11:00 to 11:20	**Title: Prevalence of depression and associated stigmatized beliefs in university students: results of a survey in the United States, Taiwan, United Arab Emirates, and Egypt** **Author(s):** Arif Pendi, Jahanzeb Ashraf, Feng-Jen Tsai, Samir Abou El Magd, Ciny Liu, Hajra Hussain, Mohamed Khalil, Kate Wolitzky-Taylor, Danny Lee, Sherif Gohar, Jeff Sugar, Kasim Pendi, Joshua Lee, Reham Abdel Maksoud, Noha Adel, David Baron. **Background**: Depressive disorders constitute a leading cause of disability worldwide. Among university students, a high prevalence of depression is complemented by personal and perceived (of others) stigmas, preventing students from seeking mental healthcare. Furthermore, the burden of depressive disorders and stigmatized beliefs among university students may differ inter-nationally. **Methods**: An anonymous socio-demographic survey, Patient Health Questionnaire-9 (PHQ-9), and Depression Stigma Scale (DSS) were sent to students from universities in the United States, Taiwan, United Arab Emirates, and Egypt. Depression prevalence and severity were determined from the PHQ-9. Stigmatization of beliefs was calculated from DSS scores and the *t*-test was used to compare stigmatization of personal and perceived beliefs. Students from each country were compared in terms of depression severity, personal stigmatized beliefs, and perceived stigmatized beliefs using ANOVA. Post-hoc Tukey tests were performed to further analyze mean differences. **Results**: A total of 2131 completed responses were submitted by students from the United States (n=1675), United Arab Emirates (n=134), Taiwan (n=217), and Egypt (n=105). Overall, 593 students (27.8%) screened positive for depressive disorder and Emirati students exhibited the highest depression severity, which was significant compared to American students ($p<0.001$). American students were also significantly more depressed than Taiwanese students ($p<0.001$). Overall, students exhibited far more stigmatized perceived beliefs than personal ones ($p<0.001$). There was also a difference in terms of personal stigma due to Egyptian students exhibiting more personal stigma than American ($p<0.001$), Emirati ($p<0.001$), and Taiwanese ($p<0.001$) students. Differences in perceived stigma were insignificant ($p=0.196$). **Conclusions**: The prevalence of depression (27.8%) has risen among university students, requiring greater attention by mental healthcare providers to address this burden. However, resource allocation may differ from nation to nation given the differences in disease prevalence. University-led efforts may need to be especially focused to reduce perceived stigma, but Egyptian students in particular may benefit from mental health literacy campaigns to reduce personal stigma.
11:20 to 11:40	**Title: Changes in mental health with opioid analgesia for chronic non-cancer pain** **Author(s):** Sara Meunier, Rob Tanguay **Background**: Multidisciplinary chronic pain centers are considered to be the gold standard treatment for the treatment of chronic non-cancer pain (CNCP). Despite a lack of authorized indications and in some cases, sufficient evidence, opioid analgesia is commonly prescribed for most CNCP conditions. Chronic opioid analgesia is associated with common adverse effects including sleep disturbances, cognitive dulling and sedation. These are symptoms also identified for patients with depression and anxiety. At present, we do not associate chronic opioid analgesia use with adverse mental health outcomes. **Methods:** A prospective analysis of The Neuropathic Pain Database (NePDAT) cohort, performed at several Canadian multidisciplinary pain centers, was performed. We hypothesized that chronic use of opioids for CNPC is associated with poor mental health (MH) outcomes and quality of life (QOL). Utilizing the Canadian Neuropathic Pain Database (Moulin et al. 2015) we identified patients not being treated with opioids upon entering a multidisciplinary pain treatment clinic and preformed a prospective longitudinal analysis comparing mental health, quality of life, and functioning between patients initiated on opioids within the 1 year follow up period and those who were not.

