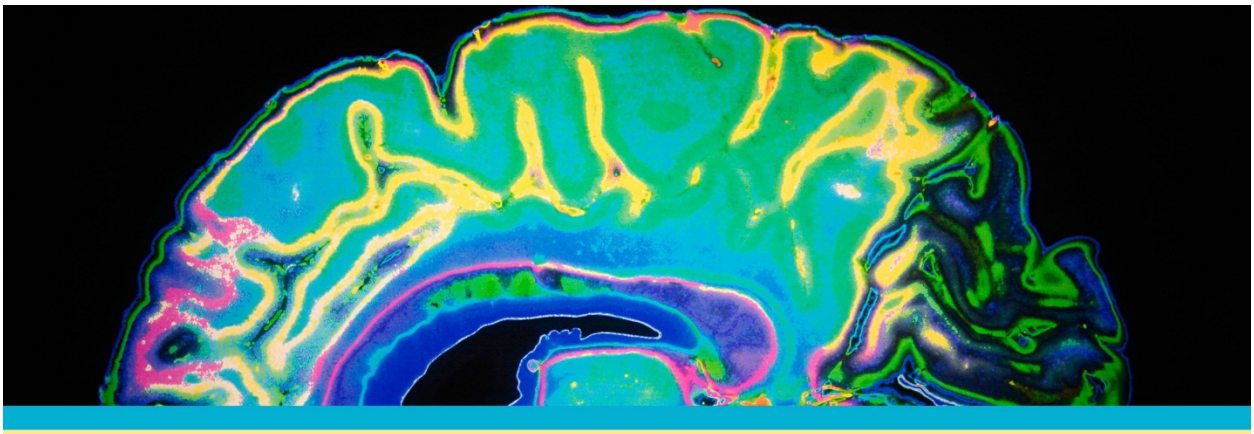


UNIVERSITY OF ALBERTA
FACULTY OF MEDICINE & DENTISTRY

15th Annual Department of Psychiatry Research Day

Abstract Book

Presented by
the Department of Psychiatry
June 22, 2016

CHAIRS MESSAGE

Welcome to the 15th Annual Research Day of the Department of Psychiatry at the University of Alberta!

Going into its 15th anniversary, Psychiatry Research Day 2016 showcases and celebrates recent findings from our basic and translational research programs including developments in neurochemistry, genetics, imaging, neuropsychiatry, and psychotherapy. Many of these programs involve collaborative research with colleagues from other departments and institutions locally, nationally and internationally. Over the years, the Department of Psychiatry has developed very strong MSc and PhD programs to complement our excellent residency program, with some of our residents enrolled in our MSc program. Our trainees represent our department exceedingly well by winning many national, provincial, university and faculty scholarships and awards and by disseminating their research at scientific conferences throughout the world.

Research Day this year has a focus on addictions, and our invited speakers cover a range of topics from this area, including a lived experience presentation by Dennis Anderson at the start of the day, guest speaker Dr. Stefan Brennan providing the lunch-time presentation as a part of Psychiatry Grand Rounds, and last but not least our keynote lecture by Dr. Marco Leyton in the afternoon. For the first time, many of our graduate students will present their work in mini-talks, and we are excited to hear from Brad Necyk, Ericson Dametto, Rohit Lodhi, Huining Guo, Chandra Ashton, Manoj Malik, James Benoit, Deena Hamza, Dimitar Ourdev, Wesley Paylor , Erin Martin, Michal Juhas, Sudhakar Sivapalan, and Daniela Gomez. Poster presentations from our trainees and collaborators will also be presented throughout the day. The top presentations by research trainees will be acknowledged with awards.

Our keynote speaker for this year's event is Dr. Marco Leyton, of the University of McGill. Dr. Leyton is the past President of the Canadian College of Neuropsychopharmacology (CCNP), and a founding member of the Scientific Advisory Committee on Substance Abuse (CCSA), Dr. Leyton has been studying the neurobiology of reward-seeking behaviour for 25 years. His research spans basic science in laboratory animals to clinical science in humans and he has published more than 100 publications in high-ranking journals in the field of psychiatry and neuroscience. We are extremely excited to host Dr. Leyton at our event and anticipate that his talk will be substantial, interesting, and informative for members of our faculty and external attendees. Dr. Leyton's keynote lecture is entitled, "Vulnerability to addictions: a potential dopamine-related pathway in humans."

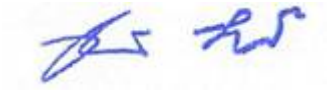
We are grateful to all our research trainees and their supervisors for their contribution to the vital research in our department. Special thanks to our organizing committee for Research Day: Michael Juhas and Brad Necyk (our graduate student representatives), John Wesley Paylor

(ad-hoc member), Tara Checknita (heart & soul of Research Day), and Dr. Esther Fujiwara for their tireless efforts in organizing this year's Research Day. Thanks also go to Karyn Crawford for administrative support.

Dr. Leyton's visit to our department was supported in part by the Faculty of Medicine and Dentistry via the Walter Mackenzie Visiting Speaker Fund, and we are extremely grateful for this generous support. Last but not least, we gratefully acknowledge generous financial support from our sponsors Leica Microsystems, Janssen Inc., and Otsuka Canada Pharmaceutical Inc., Sunovion Pharmaceuticals Canada Inc. for this important venture.

Thank you for joining us in celebrating our research accomplishments for the past year.

