needs and instances of stigmatization by healthcare professionals. They also described resilience and desires for community participation. Helpful intervention ingredients included system navigation, advocacy, intermediation, and practical needs assistance. Service users valued service provider characteristics grounded in relatability, non-judgmental partnerships, recovery driven approaches, and the promotion of their personal growth.

Frequent ED users experience complex needs, as well as desires for societal contribution. Interventions targeting this population may be enhanced by a focus on service users’ strengths and community engagement, and service provider selection and training to support comprehensive care advocacy and system navigation from a client driven, recovery oriented perspective.
In 2012, adult ambulatory psychiatric services at St Joseph’s Health Centre were restructured to: 1) enhance access to timely ambulatory psychiatric care 2) improve patients’ post-discharge transition and 3) reduce 30-day psychiatric readmissions.

Access to ambulatory appointments in the Collaborative Care Clinic (CCC) has been facilitated by the implementation of an open-access online scheduler. Using the Model for Improvement (Plan-Do-Study-Act cycles), several change initiatives have been introduced, such as: standardization of appointment reminder phone calls, patient experience questionnaires, and medication reconciliation. Outcome measures include: attendance of the initial post-discharge ambulatory appointment, percentage of discharges having discharge medication records faxed to community providers, and 30 day readmissions to SJHC.

Over 600 post-discharge ambulatory appointments were scheduled for discharged inpatients between 2013 and 2015. Non-attendance of scheduled post-discharge appointments has decreased from 37% in 2013 to 6.7% (June to December) 2015. Communication of discharge medication records has improved from an average delay of 52.8 days to 0 days (100% on day of discharge). The 30-day readmission rate has been reduced from 13.7% in 2013 to 11.9% in 2015.

The open-access online appointment scheduler has enhanced and sustained access to ambulatory psychiatric care. Multiple initiatives are required and have been tested to enhance continuity of psychiatric care. We have preliminary evidence to suggest the CCC model and continued evaluation is reducing psychiatric readmissions; however, data on 30-day readmissions to other institutions, following an index hospitalization at SJHC, is not yet available to inform our evaluation.
Our Mental Health Care system Framework intends to aid organizations, policy planners and clinicians in clarifying responsibilities, roles and best practices. We applied a Bauhaus design lens (1) such that our framework's form follows patient and healthcare centered needs. Ethics and values of social responsibility, population health and principles of quality of care inform our framework.

Our Mental Health Care system is fragmented. Patients may not access clear entry points or progress through care optimally (2). Similar to other institutions, wide-ranging and growing clinical demands at our community academic general hospital resulted in us trying to better understand our mandate to meet patient needs. We will review evidence for this framework (based on need, acuity, risk, service intensity and provider level) describing patient care pathways from intake/triage to three patient-centered levels of care: (1) lower needs and service intensity (e.g., primary care); (2) moderate needs and service intensity (e.g., acute ambulatory care); and (3) high needs and service intensity (e.g., complex chronic care, emergency, crisis and acute inpatient care). Within each tier, various models of care are organized from low to high service intensity as informed by a report from the British Columbia Ministry of Health. We will argue that despite traditional designations of primary, secondary and tertiary care, providers and models of care may not be functioning within proposed mandates. Our model may help to better conceptualize and organize our mental health care system and help providers clarify roles (3), responsibilities and accountabilities to improve quality of care.
Oral Presentation: B6. Advances in Health Systems Solutions

Using Innovation to Support Evidence Based Distress Management in Cancer Care

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Mary Jane Esplen, de Souza Institute, University Health Network, University of Toronto

The number of cancer cases is increasing and 1 in 4 Canadians are estimated to die from the disease (Canadian Cancer Society 2015). Cancer related distress, i.e., anxiety and depression are experienced by a significant numbers of patients. Unresolved distress can impede treatment adherence, increase health care service utilization, reduce quality of life and affect a person’s relationship with others. The Canadian Association of Psychosocial Oncology (CAPO) has developed clinical practice guidelines on evidence based distress management. Despite the guidelines, many providers report a lack of confidence in assessing and managing the complex emotional and physical distress experienced by cancer patients.