	Results: Total Mood Disturbance using the POMS questionnaire was significantly higher in the opioid group (p=0.0051), with MH sub-scores of Depression (p=0.0242) and Tension (p=0.0116) being significantly higher than in the non-opioid group. EQ-5D scores for QOL revealed improved QoL following treatment at the multidisciplinary pain center without similar improvement observed in the opioid group (p=0.0123). Scores did not worsen with post-admission opioid use, but rather, they did not improve as identified in the non-opioid group. **Conclusions:** These results suggest that the use of opioids in the treatment of CNCP may impede or fail to contribute benefit to the treatment for mental health difficulties associated with CNCP at multidisciplinary pain centers.
11:40 to 12:00	**Title: The Utility of the Mild Behavioral Impairment-Checklist in Detecting Mild Cognitive Impairment and Dementia** **Author(s):** Sophie Hu, Zahinoor Ismail, Scott Patten **INTRODUCTION:** By 2036, 1 in 4 Canadians will be 65 or older and many will suffer cognitive decline and/or dementia. Although memory loss is a hallmark of dementia, neuropsychiatric symptoms (NPS) are early markers. Mild Behavioral Impairment (MBI) is a syndrome of sustained NPS as an at-risk state for cognitive decline and dementia. However, NPS have been historically viewed in the context of dementia populations rather than pre-dementia populations with mild cognitive impairment (MCI). The MBI Checklist (MBI-C) was developed with applicability to populations with normal cognition or MCI. The MBI-C assesses motivation, mood, impulse control, social appropriateness and perception. As the MBI-C is a new instrument, its utility will be compared to the gold standard Neuropsychiatric Questionnaire (NPI-Q) for normal cognition, MCI and dementia patients. **RESEARCH QUESTION:** How does the MBI-C compare to the NPI-Q in detecting NPS in a cognitive neurology clinic? **OBJECTIVE:** To determine the sensitivity of MBI-C scores in comparison to the NPI-Q to detect NPS in normal cognition, MCI and dementia. **METHODS:** The MBI-C is routinely administered in the Cognitive Neuroscience Clinic at the University of Calgary. We will retrospectively analyze MBI-C and NPI-Q scores in normal cognition, MCI and dementia patients using 2-sample t-tests and logistic regression. **RESULTS:** Normal cognition patients (n=18) had an average NPI-Q score of 3.22 ± 0.83 (p=0.22) and MBI-C score of 9.56 ± 1.76 (p=0.25). MCI patients (n=92) had an average NPI-Q score of 3.86 ± 0.43 (p=0.63) and MBI-C score of 12.02 ± 1.03. Dementia patients (n=58) had an average NPI-Q score of 4.72 ± 0.63 (p=0.06) and MBI-C score of 12.28 ± 1.28 (p=0.14). **CONCLUSIONS:** As cognitive decline progresses, NPI-Q and MBI-C scores increase. The MBI-C may be used to detect NPS in normal cognition and MCI patients, and to predict incident cognitive decline and dementia. Historically, NPS have been exclusion criteria for dementia clinical trials, but this may change if evidence supports the utility of MBI in dementia prognostication.
12:00 to 13:00	**Poster Viewing & Lunch Break**
13:00 to 14:00	**Dr. David Baron, University of Southern California: Concussion and Psychiatry: Past, Present and Future Clinical and Research Translational Considerations**

14:00 to 14:20	**Title: Validity of the PHQ-9 In Neurological Populations** **Author(s):** Kimberly Williams, Michael Sanderson, Nathalie Jette, Scott B Patten **Background:** The objectives of this study was to evaluate the validity of the Patient Health Questionaire-9 (PHQ-9) for detecting Diagnostic and Statistical Manual (DSM)-defined major depressive episodes in people with neurological conditions. The objectives of this study was to evaluate the validity of the Patient Health Questionaire-9 (PHQ-9) for detecting Diagnostic and Statistical Manual (DSM)-defined major depressive episodes in people with neurological conditions. **Methods:** Participants were recruited from outpatient clinics for Multiple Sclerosis, epilepsy, migraine, Parkinson's Disease and stroke. Participants were administered a questionnaire (this included the PHQ-9), chart review and a follow up telephone interview. The Structured Clinical Interview for Depression was used as the reference standard for psychiatric diagnoses. The performance of PHQ-9 was analyzed using sensitivity, specificity, diagnostic odds ratios (DOR) and receiver operator curve analysis. **Results:** All neurological subpopulations had a specificity greater than 78% and sensitivity greater than 79% at a cut point of 10. Using a random effects model the I^2 value was 13.7% and Tau^2 was 0.05, showing homogeneity across the neurological subpopulations. The pooled DOR was 25.3 (95%CI 14.9 – 42.8). Meta-analytic analysis for sensitivity found the pooled estimate was 90% (95%CI 81-97) and for specificity was 85% (95%CI 79-90). **Conclusion:** Despite theoretical concerns about its validity, the PHQ-9 performed well at its standard cut-point of 10. Consistent with literature, being able to use a validated, brief tool which is available publically should improve case finding of depression in neurological populations. When considering clinical practicality along with the findings of this analyzed this study confirmed that the PHQ-9 is valid in a general outpatient neurological population.
14:20 to 14:40	**Title: Risk of Preterm Birth among Women Living in Deprived Neighbourhoods Differs by Women's Depression and Anxiety Status** **Author(s):** Kamala Adhikari Dahal, Scott Patten, Tyler Williamson, Alka Patel, Shahirose Premji, Suzanne Tough, Nicole Letourneau, Gerald Giesbrecht, Amy Metcalfe **Objective**: This study examined whether anxiety, depression, or comorbid anxiety and depression during pregnancy modifies the relationship between neighborhood SES and PTB. **Methods:** Individual-level data from two prospective cohort studies in Alberta Canada (All Our Families and Alberta Pregnancy Outcome and Nutrition (n=5,538)) were linked to neighborhood SES data measured by the Pampalon deprivation index. Depression was defined as an Edinburgh Postnatal Depression Scale (EPDS) score of ≥10, anxiety was defined as an EPDS anxiety-subscale score of ≥6, and comorbid anxiety and depression was defined as meeting both anxiety and depression definitions. Multilevel logistic regression models were developed including confounding variables (parity and ethnicity) and the interaction-term of neighborhood-deprivation with anxiety and/or depression. **Results:** The rates of PTB in the least and most deprived-neighborhoods were 7.5% and 10.6%, respectively. However, the PTB rate in the most deprived-neighborhoods differed by anxiety and depression status: the rate was 9.5% (95% confidence interval (CI): 6.8, 13.3) for women without depression or anxiety, 14.7% (95% CI: 6.0, 31.9) for anxious women, 16.2% (95% CI: 10.0, 24.9) for depressed women, and 6.9% (95% CI: 3.1, 14.7) for women with comorbid anxiety and depression. The presence of anxiety, depression, and comorbid anxiety and depression increased the risk of PTB by 1.4, 2.4, and 1.9 times, respectively (p-value for interaction: 0.07, 0.03, and 0.04, respectively) for women living in the most deprived-neighborhoods. **Conclusions:** Study findings suggest that anxiety and depression associated with the challenges of deprivation may extend stress-response activation, resulting in increased risk of PTB. This understanding may guide identification of high-risk women for PTB and allocation of resources to develop interventions for early identification and management of anxiety and depression, and ultimately the reduction of PTB, in vulnerable populations.