Best wishes,



Dr. Xin-Min Li, MD, PhD, FRCPC
Professor and Chair, Department of Psychiatry
Faculty of Medicine and Dentistry, University of Alberta

ACKNOWLEDGEMENTS

The Department of Psychiatry is grateful to the following for their financial support (listed alphabetically):

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15th Annual Psychiatry Research Day

8:45 am – 9:00 am	**Opening Remarks** by Dr. Xin-Min Li, Chair
9:00 am – 9:45 am	**Guest Speaker** - ***Mr. Dennis Anderson*** "Mental health is life, not just Psychiatry"
9:45 am – 10:00 am	**Coffee Break**
10:00 am – 11: 00 am	**5-Minute Thesis Talks** by Graduate Students *1. Brad Necyk* *5. Ericson Dametto* *2. Rohit Lodhi* *6. Huining Guo* *3. Chandra Ashton* *7. Manoj Malik* *4. James Benoit* *8. Deena Hamza*
11:00 am – 12: 00 am	**Poster Session**
Starting 11: 30 am	**Lunch Buffet – L1-420**
12:00 pm – 1:00 pm	**Guest Speaker** - ***Dr. Stefan Brennan*** "Substance use and mental health disorders: Understand both to achieve better outcomes."
1:00 pm – 2:00 pm	**5-Minute Thesis Talks** by Graduate Students *9. Dimitar Ourdev* *12. Wesley Paylor* *10. Erin Martin* *13. Michal Juhas* *11. Sudhakar Sivapalan* *14. Daniela Gomez*
2:00 pm – 2:30 pm	**Poster Session** and Coffee Break
2:30 pm –3:30 pm	**Keynote Address** - ***Dr. Marco Leyton*** "Vulnerability to addictions: a potential dopamine-related pathway in humans."
4:00 pm - 4:15 pm	**Student Awards Presentation and Closing Remarks** by Dr. Esther Fujiwara, Graduate Program Director

5-Minute Thesis Talks by Psychiatry Graduate Students

POSTER PRESENTATIONS

11:00am - 12:00pm & 2:00pm - 2:30pm

The Trauma and Attachment Group (TAG) Program: an ethnographic exploration of an intensive dyad-based group intervention for traumatized youth

Chandra K. **Ashton** (Department of Psychiatry, University of Alberta), Anna O'Brien-Lange, (Research Officer, CASA Child, Adolescent, and Family Mental Health, Edmonton, Alberta) Karin Olson, (Faculty of Nursing, University of Alberta), Peter H. Silverstone (Department of Psychiatry, University of Alberta)

Advances in neuroscience since the early 1990s have uncovered compelling conclusions regarding the impact of early trauma on human growth and development. Firstly, that our brains are constructed by early experience, secondly, that the body's stress response systems, cardiovascular and immune systems, and metabolic regulatory controls, are all significantly disrupted by early adversity, and lastly, that these disruptions can lead to life-long impairments in physical and mental health. Some children who have experienced early attachment related trauma do not readily attach to new caregivers, which may be reciprocated especially if emotions and behaviours associated with past experiences of terror and shame cause a disruption in the relationship and further exacerbate the attachment opportunity. Researchers have proposed that when reciprocal relationships are established, children placed in to care later in their lives can demonstrate flexibility in attachment capacity, which may improve long-term negative outcomes. Through an ethnographic lens, we demonstrated that CASA's Trauma and Attachment Group (TAG) program for youth in middle childhood significantly improved caregiver/child attachment relationships, reduced children's symptoms of attachment trauma, and increased the caregiver's ability for self-reflection. Themes uncovered in our focus group and interviews suggest providing trauma focused psychoeducation in a group setting to the caregiver/child dyad, may be the key mechanism to promoting these changes in relationships that have been challenged by adverse effects of early developmental trauma. Further evaluation may help to identify other components that contribute to the success of the program.

Presentation: Thesis Talk

Two-photon calcium imaging depicts population encoding of vibrotactile information within excitatory and inhibitory networks of the limb associated mouse somatosensory cortex

Mischa V. **Bandet** (Neuroscience and Mental Health Institute, and Neurochemical Research Unit, University of Alberta), Ian R. Winship (Neuroscience and Mental Health Institute, Neurochemical Research Unit, and Department of Psychiatry, University of Alberta)

To distinguish between various somatic stimuli, the somatosensory cortex should process dissimilar stimuli with different patterns of neuronal activation. However, a large scale population based examination of somatosensory tuning to complex somatosensory stimuli has never been reported within the limb associated somatosensory cortex of rodents. Here we used in vivo two-photon Ca2+ imaging to measure HL and FL somatosensory responses of populations as large as 250 neurons per optical section. We show that individual neurons within the somatosensory cortex can be precisely tuned to particular frequencies of vibrotactile limb fluctuation or broadly tuned to multiple frequencies of fluctuation, thereby forming a population code for sensory processing. These population codes may result from preferential activation of different subsets of cutaneous and musculoskeletal receptors that respond to particular stimuli features and may be needed for fine adjustment of motor control during limb movement. Here we also expressed an AAV for GcAMP6S under a neuron specific promoter and an AAV for tdTomato selectively in parvalbumin positive (PV+) inhibitory interneurons under CRE dependent control in PV-CRE mice. We demonstrate that long duration high frequency limb fluctuation results in increased PV+ cell activity within the somatosensory cortex as a potential means to actively inhibit prolonged responses of non-PV+ cortical neurons. As PV+ cell dysfunction is thought to be a contributor to sensory abnormalities in disorders such as schizophrenia and stroke, these results will be highly useful as a comparison for cell population specific changes in activity in these disorders.