We developed an innovative training program to help clinicians to implement CAPO guidelines in their day to day practice. This includes in person workshop, weekly videoconferencing sessions and self-directed online learning. Theoretical framework, interactive activities and case studies were incorporated to highlight psychosocial aspect of cancer care; and to introduce psychotherapeutic tools such as the BATHE technique to manage cancer distress. A rigorous evaluation process was included to assess and compare the effectiveness of different training methods.

277 healthcare providers participated in our training program. Statistically significant improvements were reported in all 3 training methods in areas such as distress screening, addressing patients’ information needs, fear of death, losses and bereavement, and the provision of psychosocial care and referrals.

We will review quantitative and qualitative data on each teaching method and discuss their unique contribution in content delivery, learner engagement, knowledge retention and application.
Collaborative mental health care models have demonstrated effectiveness but suffer from variable uptake in naturalistic primary care settings, leading to a "quality chasm" between evidence and practice. There are no existing quality measurement frameworks by which to evaluate Collaborative Care implementation in primary care settings; thus we aimed to develop one.

To identify existing measures of Collaborative Care performance we conducted a scoping review of published and 'grey' literature. Next we interviewed healthcare providers and service users of collaborative care to elicit their perspectives on Collaborative Care implementation and priorities for measurement and improvement. We synthesized the findings into a quality framework with broad domains and specific dimensions of Collaborative Care implementation. A knowledge translation advisory group that included people with lived experience (PWLE), health care providers, quality experts, researchers and policymakers helped interpret the findings and shape the framework through iterative surveys and meetings.

From the literature we extracted and critically appraised 272 unique quality indicators, including many indicators of clinical effectiveness; some indicators of accessibility, efficiency, and equitability of care, and; almost no indicators of patient-centeredness or patient safety. Interviews elicited many dimensions of quality that were unaddressed in the literature, particularly regarding patient-centeredness, teamwork, and continuity of care.

This study delivers an evidence informed quality framework and indicators by which to measure Collaborative Care implementation in Ontario’s primary care settings. Our next phase of research will pilot the quality measures to determine their relevance, soundness, feasibility, and ability to drive improvements in care.
Project ECHO (Extension for Community Healthcare Outcomes) uses tele-education to bridge knowledge gaps between specialists in academic centres and primary care providers (PCPs) from remote locations. It has been implemented for multiple medical conditions in various international clinical settings with positive patient outcomes. Current evidence on ECHO models feasibility and outcomes was reviewed.

PubMed, MEDLINE, EMBASE, PsychINFO, and ProQuest databases were searched for the key word Project ECHO and Project Extension for Community Healthcare Outcomes from January 2000 to August 2015. Additional articles were generated through reference searches. Articles were limited to those published in English, peer-reviewed works, and studies that primarily focused on Project ECHO. Articles containing the same data pools were included as long as they were analyzed for different outcomes. Editorials, commentaries, grey literature and non-peer reviewed articles were excluded. Moore’s evaluation framework was used to organize study outcomes for quality analysis.

39 papers describing Project ECHOs involvement in 17 different medical conditions were identified. ECHO evaluation has been predominantly limited to levels 1 (participants) to 4 (providers competence) outcomes (n= 2238 studies, with some studies containing data from multiple levels). Preliminary data from 9 studies suggest that ECHO can change provider behaviour (n=1), patient outcomes (n=6) and can be cost-effective (n=2).

ECHO is a feasible and potentially cost effective model that can increase patient’s access to health care in under-resourced and remote locations, but further research examining its efficacy will be needed given study limitations to date. Identifying and addressing potential barriers to its implementation will further support the dissemination of ECHO as an education and practice improvement initiative.
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