14:40 to 15:00	**Title**: **Long term neuropsychiatric outcomes of intensive care unit patients: A systematic review and meta- analysis** **Author(s):** Kyla N Brown, Simon Olivier Guienguere, Brianna Rosgen, Kirsten M Fiest, Thomas Stelfox **Background**: Studies suggest that patients who survive a stay in the intensive care unit (ICU) may be at increased risk of developing neuropsychiatric disorders, such as post-traumatic stress disorder (PTSD), depression, and anxiety. This risk may be attributed to the severity of illness experienced and the nature of therapies provided in the ICU. Approximately half of ICU patients develop delirium, an acute confusional state, during their ICU stay. It is unknown whether delirium is associated with the onset of subsequent neuropsychiatric diagnoses. This study aims to determine whether the presence of delirium during a stay in a medical-surgical ICU is associated with a subsequent diagnosis of a neuropsychiatric disorder in adult ICU patients. **Methods**: Using systematic review methodology, keywords and subject headings were searched in MEDLINE, EMBASE, PsycINFO, and CINAHL from 1980-October 5, 2017. Two reviewers screened abstracts, assessed full-text eligibility, and extracted data independently, and in duplicate. Included studies were observational and reported on the prevalence or incidence of neuropsychiatric outcomes in adult patients following a stay in the ICU. Each included study was evaluated for potential biases using the Newcastle-Ottawa Scale. Heterogeneity was assessed using the I-squared statistic. Publication bias was assessed visually using funnel plots and statistically using Begg's and Egger's tests. **Results**: 4,150 titles and abstracts were screened, and after reviewing 373 full text articles, 53 articles were eligible for inclusion, of which 16 reported an estimate of delirium in the ICU. Studies analyzed: PTSD (n=26), depression (n=22), anxiety (n=17), and neurocognitive disorders (n=8). The prevalence of delirium ranged from 6-84%, with the majority (n=10) using the CAM-ICU to assess the presence of delirium. Four studies reported an association between delirium and subsequent neuropsychiatric disorder. Three of the four studies (2 reporting neurocognitive disorders, 1 reporting PTSD) identified a significant association, suggesting that the presence of delirium in the ICU is a risk factor for developing a neurocognitive or PTSD disorder. The pooled prevalence of PTSD was 24% (95% Confidence Interval [CI] 19%-29%), depression 36% (95% CI 29%-44%), anxiety 35% (95% CI 28%-42%), and neurocognitive disorders 43% (95% CI 25%-60%). **Conclusions**: This systematic review is the first to summarize the literature on whether there is an association between delirium in ICU patients and subsequent neuropsychiatric outcomes. Expected findings of this research will enhance current provider and patient knowledge around the impact of delirium in the ICU and neuropsychiatric outcomes following a stay in the ICU.
15:00 to 15:10	**Poster Viewing - Coffee Available**
15:10 to 15:30	**Title: Investigating the Effect of Glutamate on Executive Functions in Children with Attention-Deficit/Hyperactivity Disorder using Magnetic Resonance Spectroscopy** **Author(s):** Tasmia Hai, Hanna Kubas, Jean-Francois Lemay, Rose Swansburg, Frank P. MacMaster **Background:** Attention-deficit/hyperactivity disorder (ADHD) is a neurodevelopmental disorder in children, with a prevalence of 5-7%. Symptoms include inattention, impulsivity and hyperactivity. Previous studies have reported dysfunction in the glutamatergic pathway. However, no studies to date have linked the glutamate differences with performance in Executive Function (EF) tasks. **Methods:** 31 children with ADHD (*M* = 10.2 years, *SD* = 1.3; males = 19) and 15 control participants (HC; *M* = 10.0 years, *SD* = 1.4 years; males = 6) took part. Short echo proton magnetic resonance spectroscopy (1H-MRS; TE = 30ms) were used to study the changes in in the right prefrontal cortex (R-PFC) and left striatum (LS). Both groups completed an EF assessment battery, Digit Span (DSB), Letter Fluency (LF) and Trail Making Test–Part B, (TMT-B).