Presentation: Poster

Classifying MDD severity and treatment response using machine learning

James **Benoit** (Dept of Psychiatry, University of Alberta), Matt Brown (Dept of Psychiatry, University of Alberta), Andy Greenshaw (Dept of Psychiatry, University of Alberta), Serdar Dursun (Dept of Psychiatry, University of Alberta), Rajamannar Ramasubbu (Dept of Psychiatry, University of Calgary)

Machine learning approaches are increasingly being used in the development of diagnostic and prognostic tools for Major Depressive Disorder (MDD). Differences in brain white matter shown by Diffusion Tensor Imaging (DTI) scans may serve as a proxy for MDD symptom severity. Here, machine learning methods were applied to DTI scans to examine the diagnostic accuracy of white matter integrity in predicting MDD symptom severity and treatment response. Participants were forty-six medication-free patients with DSM-IV-defined MDD, and eighteen healthy controls. MDD patients were divided by tertile based on Hamilton Rating Scale for Depression (HRSD) scores: mild to moderate depression (HRSD 14-19), severe depression (HRSD 20-23), and very severe depression (HRSD ≥ 24). MDD patients were also divided by treatment response: medication responders (HRSD score reduced by >= 50%), non-responders (HRSD reduced by <50%, and symptom remitters (HRSD < 7). DTI scans were analyzed using the TBSS (Tract-Based Spatial Statistics) modules of the FMRIB Software Library (FSL) 5.0. This allowed for creation of an alignment-invariant map of the brain's white matter. These white matter maps were then used to train a classifier to differentiate healthy controls from severity tertile, healthy controls from treatment response group, severity tertiles from each other, and treatment response groups from each other. Classification of DTI data using machine learning showed statistically significant diagnostic classification between healthy controls and treatment non-responders. Results indicate that there is some added diagnostic value to applying a machine learning classifier to TBSS-based white matter maps of participants exhibiting MDD symptoms.

Presentation: Thesis Talk & Poster

Neuroimaging in neurocysticercosis

Ericson **Dametto** (Department of Psychiatry, University of Alberta), Manoj K Malik, Michal Juhas, Matthew Brown, Rajiv Kumar Azad (Neuroradiology, Shri Guru Ram Rai Institute of Medical & Health Sciences, Dehradun, India), Andrew Greenshaw (Department of Psychiatry, University of Alberta)

Neurocysticercosis is a parasitic infection of larval stages of Taenia solium. It is considered the most frequent helminthiasis of the central nervous system. Neurocysticercosis (NCC) is a pleomorphic disease concerning to the diversity of signals and symptoms that are linked to its manifestations. The most consistent groups of manifestations encompasses neurological and psychiatric symptoms. The frequency of symptoms decreases from epilepsy, to headaches, neurological deficits and intracranial pressure changes. Among psychiatric manifestations, association was found to depression, cognitive decline, schizophrenia, bipolar disorder, etc. Heterogeneity of psychiatric presentations encourage physicians to add NCC to their list of differential diagnoses, especially in endemic countries. The multiplicity of brain areas affected by lesions is believed to partly explain the variety of NCC's manifestations. In addition, the signs and symptoms associated with NCC depend on the larvae's number, developmental stage, on the duration of the infection and the host's immune response. Neuroimaging of cysts in various areas of the brain and in different stages illustrate the importance of considering neurocysticercosis as a co-morbid diseases related to psychiatric disorders.

Presentation: Thesis Talk

Determinants of risk taking and impulsiveness in individuals with HIV+ infection

Daniela **Gomez** (Department of Psychiatry, University of Alberta), Christopher Power (Department of Medicine, Div. Neurology, University of Alberta), M. John Gill (Department of Neurology, University of Calgary), Esther Fujiwara (Department of Psychiatry, University of Alberta)

Risk-based decisions involve making choices with positive or negative outcomes and fixed probabilities. Risky decision making is of key interest in the context of HIV, probing fronto-striatal brain areas vulnerable to HIV-infection. Despite improved treatment, some HIV+ patients develop HIV-associated neurocognitive disorders (HAND). A few previous studies using the risk-based Game of Dice Task (GDT) pointed to deficits in HIV+ patients, but the role of HAND has not been studied. This study aimed at elucidating the contribution of cognitive deficits in HIV+ patients' risk-based decision making. We further tested predictors of GDT deficits in HIV+ patients. A total of 288 HIV+ patients were tested at the Southern Alberta HIV Clinic in Calgary, with a HAND diagnosis ascertained by clinical and neuropsychological data in 70 patients (24.3%). The remaining 218 patients had normal neurocognitive (NN) performance. Compared to NN patients, HAND patients were impaired in all GDT measures, but substantial demographic differences were observed between the groups. Using principal component analysis to summarize sample characteristics, logistic regressions showed that in the entire population, low GDT performance was predicted by a combination of female gender, substance abuse, psychiatric comorbidities, low IQ, and poor executive functions. Examining only the GDT-impaired HAND group, effective past or present immunosuppression emerged as the most important predictor of GDT performance, indicating possible legacy effects of HIV infection on the CNS underlying decision making deficits in HIV. Identifying determinants of risk behaviour in HIV is needed for better health management, and could provide targets to promote cognitive maintenance.

Presentation: Thesis Talk & Poster

Treating depression with ultrasound: an exploratory study

Huining **Guo** (Department of Psychiatry, University of Alberta), Jie Chen (Department of Electrical and Computer Engineering, University of Alberta), Xin-Min Li (Department of Psychiatry, University of Alberta)

Depression has become one of the leading health-care burdens in North America. Despite the wide application of antidepressants, a significant portion of patients do not benefit sufficiently from the standard medications. Therefore alternative safe and effective treatment options are needed. Previous studies have shown that transcranial ultrasound could noninvasively modulate neurons and neural network activities. However, the potential of ultrasound as a treatment for depression still needs to be elucidated. Here we investigated the application of low-intensity pulsed ultrasound (LIPUS) as a therapeutic option for depression. We found that LIPUS significantly increased the viability of both neuronal-like cells and primary glia cells in vitro. Protein analysis revealed that LIPUS promoted the phosphorylation of β-catenin and elevated the level of BDNF in both cell types. In animal study with repetitive restraint stress (RRS) model, LIPUS significantly alleviated the depression-like behaviors of mice exposed to RRS. Pathological tests indicated that the potential mechanisms for these beneficial effects of LIPUS were associated with promotion of neurogenesis and elevating the level of BDNF. Later in the cuprizone (CPZ) induced demyelination animal model, we found that LIPUS attenuated the depressive-like behaviors in mice exposed to CPZ. Pathological tests showed that LIPUS alleviated injuries to both mature myelin and oligodendrocyte progenitor cells that were caused by CPZ exposure. These findings indicated that LIPUS could serve as a promising therapeutic option for depression, not only by promoting neurogenesis and elevating the level of BDNF, but also by the protection and promotion of myelin and oligodendrocytes.

Presentation: Thesis Talk

A novel multimodal school-based program, EMPATHY, significantly decreases long-term drug and alcohol abuse as measured by CRAFFT scores in 6,227 youth aged 11-18

Deena M. **Hamza** (Department of Psychiatry, University of Alberta), Marni Bercov (Strategic Clinical Network for Addiction and Mental Health, Alberta Health Services), Victoria Y.M. Suen (Strategic Clinical Network for Addiction and Mental Health, Alberta Health Services), Andrea Allen (Strategic Clinical Network for Addiction and Mental Health, Alberta Health Services), Ivor Cribben (Department of Finance and Statistical Analysis, University of Alberta), Jodi Goodrick (Red Deer Public Schools), Stu Henry (Red Deer Public Schools), Catherine Pryce (Strategic Clinical Network for Addiction and Mental Health, Alberta Health Services), Pieter Langstraat (Superintendent, Victoria Public Schools), Katherine Rittenbach (Strategic Clinical Network for Addiction and Mental Health, Alberta Health Services), Samprita Chakraborty (Department of Economics, Faculty of Art, University of Alberta), Rutger C. Engles (Trimbos-Institute), Andrew J. Greenshaw (Department of Psychiatry, University of Alberta), Christopher McCabe (Department of Emergency Medicine and Public Health), Peter H. Silverstone (Department of Emergency Medicine and Public Health)

Youth alcohol and drug misuse has multiple longer-term consequences. Suggestions to reduce the frequency of this include combining Screening, Brief Interventions, and Referral to Treatment (SBIRT). However, while SBIRT is well studied in adults, it hasn't been widely studied in youth. The present study was part of a larger school-based intervention program (EMPATHY), whose primary goal was to reduce depression, anxiety, and suicidal thinking. A secondary outcome was to determine if the EMPATHY program, which utilizes all aspects of SBIRT, would also decrease substance abuse. To allow better comparisons with previous research we extracted the scores for the 6-items of the CRAFFT, a scale designed to be used in youth where a score of ≥ 2 indicates an increased likelihood of substance abuse. Here, we report on CRAFFT scores at Baseline (n=3,224), 3-months (n=3,229), 7-months (n=4,860), and 15-months (4,497) over two school years. We also report on the CRAFFT score in the 1,884 students who completed all 4 assessments, as well as examining comorbidity rates and how these changed over time. Our results showed, as expected, high rates of risk for substance abuse that increased with age. We also found that the EMPATHY program, which is a version of SBIRT, led to a highly significant reduction in the total percentage of students who scored ≥ 2 from 14% to 7% at the 15-month follow-up. We found reductions in all grades, for example reductions in Grade 12 were from 31% at Baseline to 20% at 15-months, while reductions in Grade 11 were from 24% at Baseline to 15% at 15-months. We also found a significant reduction in comorbidity with both depression and anxiety over time. These findings support more widespread use of SBIRT for youth, perhaps as part of other comprehensive school-based programs, even though funding for EMPATHY itself was terminated.

Presentation: Thesis Talk & Poster

CYP2D6: detecting new structures for clinical practice

Beatriz Carvalho **Henriques** (Dept. of Psychiatry, University of Alberta), Yabing Wang (Dept. of Psychiatry, University of Alberta), Rita Whitford (Dept. of Psychiatry, University of Alberta), Ian Craig (Institute of Psychiatry, Psychology and Neuroscience, London UK) Katherine Aitchison (Dept. of Psychiatry, University of Alberta)

A gene that has been the focus of extensive pharmacogenomic research is the cytochrome P450 enzyme 2D6 (CYP2D6), a highly polymorphic gene found on chromosome 22. This project expands on work that has previously identified individuals based on their copy number call variance. Using CNV as a preliminary screening of available samples, we are interested in isolating individuals with calls compatible with *5 and *XN genotypes, most common alleles associated with poor and ultra metabolizer status, respectively, as well as calls compatible with the presence of a hybrid allele, derived from the combination of CYP2D6 with its adjacent pseudogene, CYP2D7. Our objective is to identify precisely which variants are present among our sample pool. In this manner, the improvement in technology gained will enable correct identification of a wider range of variants of this enzyme than was previously possible, for translation into clinical practice in the form of more accurate pharmacogenetics testing. The methodology applied is a long-PCR approach to identify hybrid alleles of CYP2D6 using the technique described by Kramer et al. (2009)1 and Black et al. (2012)2, with fragment delineation by both agarose gel and Agilent 2100 Bioanalyzer (Agilent Technologies, Canada) electrophoresis. Results have shown successful amplification for fragments corresponding to the presence of a *5 allele, to which a current protocol has been developed. In addition, more recent results for an individual sample confirms the presence of a hybrid allele and validates the current conditions used for detection of this variant, which will be applied to the remaining samples of similar call. Comparison made between different runs point to effective changes to the initial method. The technique employed is a modified version of that described by Kramer et al.

Presentation: Poster

Increased subcortical iron concentration in alcohol-dependent brain

Michal **Juhas** (Department of Psychiatry, University of Alberta), Hongfu Sun (Department of Biomedical Engineering, University of Alberta), Matthew Brown (Department of Psychiatry, University of Alberta), Marnie MacKay (Department of Psychiatry, University of Alberta), James Benoit (Department of Psychiatry, University of Alberta), Timothy Gillese (Alberta Health Services), Ericson Dametto (Department of Psychiatry, University of Alberta), Allan Aubry (Alberta Health Services), Glenn Walmsley (Alberta Health Services), Blayne Blackburn (Alberta Health Services), Cindy King (Alberta Health Services), Liana Urichuk (Alberta Health Services), Mark Loowell (Alberta Health Services), Alan Wilman (Department of Biomedical Engineering, University of Alberta), Serdard Dursun (Department of Psychiatry, University of Alberta), Andrew Greenshaw (Department of Psychiatry, University of Alberta).