	Results: Independent t-tests found lower concentrations of Glutamate (Glu; p = 0.009), Choline (Cho; p = 0.016) and N-Acetyl Aspartate (NAA; p = 0.029) in the R-PFC in ADHD participants compared to HC. No significant differences were seen in the LS. Positive correlation with Glu concentration and performance in DSB, LF and TMTB tasks in the control group were observed. No such correlations were observed in the ADHD group. **Conclusions:** To our knowledge, this is the first study to investigate the relationship between EF and Glu concentration. These findings suggest the decoupling effect of Glu in EF related tasks in children with ADHD compared to controls. As such, Glu concentration can be a possible ADHD biomarker and novel treatments target for future.
15:30 to 15:50	**Title: The association between maternal prenatal salivary cortisol and birth weight: A systematic review and meta-analysis.** **Author(s):** Cherak, S.J., Giesbrecht, G.F., Metcalfe, A., Ronksley, P.E., Malebranche, M.E. Low infant birth weight is an important cause of preventable morbidity and mortality worldwide. Babies who are born preterm or of low birth weight are often at higher risk for morbidity and mortality than are full-term babies with normal birth weight. To implement effective maternal treatment strategies to prevent lower birth weight infants, accurate information regarding the effects of gestational timing and fetal sex on this condition within the general population is essential. Maternal cortisol during pregnancy is a well-recognized mechanism through which maternal psychological stress has lasting effects on fetal development and contributes to a low birth weight infant. Previous systematic reviews examining the association between heightened maternal cortisol and adverse newborn outcomes have been unable to conduct meta-analysis due to significant heterogeneity between studies. To mitigate the heterogeneity, we adopted strict inclusion and exclusion criteria; exploring the association between an area under the curve with respect to ground (AUCg) of maternal prenatal salivary cortisol and newborn birth weight. From the searches run in MEDLINE, EMBASE, PsycINFO, and CINAHL, a total of nine studies were included in the systematic review and all included studies were deemed eligible for meta-analysis. For every maternal-fetal dyad, an AUCg of maternal cortisol was calculated to determine a Pearson's correlation coefficient with a continuous measure of newborn birth weight. To investigate heterogeneity, the correlation coefficients were subdivided by gestational trimester and fetal sex. What was found was a statistically significant negative correlation between maternal cortisol and newborn birth weight across all trimesters (-0.24, 95%CI -0.28 to -0.20, p<0.001, I^2=88.9%), with the strongest correlation in the third trimester (-0.30, 95%CI -0.33 to -0.26, p<0.001, I^2=85.4%). In examining the effect of fetal sex, male fetuses trended to demonstrate a stronger correlation (male, -0.25, 95%CI -0.30 to -0.21, p<0.001, I^2=91.6%; female, -0.23, 95%CI -0.27 to -0.19, p<0.001, I^2=86.9%), but the difference between male and female fetuses did not reach statistical significance. The substantial heterogeneity is thought to stem from the fact that measures of heterogeneity are sensitive and dependent on sample size; all included studies were large prospective cohorts. This study revealed the third trimester as a possible critical gestational period for heightened maternal prenatal stress to affect birth weight, and a trend towards a male vulnerability to maternal adversity possibly due to sexual differences in fetal growth strategies. Challenged faced in this body of research and recommendations for future maternal stress research are discussed.

15:50 to 16:10	***Title*: Colitis Promotes Anxiety Through a CRF-R1-Mediated Suppression of Central Anandamide Signaling** ***Author(s)*:** Haley Vecchiarelli, Kaitlyn Tan, Vincent Chiang, Maria Morena, Alessia Santori, Catherine Keenan, Kira Leitl, Martin Sticht, Winnie Ho, Keith Sharkey, Matthew Hill ***Background*:** It is well established that peripheral inflammatory diseases (e.g. inflammatory bowel disease, arthritis) are commonly associate with stress-associated neuropsychiatric disorders (e.g. anxiety, depression). To date, however, the mechanisms underlying these comorbidities have not been fully elucidated. The endocannabinoid system regulates both anxiety and inflammation, making it a potential candidate mediating these comorbidities. To examine the hypothesis that endocannabinoids are mediators of the emotional comorbidities of peripheral inflammatory conditions, we employed an animal model of colitis to explore the potential role of endocannabinoids in these processes. ***Methods*:** Colitis was induced by intracolonic administration of trinitrobenzene sulfonic acid (TNBS, 0.45 mL, 50 mg/mL, 50 % [vol/vol] in ethanol/water) to adult male rats, while control rats received the same volume of saline. Central levels of anandamide were measured using liquid chromatography/tandem mass spectrometry, and the activity of its metabolic enzyme, fatty acid amide hydrolase (FAAH), was measured using a radioligand enzymatic activity assay. Anxiety-like behaviour was assayed using the elevated plus maze during the lights-on phase of the light cycle. To investigate central mechanisms, unilateral cannulation surgeries targeting the lateral ventricle were performed one week prior to colitis onset, with acute administration of a FAAH inhibitor (PF-04457845) occurring two hours prior to behaviour testing, or sustained administration of a corticotropin releasing factor receptor 1 antagonist (antalarmin) through an Alzet mini-pump. ***Results*:** There were no differences in anandamide (AEA) levels in any region measured (amygdala, hippocampus, hypothalamus and medial prefrontal cortex), three days after the onset of colitis, when the disease is peaking; however, AEA levels were decreased in the amygdala, hippocampus and medial prefrontal cortex seven days after the induction of colitis. Concomitantly, seven days after the onset of colitis, there was an increase in fatty acid amide hydrolase (FAAH) activity, indicating that peripheral inflammation can increase central AEA hydrolysis. Additionally, we observed an increase in anxiety like-behaviour in the elevated plus maze at this time point. The increase in anxiety was reversed with an acute intracerebroventricular administration of a FAAH inhibitor (PF-04457845), which increases levels of AEA. These data suggest that AEA levels are dynamically regulated in response to colitis, with the anxiety-related reduction in AEA levels occurring following the peak of disease activity, but after a sustained period of peripheral inflammation. Additionally, central administration of an antagonist of the corticotropin releasing factor receptor 1 (CRF-R1; antalarmin) throughout the duration of colitis reversed the AEA reductions in the amygdala and hippocampus. ***Conclusions*:** Together these findings add to the understanding of central mechanisms underlying anxiety-like behaviours associated with peripheral inflammation. They suggest that similar to psychological stress-induced anxiety, inflammation-induced decreases in AEA signaling (due to CRF driving FAAH activity), are relevant for the change in anxiety-like behaviours associated with inflammation.

16:10 to 16:30	**Title: Clinical Outcomes of the Connect Parent Group in CAAMHPP** **Author(s):** Melissa Adrian; David Cawthorpe **Introduction:** In Calgary, the Connect Parent Group is a free 10 week program to support parents and caregivers of pre-teens (ages 8 to 12) and teens (ages 13-17) with behavioural and emotional problems that has been offered since 2008. This evaluation will describe the outcomes of the participants and their children's clinical profiles and outcomes associated with exposure to the Connect Parent Group. **Methods:** Pre and post surveys of the Parenting Relationship Questionnaires (PRQ) were collected for a sub-sample of participating parents. Additionally, the clinical profiles (MTP, WCWL-CMH-PCS, System Variables – e.g., repeat admissions) of the CAAMHPP enrolled children associated with parental exposure were compared to enrolled children who were not exposed and admitted over the same time period. **Results:** Parents demonstrated improvement on standard measures post-group. The enrolled children whose parents were exposed to the group were clinically more severe, impaired and urgent compared to non-exposed children. The number of enrollments post-group-exposure reduced 61% compared to pre-group-exposure. **Conclusions:** Children of parents exposed to the Connect Parent Group are clinically distinct. The results of exposure to the Connect Parent Group have substantial effects in terms of reduced subsequent admissions to CAAMHPP services that support wider implementation of multi-family-interventions.
16:30 to 16:40	**Awards and Closing Comments - Auditorium**

AUDITORIUM FOYER
POSTER PRESENTATIONS

Title: Case Report - Clinical Variant or Primary Psychosis? Charles Bonnet Plus Syndrome
Author(s): Jaylynn Arcand, Juliana Kirova
Introduction: Late onset Schizophrenia is uncommon (1). Additionally, in patients with Schizophrenia, the prevalence of visual hallucinations compared to auditory hallucinations is low (2). In both of these cases, a thorough consideration of the differential diagnosis is paramount. In patients with low visual acuity, the differential diagnosis for visual hallucinations would include Charles-Bonnet Syndrome, a condition characterized by neutral themed visual hallucinations without other sensory modality hallucinations or other symptoms of psychosis. However, there are a handful of case studies suggesting cases of multimodality presentations of Charles-Bonnet Syndrome. **Case Description:** 47-year-old gentleman with a history of glaucoma, chronic uveitis, and 3 brief psychotics episodes in the last 1.5 years, presents with acute agitation secondary to auditory and visual hallucinations. The auditory voices are coming from visual hallucinations of cartoon-like faces which began in the context of sensory deprivation (dark and silent) and are never present singularly. At each presentation the patient also presented with red, tearing eyes requiring a consultation to ophthalmology because of worsened vision and was treated with eye drops. He was given risperidone and responded to treatment within 1-3 days. 7 days prior to the patient's presentation he ran out of prescription eye drops but continued on his risperidone. After 3 days without drops, he had acute worsening of his vision and 2 days following the vision changes he became troubled by auditory and visual hallucinations. Although he was acutely agitated by the hallucinations, his insight remained intact. This is similar to the week prior to each previous presentation for psychosis.
Discussion: Late-onset Schizophrenia is a possibility for the presentation of this patient. However, given the patients acute onset of vision loss, presentation of co-morbid auditory and visual hallucinations, age,

level of insight and the presentations upon sensory deprivation are more in keeping with Charles-Bonnet Plus Syndrome. Although there are only a few case studies of this condition, it could easily be mistaken for Schizophrenia when considering a thorough differential diagnosis. It is important that we continue to evaluate for similar cases, as the treatment and prognosis is very different for patients with Charles-Bonnet, then those for Schizophrenia.

Title: ***Attenuated Psychotic Symptom Interventions in Youth at Risk of Psychosis: A Systematic Review and Meta-Analysis***