Alcohol use disorder (AUD) is a chronic, recurrent disorder with large personal and societal problems. The neurobiological mechanisms driving adaptive brain changes during AUD and its recovery still remain not fully understood. Recently developed innovative neuroimaging techniques such as the quantitative susceptibility mapping (QSM) magnetic resonance imaging (MRI) contrast permit us to measure increased iron concentration in deep-brain structures even retrospectively on already acquired echo planar MRI volumes. In this study, we have taken advantage of this new innovation to retrospectively calculate the QSM maps on 20 male AUD (DSM-IV-TR) and 15 healthy male control functional MRI scans. We have then manually traced the 3D subcortical brain regions and compared the average iron concentration in each region of interest between the two groups. The results agree with our apriori hypothesis of increased iron concentration in the alcohol-dependent patient brains, with the highest differences observed in the most susceptible regions. On average, the AUD patients exhibited 9 to 15% increased deep gray matter iron concentration compared to the matched controls. This new evidence provides additional support to proposed mechanism of oxidative brain damage associated with brain atrophy in chronic alcohol abuse. Our study has successfully demonstrated new innovation opportunities which allow clinical researchers to leverage existing datasets to explore potential new biomarkers in psychiatric disorders to help not only with better understanding of their mechanism but also with their proper evidence-based classification. This is the first study to our knowledge to measure subcortical iron concentration in alcohol-dependent patients.

Presentation: Thesis Talk & Poster

Cognitive significance of deep grey matter iron accumulation in multiple sclerosis

Jonn **Kmech** (Department of Psychiatry, University of Alberta), Esther Fujiwara (Department of Psychiatry, University of Alberta), Dana Cobzas (Department of Computer Science, University of Alberta), Hongfu Sun (Department of Biomedical Engineering, University of Alberta), Peter Seres (Department of Biomedical Engineering, University of Alberta), Gregg Blevins (Department of Medicine, Division of Neurology, University of Alberta), Alan. H. Wilman (Department of Biomedical Engineering, University of Alberta)

Deep grey matter (DGM) iron accumulation is increasingly recognized in association with Multiple Sclerosis (MS) and can be measured in-vivo with MRI. Cognitive implications of this pathology are not understood well, especially vis-à-vis DGM atrophy. Our objective was to investigate relationships between cognition and DGM iron in MS using two MRI-based iron measures. 40 MS patients (EDSS = 5.25; relapsing: N = 16; progressive: N= 24) and 27 controls were imaged at 4.7T using transverse relaxation rate (R2*) and quantitative susceptibility mapping (QSM). R2* and QSM values and volumes of caudate, putamen, globus pallidus, and thalamus were determined by multi-atlas segmentation. Cognition was assessed with the Brief Repeatable Battery of Neuropsychological Tests. Relationships between cognition and DGM iron were examined by hierarchical regressions. Compared to controls, patients showed reduced memory and processing speed, smaller putamen, globus pallidus, and thalamic volumes,
and increased QSM indicative of iron accumulations in putamen and globus pallidus. Thalamus and putamen volume predicted cognition in patients. Controlling for atrophy, QSM values in the globus pallidus also predicted cognition. QSM was more sensitive compared to R2* in detecting DGM iron accumulation. DGM atrophy and DGM iron have negative and separable relationships to cognition in MS.

Presentation: Poster

COMT Val158Met polymorphism and lifetime cocaine use

Rohit J. **Lodhi*** (Department of Psychiatry, University of Alberta), Yabing **Wang*** (Department of Psychiatry, University of Alberta), Georgina Macintyre (Department of Medicine, University of Alberta), Candice Crocker (Department of Psychiatry, Dalhousie University), Hongyan Ren (Department of Psychiatry, University of Alberta), David Rossolatos (Department of Psychiatry, University of Alberta), Alexandra Bowker (Neuropsychology Department, Alberta Hospital Edmonton), Alexandra Loverock (Neuropsychology Department, Alberta Hospital Edmonton), Brett Granger (Neuropsychology Department, Alberta Hospital Edmonton), Virginia Newton (Neuropsychology Department, Alberta Hospital Edmonton), Philip Tibbo (Department of Psychiatry, Dalhousie University), Scot E. Purdon (Neuropsychology Department, Alberta Hospital Edmonton; Department of Psychiatry; University of Alberta; Edmonton Early Psychosis Intervention Clinic), Katherine J. Aitchison (Departments of Psychiatry and Medical Genetics, University of Alberta; Edmonton Early Psychosis Intervention Clinic)

*Joint first authors

Altered functioning of the dopamine and related systems system is an important factor in the development of addiction. Variations in the gene coding for the dopamine catabolizing enzyme catecholamine-O-methyltransferase have been related to substance use, specifically lifetime cannabis use. It has been reported in an African-American sample that Met/Met homozygotes of the COMT Val158Met variation have a greater risk of cocaine addiction compared to Val/Val. In addition, lifetime cannabis use is postulated to have a "gateway effect" of increasing the risk of using other illicit substances such as cocaine. We examined the association between lifetime cocaine use (LCU), COMT and frequency of lifetime cannabis use (LCaU) in a Canadian sample. 209 patients referred to a study of genetic factors in psychosis recruited from Edmonton and Halifax with relevant data were analyzed. Logistic regression was used to assess the effect of COMT and LCaU on LCU. Subsequently, the COMT-LCU relationship was examined after adjusting for LCaU, gender and psychiatric diagnosis. LCaU was significantly related to LCU (OR=3.48, $p<0.0001$). Val/Val COMT genotype individuals were 2.6 times more likely to have a history of LCU than those of Met/Met (OR=2.607, $p=0.014$). The COMT-LCU association remained significant even after adjustment for LCaU, gender and diagnosis and when the sample was restricted to Caucasians only.