Author(s): Dan Devoe, Megan Farris, Parker Townes, Jean Addington

Aim: Attenuated psychotic symptoms (APS) have been the primary emphasis in youth at clinical high risk (CHR) for psychosis for assessing symptomology and determining subsequent transition to a psychotic disorder. Previous reviews primarily focused on the efficacy of cognitive behavioral therapy (CBT) on APS, however a comprehensive assessment of other interventions to date is lacking. Therefore, we conducted a systematic review and meta-analysis of all intervention studies examining APS in CHR youth. **Method:** The authors searched Embase, CINAHL, PsycINFO, Medline, and EBM from inception to May 2017. Studies were selected if they included any intervention that reported follow-up APS in youth at CHR. Interventions were evaluated and stratified by time using both pairwise and network meta-analyses (NMA). Due to the differences in APS scales, effect sizes were calculated as Hedges g and reported as the standardized mean difference (SMD). **Results:** Forty-one studies met our inclusion criteria. In pairwise meta-analyses, CBT was associated with a significant reduction in APS compared to controls at 18 to 24-month follow-up (SMD, -0.22; 95% CI, -0.43 to -0.01; I2=0%; P=0.04, 3 studies, N=356). In the NMA, integrated psychological therapy, CBT, supportive therapy, family therapy, needs based interventions, omega-3, risperidone plus CBT, and olanzapine were not significantly more effective at reducing APS at 6- and 12-months relative to any other intervention. **Conclusions:** CBT was more effective at reducing APS at long-term follow-up compared to controls. No interventions were significantly more effective at reducing APS compared to all other interventions in the NMA.

Title: **Structural connectivity of Neuropsychiatric Symptoms (NPS) in association with cognitive decline and dementia**

Author(s): Sascha Gill, Brandon Craig, Cheryl McCreary, Eric Smith and Zahinoor Ismail

Background: Multiple lines of evidence suggest that neuropsychiatric symptoms (NPS) can be early markers of neurodegenerative disease. Although, studies have identified decreased white matter (WM) integrity in regions associated with NPS in Alzheimer's Disease (AD), evidence in pre-clinical populations is sparse. Mild-Behavioural Impairment (MBI) is a neurobehavioural syndrome that describes later-life onset of NPS as an at-risk state for incident cognitive decline and dementia and could potentially be used for early identification of neurocognitive disorders. Diffusion imaging allows increasingly sophisticated analysis of white matter neurobiology and structural connectivity and has highlighted important pathways within the brain surrounding this field. Although understanding such pathways is informative, exploring changes at the whole brain level may be even more powerful. The whole-brain connectivity (i.e. connectome) approach may also provide biomarkers which can inform individualized predictors of NPS in Mild Cognitive Impairment (MCI) and AD populations. **Aim 1:** Describe white matter connectivity alterations in individuals with normal cognition, MCI and mild AD. **Hypothesis 1:** Degree connectivity of relevant nodes (i.e. cingulate, etc.) negatively correlates with disease severity. **Aim 2:** Investigate the correlation between NPS clustered into MBI domains, and structural connectivity

abnormalities in individuals with MCI and AD. **Hypothesis 2:** Global and nodal degree connectivity will be inversely correlated with the severity of NPS. **Methods:** We recruited participants with normal cognition (n= 20), MCI (n=20) and AD (n= 20) for cross-sectional evaluations (with >40+ scans still to be processed). Participants completed a high-resolution T1-weighted anatomical and diffusion imaging (25 directions; b=850s/mm^2) scan. T1 images are parcellated into 99 regions of interest (nodes) using a validated atlas in BrainSuite. Whole-brain WM uses deterministic tractography. Individualized WM connectomes are then quantified by calculating connection strengths (i.e. number of streamlines (NOS) at global (i.e. whole-brain) and nodal levels). Additionally, participants completed validated clinical and cognitive assessments (NPI). Using the NPI, NPS will be clustered into the 5 MBI domains, and each domain will be correlated with structural connectome properties. **Significance:** Assessing MBI domains in MCI and AD patients will improve understanding of the role of NPS in neurodegenerative disease while potentially uncovering novel imaging biomarkers for early detection/ treatment.

Title: Effects of Repetitive Transcranial Magnetic Stimulation (rTMS) on Cortical Neurophysiology in Children with Persistent Post-Concussive Symptoms

Authors: Godfrey, H., King, R., Kirton, A., Yeates, K., MacMaster, FP., Barlow, KM.

Background: Recovery from mild traumatic brain injury (mTBI) is variable, with symptoms persisting past 3 months in 10-15% of children. Mechanisms of mTBI recovery are poorly understood, however evidence suggests neurotransmission mechanisms are altered and certain anatomical areas may be altered including DLPFC. Repetitive transcranial magnetic stimulation (rTMS) is a form of neuromodulation that uses brief magnetic pulses to alter cortical excitability in specific brain regions. rTMS over the DLPFC is an effective treatment for major depressive disorder in adults and may be a treatment option for persistent PCS. The objective of this project was to determine if cortical excitability is altered following rTMS treatment for persistent post-concussive symptoms in adolescents. **Methods**: This single centre, open label, cohort pilot study is assessing the safety and feasibility of rTMS treatment in 13-18 year old children with persistent post concussive symptoms. 20 sessions of rTMS to the left DLPFC were given over 4 weeks. Each session consisted of 40 suprathreshold (120% RMT) pulses over 4 seconds (10 Hz) with an inter-train interval of 26 seconds. Cortical excitability of M1 was measured by targeting the right FDI using single and paired pulse TMS paradigms before and after rTMS treatment. Paradigms included short interval intracortical inhibition (SICI), cortical silent period (cSP), and long interval intracortical inhibition (LICI). Paired t-tests were used to examine changes in neurophysiology within subjects. **Preliminary Results**: Six participants have been studied: (mean age= 15.63 years, 33% male). SICI appeared to increase between pre and post sessions with mean SICI higher following treatment (p=0.024). There were no apparent changes in LICI or cSP measures following rTMS treatment. **Preliminary Conclusions**: rTMS appears safe and well tolerated in children with PPCS. TMS measures of M1 intracortical inhibition may change with rTMS treatment. Completion of this and larger studies are required to determine the clinical and neurophysiological effects of rTMS in this population.

Title: Pilot study of supplementary motor area rTMS for Tourette's syndrome in children

Author(s): Cynthia Kahl, Adam Kirton, Tamara Pringsheim, Paul Croarkin, Quinn McLellan, Rose Swansburg, Ephrem Zewdie, Frank P. MacMaster

Background: Tourette's Syndrome (TS) is a disorder that is characterized by brief, repetitive movements and vocalizations called tics. Treatment options for TS are limited and can carry significant risks—new interventions are needed. The goal of this study is to determine the effect of fMRI-guided, low frequency repetitive transcranial magnetic stimulation (rTMS) on the severity of tics and underlying neurobiology

in children with TS. Using rTMS, we inhibit activity in an overactive region of the brain—the supplementary motor area (SMA). We hypothesize that (1) severity of tics will decrease with treatment and (2) SMA GABA will increase in association with rTMS and clinical response. **Methods:** Children aged 7-12 are recruited from a TS clinic. The participants, MRI, and TMS robotic system are co-registered for precise targeting of the SMA. Treatment consists of 1800 low frequency (1Hz) rTMS stimulations to the SMA at 100% resting motor threshold (900 stimulations/hemisphere). Additional outcomes include mental health/symptom scales, spectroscopy, motor mapping, and neurophysiological measures. All measures are completed pre- and post-treatment. **Results:** The first three male participants show a significant decrease in tic severity (A:30%; B:23%; C:72%) and impairment (A:25%; B:50%; C:67%) after treatment; assessed using the Yale Global Tic Severity Scale. Multidimensional Anxiety Scale for Children scores decreased (A:2.4%; B:3.1%; C:5.9%), as did SMA glutamate levels (A:16.9%; B:2.2%; C:0.9%). **Conclusions:** Robot-driven, neuronavigated rTMS interventions appear feasible and well-tolerated in children with TS. Treatment combined with TMS and neuroimaging may inform mechanisms of action and predictors of responsiveness. This study is ongoing.

Title: Cortical Thickness and Treatment Response to Repetitive Transcranial Magnetic Stimulation in Youth With Major Depression

Author(s): Quinn McLellan, Adam Kirton, Ephrem Zewdie, Keon Ma, Rose Swansburg, Natalia Jaworska, Lisa Marie Langevin, Chris T. Wilkes, Frank P. MacMaster

Background: Current treatment options for adolescent major depressive disorder are limited and response is unpredictable. Repetitive transcranial magnetic stimulation (rTMS) is a novel treatment option, however, the ability to predict responses remains unclear. Pre-treatment cortical thickness measures provide an objective measure to determine individuals who may benefit most from this emergent technology. **Methods:** Youth (n=23; 12-21 years) with treatment-resistant depression (TRD) underwent 3 weeks of high-frequency rTMS (10Hz). Baseline brain structural scans were obtained. Left rostral middle frontal gyrus (lRMF) thickness at baseline was compared between eventual responders, non-responders and age-matched controls (HC; n=16). Hamilton depression and anxiety rating scales (HAM-D; HAM-A) were used to determine symptom-specific treatment response (defined as ≥50% symptom reduction). Demographic and symptom profile differences were additionally explored. **Results:** Of the 23 TRD youth, 11 (47.83%) exhibited a significant reduction in depressive symptoms, while 16 (69.57%) showed significant depressive and/or anxious symptom reductions. The lRMF was thinner in responders than non-responders, and age negatively correlated with lRMF thickness in HC but not TRD subjects. Those that failed to receive significant benefit on both anxious and depressive measures had significantly thicker lRMF than responders and controls. Exploration of demographic and clinical variables revealed HAMD responders had greater frequency of suicide attempt history and higher atypical symptom cluster score; social phobia may reduce antidepressant response. **Conclusions:** Repetitive TMS can effectively reduce depressive and anxious symptoms in adolescent TRD. A thinner treatment target site (lRMF cortex) may predict better treatment response. Our findings suggest that response to rTMS intervention may be influenced by maturational factors.

Title: Pre-operative Anxiety Management in Spine Surgery

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Background: Virtually all patients scheduled to undergo spine surgery experience some degree of

preoperative anxiety. Despite being a nearly ubiquitous phenomenon in spine surgery patients, this phenomenon remains greatly unexplored in the spine surgery related literature. Furthermore, many studies have identified the link between preoperative anxiety and poor surgical outcomes albeit in other procedures. This study was therefore performed to determine spine surgeons' views of preoperative anxiety and their current anxiety management practices. **Methods**: An anonymous survey was sent to members of the international organization AO Spine North America to determine preferences of spine surgeons regarding management and measurement of preoperative anxiety. **Results**: Of 69 respondents, the majority were orthopaedic surgeons (n=52, 75.4%), practicing at an academic setting (n=39, 56.5%), and male (n=66, 95.7%). The majority of respondents did not measure preoperative anxiety (n=46, 66.7%) and would not employ a rating scale to measure it (n=38, 55.1%). The few that did measure anxiety did so verbally (n=22, 31.9%) or with rating scale/survey (n=6, 8.7%). Nevertheless, the majority of spine surgeons would discuss preoperative anxiety if measured by the patient (n=40, 58.0%). Most spine surgeons used patient education (n=54, 78.3%) and family members' presence (n=36, 52.2%) to reduce preoperative anxiety in their patients. Spine surgeons allocated the greatest amount of responsibility for preoperative anxiety management to surgeons, anesthesiologists, and patients. **Conclusions**: Although the majority of spine surgeons did not routinely document preoperative anxiety of their patients, they expressed a willingness to address it if mentioned by the patient. Furthermore spine surgeons indicated that responsibility for preoperative anxiety management is shared by several parties, including the patient. Future studies are needed to determine if these views align with those of anesthesiologists and patients. Also, most spine surgeons preferred using preoperative education and family presence to reduce anxieties, indicating their current management practices. Notably, clinical trials are needed to determine if the management techniques commonly employed by spine surgeons are effective in reducing preoperative anxiety.