Presentation: Thesis Talk

Quick tools for detection of cannabis effects on cognition and the benefits of abstinence

Scot E Purdon, PhD, R.Psych, **Alexandra Loverock** B.Sc., Brett Granger, B.A., Carol Bolt, Dip.Beh.Sci., and Virginia Newton, PhD, R.Psych
Neuropsychology Service, Central Services Program, Alberta Hospital Edmonton
Edmonton Early Psychosis Intervention Clinic, Young Adult Program, AHS
Bebensee Schizophrenia Research Unit, Department of Psychiatry, University of Alberta

There is a high rate of cannabis use among people suffering from serious mental illness (SMI), particularly among young adults, and the acute use of cannabis has significant deleterious effects on cognition. Although cognitive deficits secondary to cannabis use have been documented, the nature, severity, and persistence of these effects with sustained abstinence is not well known in the general population or among individuals with SMI. In addition, effects of substance use may make it difficult to infer the etiology of cognitive impairments or estimate the severity of such impairments in psychiatric populations. This is problematic for clinicians within the AHE Neuropsychology Service who provide diagnostic and prognostic consultations pertaining to suspected cerebral pathology associated with SMI, particularly when referrals are received from the Young Adult Program. Differentiating cognitive deficits related to illness from those related to substance use is a complicated task that requires careful assessment of both cognition and substance use history. In an effort to address this challenge, a Screen for Cognitive Impairment in Psychiatry (SCIP; Purdon, 2005) and a computerized self-administered history of drug use (DRUGS; Purdon, 2007) have been developed and routinely implemented within the AHE Neuropsychology Service. Time required to administer these instruments is no more than 15 minutes for the SCIP and 20 minutes for DRUGS. With approval from HREB, NACTRC, and AHS, a recent review was completed on 409 service records spanning the years during which both tools were administered. Relative to a gold standard of substance use measurement (i.e., urinary cannabinoids), DRUGS demonstrated very good specificity as well as very good sensitivity when applied in conjunction with a brief test of effort. SCIP scores were lower for patients with DRUGS-detected lifetime use of cannabis. SCIP scores also showed linear improvement with longer DRUGS-documented duration of abstinence. Thus, these two brief tools, supplemented by a brief test of effort, demonstrated a cost-effective method of quantifying the cognitive contributions of substance use in a sample of patients referred to the AHE Neuropsychology Service. The early results also suggested a cognitive limitation associated with lifetime use of cannabis that is improved with sustained abstinence.

Presentation: Poster

Remote ischemic per-conditioning augments collateral circulation and reduces brain damage due to stroke

Junqiang **Ma** (Neurochemical Research Unit, Department of Psychiatry; Neuroscience and Mental Health Institute, University of Alberta), Yonglie Ma(Neurochemical Research Unit, Department of Psychiatry, University of Alberta), Ashfaq Shuaib(Neuroscience and Mental Health Institute;Division of Neurology, Department of Medicine,University of Alberta), Ian Winship(Neurochemical Research Unit, Department of Psychiatry; Neuroscience and Mental Health Institute, University of Alberta);

Stroke is a devastating disease which causes death and disability worldwide. Remote ischemic per-conditioning (RIPerC) is a therapeutic strategy where brief, repetitive, non-lethal ischemia and reperfusion cycles are induced in a distant organ (typically the limbs) to protect the brain from damage due to stroke. RIPerC has strong support as a neuroprotective strategy in animal models of stroke. However, the mechanisms of this protective effect are not well defined. Notably, the effects of RIPerC on cerebral blood flow are not known. Here, we used high resolution in vivo imaging in animal models to evaluate changes in "collateral circulation" during ischemic stroke.Collateral circulation refers to alternative routes for blood to reach ischemic tissue when primary routes are blocked, and is a key predictor of outcome after stroke. Using laser speckle contrast imaging (LSCI) and two photon laser scanning microscopy (TPLSM), our experiments precisely mapped dynamic changes in vessel diameter and blood flow velocity during RIPerC treatment in focal ischemic stroke model in rats. Focal ischemia was generated by ligation of bilateral common carotid artery (CCA)combined with ligation of middle cerebral artery (MCA). RIPerC was initiated 1 hour after ischemic onset and consisted of 3 cycles of 15 min occlusion/15 min release of the bilateral femoral arteries. Blood flow through collateral connecdtions between the MCA and anterior cerebral artery (ACA), LSCI and TPLSM. Infarct size was determined at 6 hours post stroke with TTC staining to determine the impact of RIPerC on the early ischemic core. LSCI and TPLSM data show that in untreated animals, pial MCA segments progressively constricted over time after ischemic onset, reducing flow to ischemic regions. RIPerC prevented this narrowing and improved flow to ischemic areas. Moreover, the mean infarct size of RIPerC treated rats was significantly reduced comparing to control group at 6 hours after ischemic onset. Regression analysis revealed a highly significant non-linear relationship between MCA flow and infarct size in untreated animals. Notably, this strength of this relationship was reduced by RIPerC. Remote ischemic per-conditioning improves blood flow to the ischemic penumbral cortex by preventing collapse of collateral channels over time. Significant reductions in early infarct areas suggest that RIPerC has the potential to reduce early expansion of stroke core into penumbra,possibly by augmenting collateral circulation.

Presentation: Poster

Eye-tracking measures of ambiguous emotional face processing in alexithymia

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Trait alexithymia is a phenomenon associated with a difficulty in identifying and describing emotional stimuli. Alexithymia has been linked to difficulties with emotional face processing, particularly in challenging tasks (e.g. limited exposure to emotional faces, ambiguous or subtle emotional expressions, etc.). However, the visual attention patterns underlying these difficulties are unclear. We employed non-intrusive eye-tracking technology to investigate ambiguous emotional face processing as a function of alexithymia. Participants (n=63) judged the blend percentage of 60 morphed emotional target faces in comparison to their two unblended source faces. Percentage ratios varied in 10% increments from 95:5 to 5:95. 'Ambiguous' faces were operationalized as blends with 55%, 65% and 75%, and 'clear' faces were 85% and 95% blends. Response latency, accuracy, picture fixations, and alexithymia (TAS-20) controlled for anxiety (STAI-T) were measured. As expected, participants took longer and scored worse on ambiguous trials compared to clear trials. Participants fixated longer on the target face than the reference faces, and fixated longer on all three faces in ambiguous trials than in clear trials. Alexithymia was correlated with difficulty judging ambiguous emotions, especially happy and angry faces. Alexithymia was also correlated with fewer fixations on target ambiguous faces. Task performance and visual attention patterns were largely uncorrelated, and the only link between the two was observed in participants with high alexithymia, where the number of target face fixations was negatively correlated to task performance. Visual attention patterns and behavioral responses are complementary measures of emotional processing changes in alexithymia.

Presentation: Poster

Imaging biomarkers in Alzheimer's disease for early diagnosis and prediction

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Alzheimer's disease (AD) is the most prevalent form of dementia, which affects mostly elderly people. The pathological hallmarks of AD are the extracellular aggregation of beta amyloid (Aß) and intraneuronal tau proteins in the form of plaques and neurofibrillary tangles (NFT) respectively. It is well established that all the AD patients progress through a prodromal stage known as mild cognitive impairment (MCI), which do not meet the diagnostic criteria of dementia or AD. The brain pathology in AD starts much before it appears symptomatically. However, the Alzheimer's disease Assessment Scale-Cognitive Behavior section (ADAS-Cog) is considered as a "gold standard" for diagnosis AD, but it sometimes gives false positive results for MCI patients. Previous studies suggest that the five AD biomarkers are sufficiently validated and now commonly used in therapeutic trials for diagnosis and prediction of AD. These are (1) The decreased concentration of CSF Aß42. (2) Positron emission tomography (PET) for amyloid imaging. (3) Increased level of CSF total tau and hyperphosphorylated tau. (4) Structural magnetic resonance imaging (MRI) for the volumetric measurement of atrophy in the brain. (5) Hypometabolism of fluorodeoxyglucose (FDG) on PET. However, no biomarker has 100% definitive accuracy for diagnosis of AD. Therefore, all neuroimaging modalities including functional magnetic resonance imaging (fMRI) and diffusion tensor imaging (DTI) could be combined together for early diagnosis and predicting the course of illness with a high accuracy, so that early therapeutic interventions could be used in an attempt to halt or delay the onset of this disease.

Presentation: Thesis Talk

Adult education to help reduce child sexual abuse: developing novel classroom and online approaches to change knowledge, attitudes, and behaviours

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Currently, as many as 1 in 6 girls and 1 in 12 boys experience sexual abuse involving bodily contact in Canada. Individuals who experience child sexual abuse (CSA) have higher rates of psychopathology and are at higher risk of a range of medical, psychological, behavioural, and sexual disorders than those who have not been sexually abused. We developed a Canadian content, research informed CSA education program with a classroom and online version and designed a study to measure participant's behaviour change after taking the program. We predicted that participants who take the workshop would increase their use of prevention behaviours. Using the same research protocol, we collected data on the classroom version and the online version of the program. Using online questionnaires, we collected baseline data prior to the classroom workshop (n=312) and then again 12 weeks after the program (n=209, response rate = 67%) and before taking the online version (n=126) and 12 weeks after the program (n=126, response rate = 78%). A pre-test post-test within-subject design was used to determine statistically significant and clinically meaningful change. Results of the Wilcoxon signed-rank tests indicate participants in the classroom version and the online version had statistically significant and clinically meaningful changes in CSA prevention behaviours. The Mann-Whitney U test found no statistically significant differences in behaviour change between the classroom and the online groups. Results of this research are likely to lead to meaningful improvements in preventing child sexual abuse.

Presentation: Thesis Talk & Poster

Research-creation in health research as an artist-in-residence in the clinic

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The gap between evidence generation and translation into clinically significant practice and health policy is the area that my project will creatively begin to address. As an artist/researcher I am studying the contribution of arts-based (AB) methods in making visible, helping to prioritize patient experiences, and supporting dialogue that will shape and advance health research. This arts-based work is part of a larger scholarship activity called research-creation, which, according to Chapman et al (2012), "is an emergent category within the social sciences and humanities that speaks to contemporary media experiences and modes of knowing." However, I don't see it as limited to the social sciences, but, instead, as a general strategy that can be mobilized in any discipline as a creative approach with aesthetic dimension. It is an affective learning experience in both knowledge generation and translation. As the artist-in-residence with the Friends of the University Hospitals with Alberta Health Services Transplant Services for 16 months (2015-16) I was able to meet donor families and patients in the ward. It was an incredible experience of empathetic learning that led to two solo exhibitions and two film screenings. I hope to narrate the experiences I had in the research, creation, and exhibition/dissemination of this project.