Title: Delirium and Symptoms of Major Depressive Disorder and Generalized Anxiety Disorder in Caregivers of the Critically Ill

Author(s): Brianna Rosgen, Karla D. Krewulak PhD, Henry T. Stelfox MD, PhD, E. Wesley Ely, MD MPH, Judy E. Davidson DNP, RN, and Kirsten M. Fiest, PhD

Background: Many caregivers of critically ill patients witness patient delirium, an acute confusional state characterized by impaired awareness and attention. The prevalence of major depressive disorder (depression) and general anxiety disorder (anxiety) is higher in caregivers versus the general population (depression: 36% vs 4.7%; anxiety 24% vs. 2.5%). This study aims to evaluate associations between the presence and severity of patient delirium and symptomology of depression and anxiety in caregivers of critically ill patients. **Methods**: Consecutive consenting adult patients with a caregiver (i.e. family or friend) present were enrolled in an ongoing prospective cohort study at Foothills Medical Centre medical-surgical intensive care unit in Calgary, Canada. Caregiver questionnaires were completed once daily for a maximum of five days, including the Patient Health Questionnaire 9-item and the General Anxiety Disorder 7-item to assess symptomology of depression and anxiety, respectively. Patient delirium was assessed by blinded, trained research assistants twice daily using the Confusion Assessment Method for the Intensive Care Unit (CAM-ICU-7). Descriptive statistics (proportions and means) and logistic regression analyses were calculated. **Results:** In the first two months of recruitment, 15 dyads and four independent caregivers were enrolled. Caregivers were most commonly female (73.7%, 14/19) and the spouse of a patient (47.4%, 9/19), with a mean age of 51.2 years (range 22-72). 36.8% (7/19) and 52.6% (10/19) of caregivers demonstrated symptomology of depression or

anxiety, respectively. Delirium was identified in 57.9% (11/19) of patients at least once during their stay. Median delirium severity was 5 out of 7 (range 0-7). The most common symptoms of depression were difficulties with somnolence and appetite. Trouble relaxing, feeling nervous, and worry were the most common symptoms of anxiety. There was a non-significant trend of association between more severe delirium in patients and increased odds of depression and anxiety in caregivers. **Conclusions:** Caregivers of critically ill patients have an increased burden of depression and anxiety symptomology, compared to the general population. There was a trend toward more severe delirium in the patient being associated with more caregiver depression and anxiety, though larger sample sizes are required to obtain precise estimates of effect.

Title: **Feasibility of employing family-administered delirium detection tools in the intensive care unit (ICU)**

Author(s): I. Yasmeen, K. Krewulak, B. Rosgen, J. Davidson, E.W. Ely, H.T. Stelfox, K.M. Fiest

Background: Family-administered delirium detection tools have been developed, however the use of these tools have not been assessed in the ICU. Family caregivers may be able to detect changes in patient cognition and behavior from pre-illness levels of functioning earlier than unfamiliar providers. These tools may be a valuable diagnostic adjunct in the ICU. Our objective was to determine the feasibility of employing family-administered tools to detect delirium in the critically ill. **Methods:** Consecutive patients and family caregivers (dyads) in the largest adult ICU in Calgary were recruited (Aug. 9-Sept. 11, 2017). Inclusion criteria are as follows: patients with a Richmond Agitation Sedation Scale (RASS) ≥-3; no primary direct brain injury with a Glasgow Coma Scale score of <9; ability to communicate; anticipated to remain admitted in the ICU for at least 24 hours, family caregiver present, and approval to approach patient from bedside RN. Family-administered delirium assessments were completed (FAM-CAM [Family Confusion Assessment Method] and Sour Seven). To assess feasibility, we determined the proportion of patients and family members who met inclusion criteria and who consented to participate. **Results:** Of 141 patients admitted to the ICU, 38 dyads (27%) met inclusion criteria for the study, and 17 (45%) of those eligible consented to the study. Almost 15% of admitted patients did not have family and were thus ineligible. The most common reason for lack of enrollment was refusal by the family, not the patient. A barrier encountered was unavailability of the bedside RN, due to which patient eligibility could not be confirmed (16%). No participants withdrew from the study, nor indicated the study was a burden once enrolled. **Conclusions:** These data suggest employing family-administered delirium detection tools in the ICU is feasible. Future studies will validate the use of the FAM-CAM and Sour Seven in the ICU, assess potential adverse effects, and determine attitudes towards employing these tools.

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