Presentation: Thesis Talk & Poster

Potential role of β-amyloid peptides in kainic acid-induced toxicity

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Kainic acid (KA), a degradation-resistant analogue of the excitatory neurotransmitter glutamate, is known to trigger seizures in rat models which originate from the hippocampus and can spread to other limbic structures. This is associated by the subsequent loss of neurons, mossy fiber reorganization, and astrogliosis, pathologies which closely mimic those characteristic of human temporal lobe epilepsy (TLE). KA exerts its epileptogenic effects through the activation of kainate receptors (KA-Rs) which generate synchronized network-driven glutamatergic currents. Nevertheless, the underlying cellular mechanisms by which KA triggers neurodegeneration remains unclear. A number of recent studies indicate that amyloid β (Aβ), the peptides critical for their involvement in Alzheimer's disease (AD) pathogenesis, may play a potential role in triggering seizures and the associated loss of neurons. These peptides are generated from the constitutively expressed amyloid precursor protein (APP), which is alternately processed by the non-amyloidogenic α-secretase or amyloidogenic β-secretase proteolytic pathways. However, very little is known regarding the involvement of Aβ peptides in KA-induced toxicity. To address this issue, we evaluated time-dependent alterations in the levels and cellular distribution of APP and its processing enzymes in the hippocampi of KA-treated rats. We report that KA triggers a significant increase in APP processing in proliferating astrocytes. Additionally, using rat primary hippocampal neuronal cultures, we are currently evaluating the significance of Aβ peptides in the degeneration of neurons. Our results reveal that increased endogenous levels of APP may have a role in triggering degeneration of neurons in animal models of TLE.

Presentation: Thesis Talk

Consequences of perineuronal net loss in the prefrontal cortex

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Perineuronal nets (PNNs) are organized components of the extracellular matrix which surround inhibitory interneurons in the brain. They support the function of neurons by stabilizing their physical structure and connectivity, and providing metabolic support for their physiological demands. Several recent studies have identified that PNNs appear to be deficient in the post-mortem brain tissue of patients suffering from schizophrenia. Unfortunately, there are a number of limitations to post-mortem studies which make it difficult to interpret the significance of these deficits. In my work, we utilize animal models to evaluate what role PNNs might play in schizophrenia. Previously, we have used a maternal immune activation model, which results in delayed behavioural and anatomical disturbances in offspring consistent with a schizophrenia phenotype. We demonstrated that these animals also have PNN deficits in the prefrontal cortex, which do not manifest until the same window during adolescence when behavioural dysfunction first presents. While the model and schizophrenia share this feature, it still does not tell us what functional role PNNs play. To address this we are evaluating the effects of targeted depletion of PNNs in the brain of adolescent rats. We treated animals with an enzyme which degrades PNN components in the medial prefrontal cortex, and found that this results in disturbed prepulse inhibition, a measure of sensorimotor gating, and cross-modal object recognition, a test of working memory. Both of which are known to be disturbed in schizophrenia. These findings highlight the significant and individual contribution of PNN depletion to cognitive dysfunction, outside of the confounding effects of prenatal infection. Our next step is to evaluate therapies which might prevent PNN and the efficacy in reducing symptoms of affected animals.

Presentation: Thesis Talk & Poster

GWAS of anhedonia in depression identifies signals related to neurodevelopment that negatively correlate with extraversion

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Anhedonia is a relative failure to obtain pleasure from activities previously experienced as pleasurable; although it is a core feature of major depressive disorder (MDD), its genetic underpinnings and heritability remain relatively unclear. Using a continuous factor score encompassing symptomatology based on a previously published factor analysis of MADRS, BDI and HAMD-17 (Uher et al., 2008; Uher et al., 2012), genome-wide association analysis was conducted, followed by a prioritization study. In addition, estimation of heritability (hsnp) and its genetic correlation with personality traits were conducted by taking advantage of an association study from The Genetics of Personality Consortium. After quality control and imputation, 760 individuals with 7532873 SNPs remained. Genome-wide association analysis of anhedonia identified 5 intronic SNPs in 5 genes (PRPF4B, EFCAB2, NPAS3, TAOK3 and CDH18) to be significantly associated with the anhedonia score. One SNP (rs644150), located in the intronic region of PRPF4B (pre-mRNA processing factor 4B) in chromosome 6 yielded the most significant P value (1.36 X 10-9); a gene-prioritization study found one zinc-finger related gene on chromosome 14, SLC39A9 (solute carrier family 39 member 9), prioritized with a nominally significant P value (P = 0.02). The partitioned heritability of anhedonia was estimated at 0.23 and its genetic underpinnings were found to be negatively correlated with those of the extraversion dimension in terms of personality (r=-0.6414, P < 0.001). The genetic underpinnings of anhedonia in MDD appear to be related to neurodevelopment and cellular components such as Golgi and the negative overlap with extraversion is interesting.

Presentation: Poster

Non-verbal skills positively associate with mildly elevated fasting blood glucose in individuals presenting with a psychotic illness

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The metabolic syndrome (MetS) is a cluster of symptoms identified as significant risk factors in the development of cardiovascular disease and is very relevant to the psychiatric population. This study explored the relationship between MetS and cognitive functioning in a younger population presenting with early psychosis (having less than one year of treatment) to the Edmonton Early Psychosis Intervention Clinic. Clinical assessment included an evaluation with the MATRICS Consensus Cognitive Battery and MetS factors as defined by the NCEP ATP-III criteria. We hypothesized that individuals with a psychotic illness and having MetS would have increased cognitive dysfunction in one or more domains, relative to having a psychotic illness alone. Additionally, we expected impairment in glucose regulation to be associated with impairment of attention and processing speed. Our findings demonstrated that fasting blood glucose values were generally within the normal range in this population. These values were not associated with measures of sustained attention or processing speed; however, they were directly associated with performance on several non-verbal tasks sensitive to spatial working memory, learning and memory of designs, and executive skills related to reasoning and problem solving with spatial materials. This relationship was not predicted but the consistency across non-verbal instruments suggests a potentially reliable result that may implicate relatively circumscribed cerebral effects of glucose in relation to relevant neuroanatomy. Although provocative, replication will be necessary to gain confidence in the stability of this finding and the validity of inferences regarding potential mechanisms possibly underlying this association.

Presentation: Thesis Talk & Poster